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REGENERACIÓN OSEA CON DENTINA

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RESUMEN

- **INTRODUCCIÓN:**

  Después de una exodoncia se pone en marcha un proceso dirigido a la curación de la cresta alveolar. La remodelación tisular conlleva pérdidas de volumen. Esto supone un problema a la hora de rehabilitar protésicamente la zona. Así, se empieza a hablar de preservación alveolar. Los injertos "clásicos" se han usado con éxito hasta hoy, pero sus inconvenientes han llevado muchos a buscar alternativas; la dentina autóloga no tiene problemas de disponibilidad ni morbilidad (como el hueso autólogo), ni la posible antigenicidad o infecciosidad de otros tipos de injertos.

- **OBJETIVOS:**

  Establecer la magnitud de perdida ósea posterior a una extracción, comparar las tipologías de injertos y las técnicas de procesamiento de la dentina.

- **METODOLOGÍA:**

  Este trabajo se ha realizado mediante una búsqueda bibliográfica en las bases de datos de *Pubmed/Medline*, SciELO, *Google Scholar* y *The Cochrane Library*, sobre artículos en español e inglés desde el 1990.

  Quedan excluidos los estudios sin abstract.

  Se seleccionaron 66 artículos.

- **RESULTADOS:**

  Se analizaron 66 estudios. A partir de estas publicaciones se evidencia una pérdida de hasta 3,8 mm en anchura y 1,2 mm en altura en 6 meses post-extracción. El hueso autólogo presenta optimas propiedades, pero necesita de cirugía para su obtención, lo cual complica su uso. En cuanto a las técnicas de procesamiento, la de

desmineralización de la matriz con EDTA, HCl o HNO_3 se ha demostrado la más eficaz, si bien la preparación por extracción de los NCPs con cloruro de guanidinio, MTA y $Ca(OH)_2$ también dio buenos resultados.

- **CONCLUSIÓN:**

El proceso de cicatrización determina pérdidas de hasta el 50% de tejido alveolar en un año y afecta particularmente la pared vestibular. El hueso autólogo es el mejor material de injerto “clásico”, pero presenta inconvenientes. La desmineralización de la matriz dentinaria resulta ser una técnica muy prometedora en la preparación dentinaria.

ABSTRACT

•INTRODUCTION:

After an extraction, a process aimed at healing the alveolar ridge begins. Tissue remodeling leads to volume losses. This is a problem when it comes to prosthetically rehabilitating the area. Thus, one begins to speak of alveolar preservation. The “classic” grafts have been used with success until today, but their drawbacks have led many to look for alternatives; autologous dentin has no availability or morbidity problems (like autologous bone), nor the possible antigenicity or infectivity of other types of grafts.

•OBJECTIVES:

Establish the magnitude of bone loss after extraction, compare the types of grafts and dentin processing techniques.

• METHODOLOGY:

This work has been carried out by means of a bibliographic search in the databases of Pubmed / Medline, SciELO, Google Scholar and The Cochrane Library, on articles in Spanish and English since 1990.

Studies without abstract are excluded.

66 articles were selected.

• RESULTS:

66 studies were analyzed. These publications show a loss of up to 3.8 mm in width and 1.2 mm in height in 6 months post-extraction. Autologous bone has excellent properties, but requires surgery to obtain it, which complicates its use. Regarding the processing techniques,

the demineralization of the matrix with EDTA, HCl or HNO_3 has been shown to be the most efficient, although the preparation by extraction of the NCPs with guanidinium chloride, MTA and $Ca(OH)_2$ also gave good results.

•CONCLUSION:

The healing process determines losses of up to 50% of alveolar tissue in one year and particularly affects the vestibular wall. Autologous bone is the best "classic" graft material, but it has drawbacks. Demineralization of the dentin matrix turns out to be a very promising technique in dentin preparation.

ÍNDICE

1. INTRODUCCIÓN.

Remodelación ósea posterior a una exodoncia

Después de una exodoncia se ponen en marcha una serie de procesos biológicos que resultan en la degeneración y reabsorción del tejido óseo alveolar, ocasionando una reducción del reborde alveolar tanto en sentido vertical como horizontal.
Distintos estudios, a lo largo de los años, han documentado y analizado este fenómeno[1,2,3].

En 1957 Atwood et al.[1], uno de los primeros investigadores en analizar a nivel bioquímico la curación del reborde alveolar posterior a una extracción, observaron que en este proceso los osteoclastos liberan colagenasa, que eliminaba los iones $Ca2+$, $Mg2+$ y PO_4^{3-} y los productos del colágeno, causando así la desaparición de la lámina dura y dejando, en un principio, una fina cortical ósea. A continuación, empezaba a generarse gradualmente un entramado de hueso reticular (o esponjoso primario) que ocuparía el espacio alveolar constituyendo un soporte y una fuente de células osteoprogenitoras fundamentales para que se lleve a cabo el proceso de mineralización de esta matriz[1].

Años más tarde, Lindhe et al.[2] analizaron cuantitativamente las restricciones que se verifican en el reborde alveolar después de una exodoncia; se constató que, ocho semanas después de la extracción, el tejido óseo de la pared lingual se había conservado en buena medida, mientras que en el lado vestibular se objetivó un desplazamiento hacia apical de unos milímetros. Según Araujo et al. esto es debido a la composición de la pared vestibular, constituida en sus primeros 1-2 mm cervicales por hueso esponjoso que se reabsorbería más rápidamente después de una exodoncia[2].

Otro estudio que se centró en analizar cuantitativamente e histológicamente el proceso de cicatrización alveolar fue el de Cardaropoli et al.[3], en 2003 para ello utilizaron 9 perros

mestizos, a los que se extrajeron los 4 premolares mandibulares. Los autores observaron así una serie de etapas fundamentales que, según ellos, caracterizaban este proceso:

- 1° etapa: hasta los primeros 3 días, caracterizada por la formación del coagulo.
- 2° etapa: al terminar la primera semana de la extracción ya se evidenciaría la formación de una matriz provisional de tejido conectivo compuesta por vasos sanguíneos, células mesenquimales, leucocitos y fibras colágenas.
- 3° etapa: entorno al día 17 comienza el depósito de osteoclastos en las paredes del alvéolo.
- 4° etapa: al mes el hueso mineralizado ya está ocupando el 88% del volumen del alveolo[3].

Irinakis et al.[4] llegaron a conclusiones similares afirmando que el proceso de restablecimiento de la cresta alveolar se podía dividir en 5 diferentes etapas:

- 1° etapa: inmediatamente se forma el coagulo inicial, estando constituido por glóbulos rojos y blancos.
- 2° etapa: a los 4-5 días, el tejido de granulación empieza a reemplazar el coagulo en el alveolo. Empieza el proceso de angiogénesis a través de cordones de células endoteliales, y se empiezan a formar los primeros capilares.
- 3° etapa: a los 14-16 días, el tejido conectivo, constituido principalmente por fibras de colágeno y fibroblastos en forma de huso empieza a reemplazar gradualmente el tejido de granulación.

• 4° etapa: a los 7-10 días, la calcificación del tejido osteoide se hace evidente, y comienza a difundirse desde la base y las paredes del alveolo. A las 6 semanas de la extracción, las trabéculas óseas llenan casi completamente el espacio alveolar. Entre la cuarta y la sexta semana de la extracción, se alcanza la mayor actividad osteoblástica, y se registra una proliferación del tejido celular y conectivo. Los osteoblastos se depositan alrededor de islotes de hueso inmaduro y secretan tejido osteoide. A la octava semana, el proceso osteogénico se empieza a ralentizar.

• 5° etapa: entre la cuarta y la quinta semana se logra el completo cierre epitelial del alveolo. Entre la quinta y la décima semana el espacio alveolar esta casi totalmente lleno de tejido osteoide. A la decimosexta semana el alveolo se encuentra totalmente relleno de hueso y se sigue objetivando una ligera actividad osteogénica que continuará también en los meses siguientes, si bien no se llegará al nivel de densidad ósea de los alveolos adyacentes[4].

Según Cardaropoli[3], son múltiples los factores que influyen en el proceso de reabsorción ósea. Entre ellos, los más destacables son: la posición del diente en la arcada; el estado del alveolo previamente a la extracción; el biotipo gingival; la dimensión inicial del reborde; la presencia de enfermedades sistémicas con afectación vascular (diabetes); el número de dientes a extraer; hábitos como el consumo de tabaco, alcohol y drogas; el uso de técnicas y materiales de preservación alveolar y por último el uso de prótesis (y su tipología) debido a que portar una prótesis removible favorece inevitablemente una reabsorción más rápida del hueso alveolar. Una prótesis fija, en cambio, permite un mayor mantenimiento de hueso a largo plazo[3].

Con el nacimiento de las prótesis fija, también se hizo necesario elaborar una clasificación de los defectos del reborde. El primero en responder a esta instancia fue, en 1983, Seibert[5], el

cual dividió los defectos en 3 categorías, atendiendo a la dimensión en el espacio de tales defectos **(Figura 1)**:

- **Clase I**: Reabsorción horizontal, vestíbulo-lingual, preservándose la altura de la cresta.
- **Clase II**: Reabsorción vertical, ápico-coronal, manteniéndose la anchura alveolar normal de la cresta.
- **Clase III**: Reabsorción en los dos ejes del espacio, tanto en sentido vestíbulo-lingual como ápico-coronal, perdiéndose altura y anchura de la cresta.

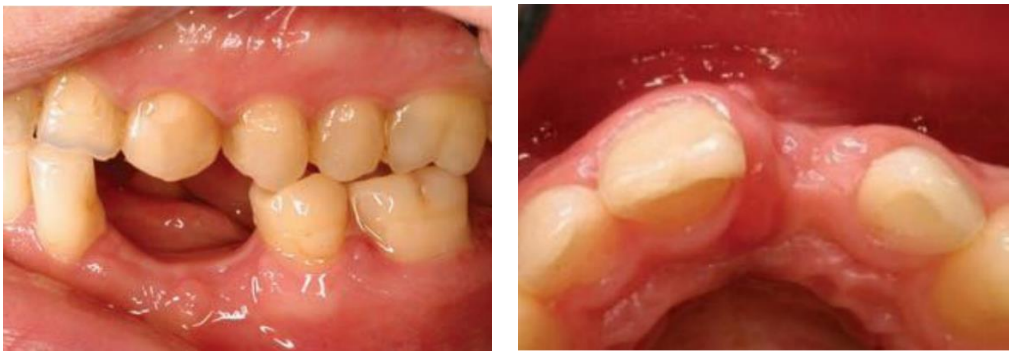

Fig. 1. Reabsorcion de la cresta alveolar en sentido corono-apical (izquierda) y en sentido vestibulo-lingual (derecha) [4].

Esta clasificación fue superada, un par de años más tarde, por Allen, que introdujo el concepto de severidad, cuantificando la extensión de los defectos alveolares en comparación con la cresta normal adyacente[6].

- Leve: Hasta 3 mm.
- Moderado: De 3 a 6 mm.
- Severo: Por encima de 6 mm.

Los estudios anteriores[1,2,3] evidencian la magnitud de la perdida de tejidos duros y blandos que ocurren después de una extracción **(Figura 2)**, y destacan la importancia de preservar cuanto más posible la integridad del reborde alveolo de cara a una futura posible rehabilitación con prótesis fija.

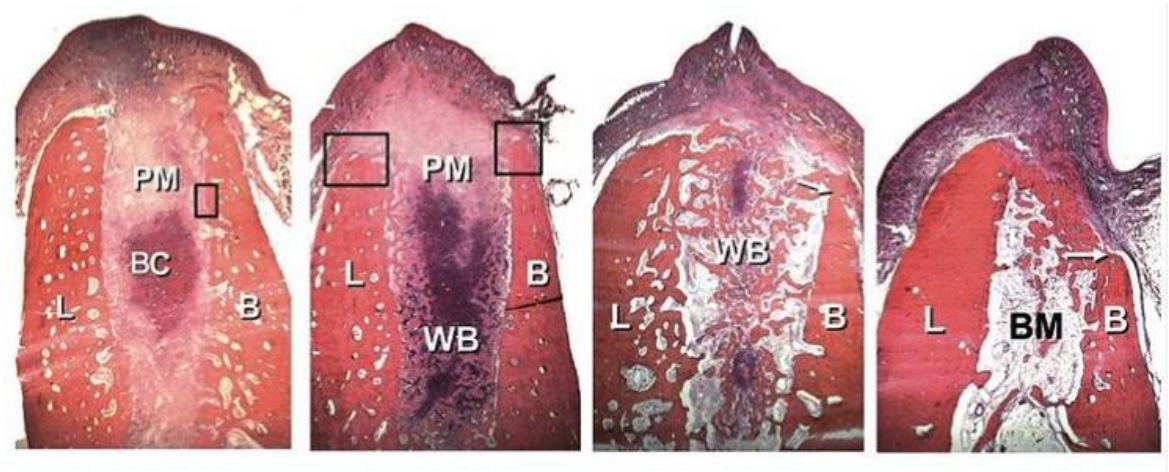

Fig. 2. Cambios dimensionales a las 1, 2, 4 y 8 semanas. Se puede observar una reducción significativamente mayor en la pared vestibular del alveolo (2,2 mm más que en lingual). PM=Matriz provisional, BC=coagulo de sangre, WB=Tejido óseo, BM=Medula ósea, B=Lado vestibular, L=Lado lingual)[2].

Preservación alveolar

A lo largo de los años se han elaborado muchas técnicas de preservación alveolar, cada una caracterizada por procedimientos y materiales distintos para tratar de alcanzar resultados cada vez mejores.

Entre los distintos tipos de injertos se encuentran los injertos autólogos (o autógenos), que provienen del mismo individuo; los aloinjertos, que provienen de un individuo de la misma especie (normalmente cadáveres); los xenoinjertos (o injertos heterólogos) que se obtienen de especies animales; y por ultimo los injertos aloplásticos, compuestos sintéticos artificiales con características semejantes a las del hueso[7].

Estos tipos de injertos se pueden utilizar solos o en combinación con compuestos de naturaleza proteica. Entre ellos, sustancias como las proteínas morfogenéticas óseas (*Bone Morphogenetic Proteins*, de aquí en adelante BMPs), el plasma rico en plaquetas (PRP) y las proteínas derivadas del esmalte (MDE) tienen la propiedad de conferir al injerto mayor capacidad osteoinductora, permitiendo así lograr mejores resultados en la preservación alveolar[7].

Clasificación de los tipos de injertos**:**

- ***Injertos alogénicos*** (corticales, esponjosos o corticoesponjosos): provienen de un individuo de la misma especie (otro ser humano). Suelen ser de dos tipos: mineralizados congelados-secados ("*freeze-dried bone allograft",* de aquí en adelante FDBA) y desmineralizados congelados-secados (*"demineralized freeze-dried bone allograft",* de aquí en adelante DFDBA)[8,9]. La desmineralización permite exponer las BMPs ayudando así la diferenciación de células pluripotenciales indiferenciadas hacia osteoblastos (osteoinducción)[7].

  A diferencia del hueso autólogo, no conllevan los problemas de morbilidad en el sitio donante ni de limitada disponibilidad; su amplia y rápida accesibilidad se debe a la creación de apósitos "Bancos de hueso". Se han vuelto muy populares en los últimos años gracias a sus propiedades, que les otorgan alta predictibilidad y eficacia en las cirugías. Tienen propiedades de osteoconducción y osteoinducción y pueden proceder tanto del hueso cortical como del hueso trabecular[10].

  A pesar de sus ventajas no están libres de controversias ya que, al proceder de cadáveres, si no tratados adecuadamente podrían presentar inconvenientes relativos a posibles

comportamientos infecciosos y antigénicos, llevando además a una posible incompatibilidad inmunológica[10].

Estos peligros, de toda forma, se hacen virtualmente imposibles gracias al tipo de procesamiento al que están sometidos los tejidos óseos, que implica su desmineralización y congelación[11].

Además de las criticidades de naturaleza infecciosa e inmunológica, este tipo de injertos, debido a su propia naturaleza y en particular a su origen humano, conlleva una serie de implicaciones de naturaleza ética[12].

Como se mencionó anteriormente, esta clase de biomateriales está ganando popularidad y difusión cada vez mayores. Se hace necesario, por tanto, reglamentar por medio de oportunas instituciones y de forma estrecha la gestión y distribución de los aloinjertos, para evitar fenómenos de contrabando y/o tráfico de órganos humanos[12].

Como se ha comentado, los bancos de órganos deberían cubrir este papel, ejerciendo los necesarios controles sobre el origen de los tejidos; estos tienen que ser donados libremente, sin esperar retornos económicos y en ausencia de cualquier tipo de condicionamiento. Estas condiciones no siempre se verifican, y son difíciles de cumplir, en particular en las áreas más pobres del planeta[12].

- ***Injertos heterólogos o xenoinjertos*** (corticales o esponjosos): incluyen una vasta gama de materiales. Proceden de animales de especies distintas al ser humano y poseen exclusivamente propiedades osteoconductivas[13].

Se utilizan mayormente en implantología y cirugías periodontales y suelen proceder sobre

todo de especies bovinas, porcinas o incluso aviares[4]. El hueso obtenido del animal está sometido a un proceso de desproteinización antes de ser utilizado en las intervenciones; esto incluye la extracción de sus componentes orgánicos, la exposición a agentes viricidas y finalmente su esterilización[4].

Varios ensayos clínicos[14,15] probaron sus buenos resultados en la preservación alveolar, ya que estos materiales han demostrado conservar en buena medida el proceso alveolar.

Sin embargo, algunos ensayos prospectivos han evidenciado como los injertos heterólogos de origen bovino en algunas ocasiones inhibirían el remodelado de las paredes del alveolo después de una extracción, por tanto su utilización podría suponer un problema por la posible escasa predictibilidad de este tipo de injertos[15,16].

- ***Injertos aloplásticos*:** se trata de materiales sintéticos fabricados artificialmente con el propósito de tener propiedades similares a las del hueso humano. Sirven como andamiaje y sostén para las células formadoras de hueso (presentan propiedades osteoconductivas). Pueden estar compuestos por hidroxiapatita, cristales bioactivos o ser de naturaleza cerámica, en cuyo caso se dividen en dos familias: la de los fosfatos de calcio y la de los sulfatos de calcio que, si bien relacionadas desde un punto de vista químico, presentan distinta morfología, manejo, propiedades químicas y mecánicas[17,18].

  Se presentan en forma de bloque granular variando el tamaño de sus poros, pudiendo ser bien macroporosos y microporosos[19]. Se dividen, además, en cristalinos y amorfos. Sus propiedades e indicaciones varían en función de todos los anteriores parámetros[20].

El objetivo de estos compuestos cerámicos es lo de sustituir el hueso en su fase mineral y por lo tanto solo presentan propiedades osteoconductivas. A nivel clínico, los injertos aloplásticos se utilizan generalmente en defectos "menores" y de pronóstico más favorable, en los cuales no haga falta recurrir a otros tipos de injertos más efectivos como los autólogos o los alogénicos[18].

Tienen el inconveniente de degradarse con el paso del tiempo, debido a dos distintos mecanismos: el primero de simple disolución fisicoquímica y el segundo de reabsorción mediada por los osteoclastos[17].

- ***Injertos autólogos*** (cortical, esponjoso o corticoesponjoso): utilizados en múltiples cirugías ya a partir de 1944[21], su uso ha crecido exponencialmente desde entonces. Considerado el *Gold Standard* en las técnicas de regeneración ósea y en particular en las de preservación alveolar debido a que se obtiene del propio paciente, por lo cual mantiene todas las propiedades de osteogénesis, osteoconducción y osteoinducción. Además, siendo hueso procedente del mismo individuo no tiene capacidad antigénica o infecciosa.
  Se pueden obtener de diferentes localizaciones, pudiendo ser éstas extraorales (tibia, cresta iliaca, calota, entre otras), indicadas sobre todo cuando las áreas a regenerar son extensas, o intraorales (tuberosidad maxilar, rama mandibular, mentón, *torus*).

  En un estudio realizado en 2012, Ren E. Wang et al.[22] examinaron el comportamiento clínico de diferentes tipos de injertos en distintas técnicas de preservación alveolar, posteriormente a una exodoncia. Observaron que los alveolos dejados vacíos, sin materiales de relleno, sufrieron una pérdida de dimensión horizontal de hasta 3 veces mayor que los que se rellenaron con xenoinjertos que, debido a su naturaleza solo poseen

la propiedad osteoconductora, careciendo tanto de la propiedades osteoinductora como de la osteogénica[22].

En el mismo estudio se utilizaron también partículas desmineralizadas de matriz ósea, las cuales dieron también buenos resultados clínicos. Los aloinjertos, en cambio, no se revelaron eficaces. El hueso liofilizado desmineralizado (DFDBA) y el hueso mineralizado en su estado natural (FDBA) mostraron resultados positivos. Por último, se colocaron tapones de colágeno en el alveolo, para evaluar su capacidad para estimular el crecimiento de nuevos tejidos; no se demostró, sin embargo, su utilidad en ralentizar la reabsorción de los tejidos[22].

La gran mayoría de los estudiados analizados concuerdan en afirmar que el mejor material para preservación alveolar, debido a las tres propiedades de osteogénesis, osteoconducción e osteoinducción, es el hueso autógeno, pese a presentar claros inconvenientes a la hora de obtener el injerto.

En los últimos años distintas investigaciones[23,24,25] han puesto en evidencia las múltiples limitaciones y complicaciones asociadas al uso de este tipo de injertos. De especial relevancia es la morbilidad que este tipo de injertos causa en la zona donante: en el lugar de obtención, por ejemplo, no es infrecuente que aparezcan de infecciones, fracturas, hematomas o secuelas como lesiones nerviosas y cicatrices hipertróficas. Además, la cantidad de hueso que se obtiene es variable en función del sitio anatómico, y en general es limitado. No siempre hay hueso suficiente para el defecto a rellenar. También la calidad del injerto es inconstante y varía mucho dependiendo del sitio. En algunos casos, y en función del sitio donante, los injertos han llegado a sufrir reabsorciones de hasta el 50%[26]. Estas son algunas tasas de reabsorción vertical en función del sitio extraoral de origen:

cresta ilíaca 12-60% y calota 0-15%. En relación a la reabsorción horizontal de los injertos autólogos en bloque se ha reportado entre un 10% y un 50%[27,28].

El éxito en este tipo de cirugías varía en función de distintos factores tales como la vascularización del lecho receptor, la estabilidad mecánica del injerto, la remodelación ósea y el contacto entre injerto y pared ósea[29].

Además, esta técnica implica un aumento importante en los tiempos quirúrgicos ya que se necesita una cirugía previa de obtención del injerto[29].

Por todas las razones mencionadas, resumibles fundamentalmente en la morbilidad en el sitio donante, la cantidad limitada de hueso, la calidad variable y el alargamiento de los tiempos quirúrgicos, la tendencia actual ha llevado a disminuir, cuando es posible, el uso de injertos de hueso autólogo en las de cirugías en favor de diferentes alternativas.

La búsqueda de un material que presente las mismas propiedades de osteoconducción, osteoinducción y osteogénesis propias de los injertos de hueso autólogo, sin tener sus inconvenientes, ha llevado cada vez más autores a estudiar e investigar las posibilidades terapéuticas ofrecidas por la dentina[30,31,32].

Descripción de los tejidos dentales

La dentina está siendo objeto de estudio y experimentación por su composición y propiedades relativamente similares a la del hueso. Está indicada en las técnicas de ingeniería de tejidos por servir, a la vez, de andamiaje y de fuente rica en factores de crecimiento[30].

Sus propiedades dependen, en amplia medida, de su matriz extracelular, compuesta por el 50% de minerales, por el 30% de compuestos orgánicos y por el restante 20% por agua. Esta

matriz contiene macromoléculas presentes en algunos tipos de tejidos conectivos y, a la vez, compuestos típicos de los tejidos mineralizados como el hueso[30].

Sintetizada por los odontoblastos, la dentina es rica en factores de crecimiento y sustancias bioactivas que estimulan la dentinogénesis, no solo durante la formación del diente, sino se liberan también cuando el diente se ve "agredido" por factores externos como la placa bacteriana, responsable de la caries, y sustancias acidas exógenas o endógenas, permitiendo así la formación de una dentina (denominada terciaria) de reparación[30].

La matriz orgánica de la dentina se constituye fundamentalmente por proteínas no colágenas (*Non collagen proteins,* de aquí en adelante NCPs), proteínas colágenas, proteoglicanos, glicoproteínas y lípidos. El colágeno, la gran mayoría de tipo I, constituye el 90% de las proteínas de la matriz, y forma un andamiaje reticular y compacto sobre el cual se depositan los cristales de hidroxiapatita. Contiene además factores de crecimiento como el Factor de crecimiento β (Tgf- β1), el *insulin like growth factor* (de aquí en adelante IGF), proteínas morfogenéticas de hueso (BMPs) y algunos factores de crecimiento angiogénicos.[30] Los NCPs a su vez, se dividen en distintos grupos: *dentin phosphoprotein* (DPP), *dentin sialoprotein* (DSP), y *dentin matrix protein 1* (DMP1), que se encuentran exclusivamente en la dentina. Otro grupo, constituido por *bone sialoproteins* (BSP), osteocalcina, y *bone Gla-protein* (BGP) se encuentran en hueso, dentina y cemento[30].

Se ha observado como estas sustancias, y en particular los TGF- β1, los BMPs y los distintos tipos de NCPs, juegan un papel importante en el proceso de regeneración y reparación de los tejidos mineralizados, siendo responsables de la mineralización de las fibras de colágeno y de la formación de cristales de hidroxiapatita durante la generación de nueva dentina[30].

Los BMPs, además, presentan una importante capacidad osteoinductora, ya que actúan promoviendo la diferenciación de las células mesenquimales en odontoblastos y ameloblastos. Es muy importante conservar este tipo de proteínas durante el procesado de la dentina para obtener el material de injerto alveolar, ya que son estas que le confieren sus propiedades osteoinductoras[7].

El elevado contenido en BMPs es una característica común a esmalte y dentina; estas dos estructuras presentan, en efecto, una composición biológica muy parecida. Esto se debe a que los tejidos dentales y el hueso alveolar tienen un origen embrionario común: ambos proceden de la cresta neural y ambos están compuestos por colágeno tipo I[7].

Su contenido mineral supera el de los otros materiales; además, su estructura y propiedades son muy parecidas a las del hueso autólogo: como éste también es osteocompatible y osteconductivo, constituyendo un andamiaje sobre el cual el nuevo hueso se va depositando. En cuanto al contenido mineral, en la dentina está presente un 70-75% de contenido inorgánico y un 20% de orgánico, mientras que en el hueso se encuentra un 65% de contenido orgánico y un 25% de orgánico; las propiedades de la dentina, debido a su composición muy parecida al hueso humano, se aproximan mucho a las del hueso autólogo[7].

A parte de los BMPs, y como ya se mencionó anteriormente, la dentina (y también el cemento) presentan en su interior muchas proteínas comunes al hueso: entre estas, NCPs tales como osteocalcina, osteonectina y fosfoproteína, fundamentales en el proceso de maduración del hueso.[7]

Otra importante ventaja de la dentina es que, a diferencia del hueso autólogo, su obtención no conlleva los inconvenientes propios de este último material (disponibilidad limitada, morbilidad en el sitio donante y en algunos casos altas tasas de reabsorción) [7].

Otra razón que nos orienta hacia la elección de la dentina sobre otros materiales de origen dental (como cemento o esmalte), es su mayor cantidad en el diente (ocupa más del 85% del volumen). Esto nos permite obtener, a partir de un solo diente, una cantidad de injerto suficiente a ocupar el alveolo en su totalidad, cosa que no podría ocurrir si se utilizara esmalte o cemento debido a sus escasas cantidades[7].

Por último, y como ya mencionado anteriormente, cabe recordar su proporción de contenido inorgánico/orgánico muy similar a la del hueso alveolar[7].

Por todas estas razones, en los últimos años la dentina ha adquirido un papel cada vez más importante como biomaterial de preservación alveolar y como posible sustituto del hueso autógeno en este ámbito **(Figura 3)**.

Fig. 3. Partículas dentinarias de entre 300 y 1200 μm[7].

Técnicas de obtención y tratamiento de la dentina

La primera investigación sobre las propiedades osteoinductoras de la dentina se llevó a cabo en 1967, por parte de Yeomans et al.[31], quienes fueron los primeros en demostrar la capacidad regenerativa de la matriz desmineralizada de dentina (*demineralized dentin matrix*, de aquí en adelante DDM). En este estudio se observó también como la matriz de dentina desmineralizada parecía poseer mayor osteoinductividad y menor antigenicidad que las partículas de dentina sin tratar (mineralizadas) [31].

En otro estudio del mismo año, Urist et al. demostraron a su vez que la matriz de dentina colágena, similar a la matriz de hueso, es capaz de inducir formación de hueso y tiene por lo tanto propiedades osteogénicas[33].

En una posterior investigación de 1998, Ike M. et al.[34] observaron, en cambio, que los gránulos de dentina parcialmente desmineralizados no parecían tener capacidad osteoinductora.

Algunos años más tarde, en 1991, Bessho et al.[32] consiguieron aislar por primera vez BMPs a partir de la matriz dentinaria. Aunque estas no sean completamente idénticas a las del hueso, su comportamiento como factor osteoinductor resultó ser parecido.

Los resultados conseguidos en el campo de la regeneración alveolar con dentina en los últimos años han sido notables: en muchos estudios[35,36,37] se observó la capacidad de la dentina de favorecer el crecimiento de células madre, y en consecuencia de nuevo tejido, en los defectos óseos **(Figura 4)**.

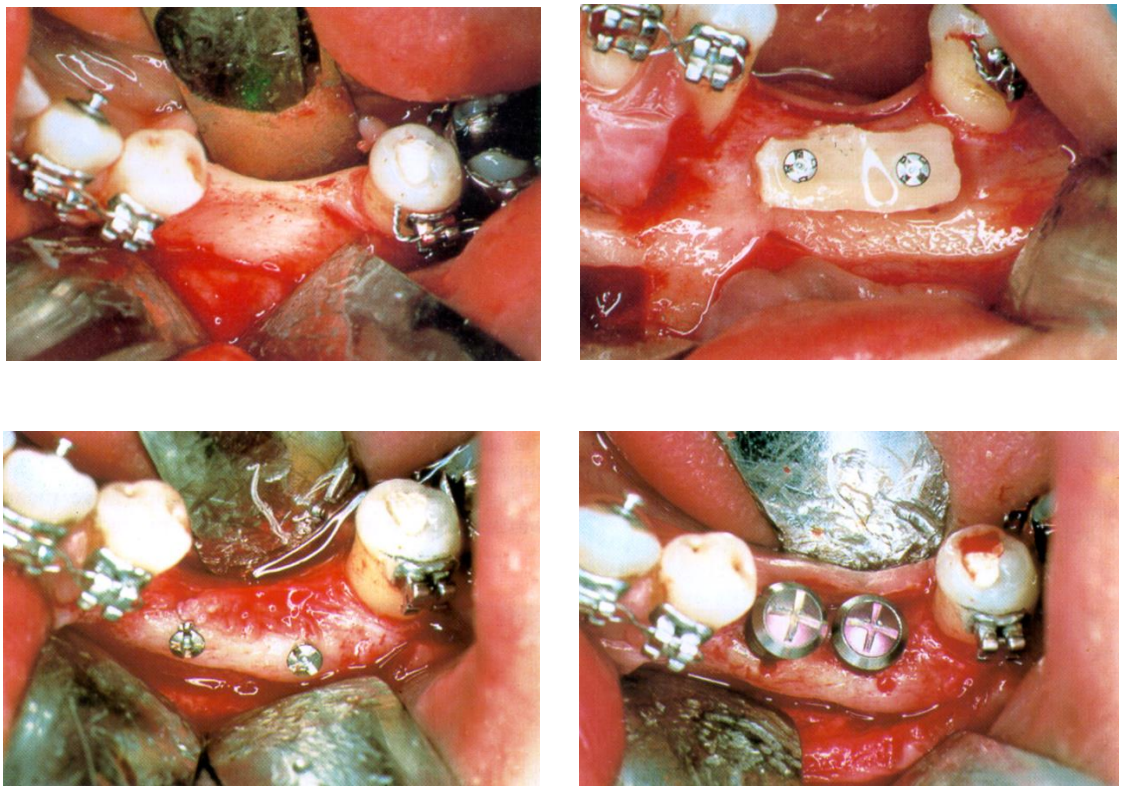

Fig. 4. Distintas etapas del proceso de regeneración alveolar con dentina, desde la colocación del injerto hasta la colocación de los implantes 6 meses después[27].

Algunas investigaciones, como la de 2020 de Andrade et al.[38] informaron de una mejor rendimiento de las partículas de dentina autólogas cuando combinadas con fibrina rica en plaquetas y leucocitos (*leukocyte- and platelet-rich fibrin*, de aquí en adelante L-PRF) y nitrógeno líquido. En esta investigación se analizó el proceso de curación de diez alveolos que después de las exodoncias se rellenaron con un compuesto de dentina y L-PRF, ambos en la misma cantidad, utilizando nitrógeno como aglutinante. A los 6 meses se realizaron las biopsias de las zonas interesadas. El proceso de cicatrización de la herida se llevó a cabo sin complicaciones en todos los pacientes. Los resultados de la biopsia mostraron una presencia en volumen de hueso, dentina y tejido conectivo de respetivamente el 57,0 %, el 0,9% y el 39,3%, evidenciando así una progresiva desaparición de la dentina en favor de la génesis de nuevo hueso. En 4 casos no quedó ninguna traza de dentina[38].

Minetti et al.[39], en una investigación de 2019, confrontaron los distintos comportamientos histológicos de una muestra de dentina mezclada con xenoinjertos y de otra muestra de dentina sola. En esta serie de casos los participantes se dividieron en dos grupos: el primero grupo recibió el injerto de sola dentina, mientras que el segundo el de dentina combinada con el material de injerto heterólogo. En ambos casos, la dentina de los dientes recién extraídos se sometió a un proceso de fragmentación y parcial desmineralización gracias a un dispositivo automatizado. Las dos muestras de injertos así procesados se colocaron en los alveolos después de la extracción y se suturó la herida. A los 4 meses se colocó un implante en cada alveolo, lo cual permitió realizar biopsias de los sitios tratados. No se encontraron signos de reacción inflamatoria o infecciosa en ningún grupo; hubo diferencia en cuanto a los resultados histomorfométricos: el grupo tratado exclusivamente con dentina (el primero) resultó presentar una cantidad de hueso neoformado mayor del 85,29% con respecto al segundo grupo, y una cantidad de injerto residual inferior a este del 83,59%, demostrando así una mayor capacidad osteogénica de la muestra con sola dentina[39] **(Figura 5)**.

Fig. 5. Procesamiento de los dientes mediante la eliminación de todos los residuos de caries, calculo y ligamento periodontal (izquierda). El material así obtenido se coloca en la cámara de trituración[7].

Recientemente, una serie de investigaciones[39,40,41] han puesto la atención sobre un aspecto muy sugestivo y hasta entonces no explorado sobre esta técnica: la capacidad osteogénicas de injertos de dentina procedentes de dientes deciduos. En estos estudios se seleccionaron dientes libres de caries, que fueron lavados cuidadosamente, cortados en fragmentos, molidos y esterilizados mediante un dispositivo especifico; se obtuvieron así unos gránulos de entre 0,4 y 0,8 mm, hechos tanto de esmalte como de dentina, que se aplicaron en el alveolo, y al final demostraron su validez como material de injerto.

Por todo lo anterior, el propósito del presente estudio es de determinar que procesos fisiológicos ocurren en el alveolo después de una exodoncia y de qué manera se modifican los tejidos a su alrededor. Para ello se analizarán las distintas técnicas y materiales propuestos para realizar preservación alveolar, destacando entre ellos el uso de dentina autógena y sus ventajas.

2. OBJETIVOS.

Los principales objetivos de esta revisión bibliográfica son:

1. **Establecer la magnitud de la perdida ósea que se produce después de una extracción.**
2. **Comparar las distintas tipologías de injertos para conservación alveolar, y su eficacia.**
3. **Comparar las distintas técnicas de procesamiento de la dentina para ser utilizada como material de injerto, y su eficacia.**

3. METODOLOGÍA.

- **Estrategia de búsqueda:**

Para realizar este Trabajo de Fin de Grado, se ha llevado a cabo una búsqueda bibliográfica en las bases de datos de Pubmed/Medline, SciELO, Google Scholar y The Cochrane Library.
Se han utilizado las palabras clase *"alveolar bone loss", "tooth extraction", "bone resorption", "alveolar preservation",* "reabsorción ósea", "exodoncia", "preservación alveolar".

- **Criterios de inclusión:**

1. Artículos de revisión sistemática y metaanálisis, ensayos clínicos aleatorizados individuales, revisiones sistemáticas de cohortes, cohortes individuales, revisiones sistemáticas de estudios de casos y controles, estudios de casos y controles individuales, series de casos y estudios en animales.
2. Estudios en pacientes humanos mayores de edad y animales.
3. Artículos redactados en español o en inglés.
4. Publicados de 1990 hasta la fecha presente.
5. En revistas reconocidas internacionalmente.

- **Criterios de exclusión:**

1. Estudios sin acceso al texto completo
2. Estudios redactados en idiomas distintos del inglés o del español.
3. Estudios sin Abstract.

Cabe destacar que la técnica estudiada en la presente revisión para realizar el Trabajo de Fin de Grado se empezó a estudiar en la década de los '70 del siglo pasado. Por esta razón, y con

la intención de ilustrar la evolución progresiva de esta técnica con el paso del tiempo, algunos artículos aquí analizados son anteriores al periodo establecido para la búsqueda bibliográfica en los criterios expuestos en la metodología.

4. RESULTADOS.

Después de aplicar los criterios de inclusión y exclusión se seleccionaron 66 artículos, según un proceso de selección y exclusión ilustrado en el siguiente diagrama **(Figura 6)** y tabla **(Figura 7)**.

Fig. 6 . Diagrama de selección de los estudios analizados.

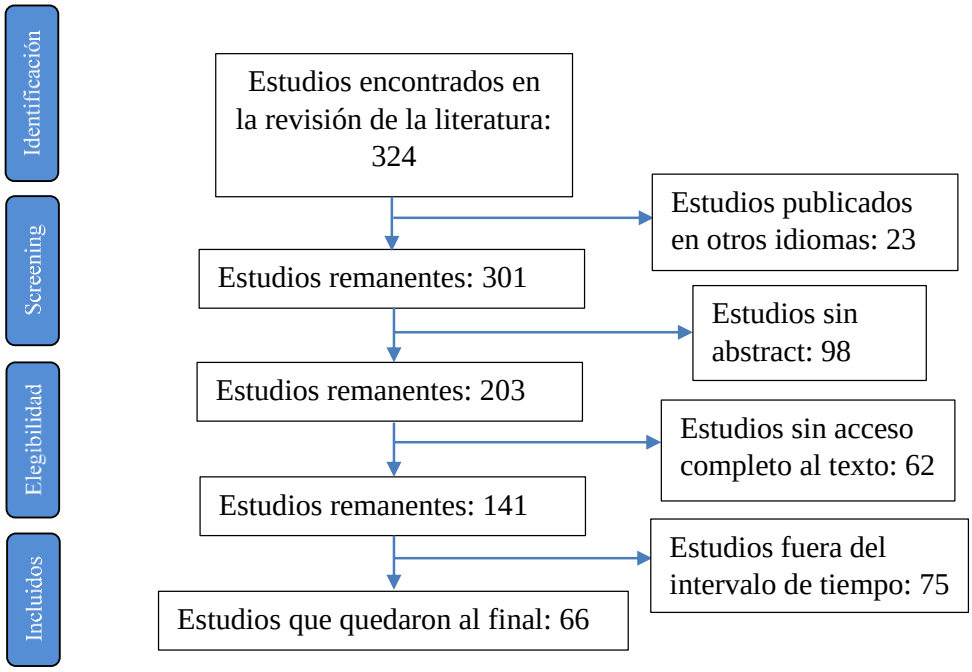

Fig. 7. Tabla de presentación de todos los estudios incluidos en el presente trabajo de revisión de la literatura.

Título del artículo.	Autores.	Journal.	Año.	Tipo de diseño.	Tamaño muestral.	Comentarios.
A Cephalometric Study of the Clinical Rest Position of the Mandible. Part II. The Variability of the Rate of Bone Loss following the Removal of Occlusal Contact.	Atwood, D.A.	J Prosthet Dent.	1957	Serie de casos.	32 participantes.	Estudio sobre la cicatrización de los rebordes alveolares después de una exodoncia, en los primeros 4 años.
Dimensional ridge alterations following tooth extraction. An experimental study in the dog.	Araujo MG, Lindhe J.	J Clin Periodontol.	2005	Estudio prospectivo en animales.	12 perros.	Descripción del proceso de cicatrización alveolar en las primeras 8 semanas post-extracción.
Dynamics of bone tissue formation in tooth extraction sites. An experimental study in dogs.	Cardaropoli G, Araujo M, Lindhe J.	J Clin Periodontol.	2003	Estudio prospectivo en animales.	9 perros.	Descripción del proceso de cicatrización alveolar en los primeros 6 meses post-extracción.
Effect(s) of the demineralization process on the osteoinductivity of demineralized bone matrix.	Zhang M, Powers RM Jr, Wolfinbarger L Jr.	J Periodontol.	1997	Estudio prospectivo en animales.	Ratones (no especifica el numero).	Se investigan las propiedades osteogénicas del hueso humano según su distinto grado de desmineralización.
Utilization of type I collagen gel, demineralized bone matrix, and bone morphogenetic protein-2 to enhance autologous bone lumbar spinal fusion.	Helm GA, Sheehan JM, Sheehan JP.	J Neurosurg.	1997	Estudio prospectivo en animales.	20 perros.	Investiga si el uso de matriz ósea desmineralizada, colágeno tipo I y BMP-2 pueden ayudar al hueso autólogo a conseguir fusión espinal.
Utilización de material dentario autólogo como injerto en el alveolo post-extracción.	Del Canto Díaz A.	TFM. Facultad de Odontología. Universidad Complutense de Madrid.	2016	Ensayo Clínico Controlado/TFM.	9 participantes.	Ensayo Clínico Controlado/TFM sobre la preservación alveolar con dentina autóloga.
A quantitative assessment of osteoinductivity of human demineralized bone matrix.	Zhang M, Powers RM Jr, Wolfinbarger L Jr	J Periodontol.	1997	Estudio prospectivo en animales.	82 ratones.	Evalúa los resultados clínicos de la regeneración ósea en ratones usando matriz ósea desmineralizada de origen humano.
Does xenogeneic demineralized bone matrix have clinical utility as a bone graft substitute?	Block JE, Poser J	Med Hypotheses.	1995	Articulo científico.	---	Análisis de distintos estudios para determinar la eficacia de DBM de origen xenogénico.
Ethical Considerations in Allograft Tissue Transplantation. A surgeon's perspective.	Nicholas, Richard MD.	Clinical Orthopaedics and Related Research.	2005	Articulo científico.	---	Consideraciones sobre las implicaciones éticas en el uso de injertos alogénicos.

Preservación de alveolos postexodoncia mediante el uso de diferentes materiales de injerto. Revisión de la literatura.	Vargas L.	TFM. Facultad de Odontología. Universidad Nacional de Colombia.	2011	Revisión de literatura/TFM.	91 publicaciones incluidas.	Revisión de literatura/TFM sobre los diferentes materiales y técnicas de preservación alveolar.
Preserving the socket dimensions with bone grafting in single sites: an esthetic surgical approach when planning delayed implant placement.	Irinakis T, Tabesh M.	J Oral Implant.	2007	Revisión de literatura.	23 estudios incluidos.	Revisión de literatura sobre las diferentes técnicas, materiales de injerto y resultados clínicos de la preservación alveolar.
Alveolar ridge sockets preservation with bone grafting – review.	Allegrini Jr. S, Koening Jr. B, Rivellino M, Yoshimoto M, Gedrange T, Fanghaenel J, Lipski M.	Ann Acad Med Estetin.	2008	Revisión de literatura.	---	Revisión de literatura sobre los diferentes materiales de injertos óseos disponibles para preservación alveolar.
Dimensional changes of the ridge contour after socket preservation and buccal overbuilding: an animal study.	Fickl S, Schneider D, Zuhr O, Hinze M, Ender A, Jung RE, Hürzeler MB.	J Clin Periodontol.	2009	Estudio prospectivo en animales.	5 perros.	Estudio comparativo con análisis clínicos y radiológicos después de utilizar diferentes materiales de injerto.
Hard tissue alterations after socket preservation with additional buccal overbuilding: a study in the beagle dog.	Fickl S, Zuhr O, Wachtel H, Kebschull M, Hürzeler MB.	J Clin Periodontol.	2009	Estudio prospectivo en animales.	5 perros.	Estudio comparativo con análisis clínicos e histológicos después de realizar preservación alveolar con xenoinjertos.
Biodegradation and bioresorption of calcium phosphate ceramics.	LeGeros RZ.	Clin Mater.	1993	Estudio *in vitro.*	---	Estudio que analiza los procesos de biodegradación y bioreabsorción de algunos tipos de injertos aloplásticos.
Calcium sulfate- and calcium phosphate-based bone substitutes. Mimicry of the mineral phase of bone.	Tay BK, Patel VV, Bradford DS.	Orthop Clin North Am.	1999	Articulo científico.	---	Articulo científico sobre diferentes tipos de injertos aloplásticos.
Radiologic and histomorphometric evaluation of maxillary sinus grafting with alloplastic graft materials.	Ozyuvaci H, Bilgiç B, Firatli E.	J Periodontol.	2003	Estudio clínico prospectivo en seres humanos.	44 participantes.	Campara varias técnicas y materiales de elevación e injerto de seno.

An evaluation of two configurations of tricalcium phosphate for treating craniotomies.	Hollinger JO, Schmitz JP, Mizgala JW.	J Biomed Mater Res.	1989	Estudio prospectivo en animales.	60 conejos.	Estudio clínico que evalúa la eficacia de injertos aloplásticos en defectos óseos de conejos.
Cancellous chip bone grafts: Report of 75 cases.	Mowlem, R	Lancet.	1944	Reporte de casos.	75 participantes.	Uno de los primeros estudios en investigar la eficacia de los injertos de hueso autógeno en la regeneración ósea.
Ridge preservation after tooth extraction.	Wang, R. E., & Lang, N. P.	Clinical Oral Implants Research.	2012	Estudio clínico prospectivo en seres humanos.	18 participantes.	Evalúa los estudios más recientes y las nuevas perspectivas sobre la preservación alveolar.
Autogenous bone graft: donor sites and techniques.	Myeroff C, Archdeacon M.	J Bone Joint Surg Am.	2011	Articulo científico.	---	Articulo científico sobre las técnicas más comunes de obtención de injertos de hueso.
Complications following autologous bone graft harvesting from the iliac crest and using the RIA: a systematic review.	Dimitriou R, Mataliotakis GI, Angoules AG, Kanakaris NK, Giannoudis PV.	Injury.	2011	Revisión sistemática de literatura.	92 estudios incluidos.	Revisión sistemática de literatura sobre las complicaciones de las cirugías de obtención de injertos autólogos.
Site selection and pain outcome after autologous bone graft harvest.	Baumhauer J, Pinzur MS, Donahue R, Beasley W, DiGiovanni C.	Foot Ankle Int.	2014	Estudio clínico prospectivo en seres humanos.	130 participantes.	Investigación de los sitios de obtención de injertos óseos y su relación con el dolor del paciente.
The TIME technique: a new technique for localized alveolar ridge augmentation prior to placement of dental implants.	Von Arx T, Hardt N, Wallkamm B.	Int J Oral Maxillofac Implant.	1996	Estudio clínico prospectivo en seres humanos.	20 participantes.	Estudio prospectivo sobre el uso de hueso autólogo para cirugías de aumento de cresta alveolar ante la colocación de implantes.
Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges.	Chiapasco M, Abati S, Romeo E, Vogel G.	Clin Oral Implants Res.	1999	Ensayo Clínico Aleatorizado.	30 participantes.	Analiza los resultados clínicos de diferentes técnicas y materiales para regenerar rebordes alveolares estrechos ante la colocación de implantes.
Horizontal-bone augmentation procedures in implant dentistry: prostethically guided regeneration.	Chiapasco M, Casentini P, Zaniboni M.	Int J Oral Maxillofac Implants.	2009	Articulo científico.	---	Análisis de los distintos enfoques quirurgicos para el tratamiento de crestas edéntulas estrechas con el fin de colocar implantes.

The biology of bone graft repair.	Burchardt H.	Clin Orthop Relat Res.	1983	Articulo científico.	---	Descripción biológica y microscópica de los mecanismo de integración de los injertos óseos.
Different dentin processing methods for bone tissue engineering application: a systematic review.	Tabatabaei FS, Tatari S, Samadi R, Moharamzadeh K.	J Biomed Mater Res.	2016	Revisión sistemática de literatura.	37 artículos incluidos.	Revisión sistemática de literatura sobre los diferentes métodos de procesamiento de dentina.
Bone induction by decalcified dentine implanted into oral, osseous and muscle tissues.	Yeomans JD, Urist MR.	Arch Oral Biol.	1967	Estudio prospectivo en animales.	48 conejos.	Compara la eficacia de injertos de dentina con la de injertos de hueso, tendón y musculo en defectos óseos de conejos.
Bone induction in excavation chambers in matrix of decalcified dentin.	Bang G, Urist MR.	Arch Surg.	1967	Estudio prospectivo en animales.	162 ratones y 24 conejos.	Evalúa la capacidad de osteogénesis de DDM en defectos óseos de distintos animales.
Recycled dentin root matrix for a carrier of recombinant human bone morphogenetic protein.	Ike M, Urist MR.	J Oral Implantol.	1998	Estudio prospectivo en animales.	118 ratones.	Estudio clínico sobre la capacidad de la matriz dentinaria como vector de BMP.
Human dentin-matrix-derived bone morphogenetic protein.	Bessho K, Tanaka N, Matsumoto J, Tagawa T, Murata M.	Journal of dental research.	1991	Estudio prospectivo en animales.	No especifica.	Estudio *in vivo* e *in vitro* sobre la capacidad osteogénica de BMP humanas en animales.
Alveolar ridge preservation with autologous particulated dentin-a case series.	Valdec S, Pasic P, Soltermann A, Thoma D, Stadlinger B, Rücker M.	International journal of implant dentistry.	2017	Reporte de caso.	1 participante.	Reporte de un caso de preservación alveolar con dentina en un incisivo central extraído.
Alveolar Ridge Preservation using Autogenous Whole-Tooth versus Demineralized Dentin Grafts: A Randomized Controlled Clinical Trial.	Elfana A, El-Kholy S, Ahmed Saleh H, Fawzy El-Sayed K.	Clinical oral implants research.	2021	Ensayo Clínico Aleatorizado.	20 participantes.	Ensayo Clínico Aleatorizado sobre la eficacia de la dentina y de una mezcla de dentina y esmalte autógenos como material de injerto.
Healing Dynamics Following Alveolar Ridge Preservation with Autologous Tooth Structure.	Mazor Z, Horowitz RA, Prasad H, Kotsakis GA.	The International journal of periodontics & restorative dentistry	2019	Estudio clínico prospectivo en seres humanos.	4 participantes.	Evaluar los resultados del hueso autólogo en la preservación alveolar para colocar finalmente implantes.

Combining autologous particulate dentin, L-PRF, and fibrinogen to create a matrix for predictable ridge preservation: a pilot clinical study.	Andrade C, Camino J, Nally M, Quirynen M, Martínez B, Pinto N.	Clinical oral investigations.	2020	Estudio clínico prospectivo en seres humanos.	4 participantes.	Describe los resultados clínicos e histológicos de una mezcla de dentina, L-PRF y fibrinógeno en la preservación alveolar.
Autologous tooth graft: a histological comparison between dentin mixed with xenograft and dentin alone grafts in socket preservation.	Minetti E, Palermo A, Savadori P, Barlattani A Jr, Franco R, Michele M.	Journal of biological regulators and homeostatic agents.	2019	Estudio clínico prospectivo en seres humanos.	6 participantes.	Comparar los resultados histológicos en la preservación alveolar utilizando dentina mezclada con xenoinjertos y dentina sola.
Demineralized deciduous tooth as a source of bone graft material: its biological and physicochemical characteristics.	Park M., Mah Y. J., Kim D. H., Kim E. S., Park E. J.	Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology.	2015	Estudio prospectivo en animales.	20 ratones.	Evaluación radio e histológica de las propiedades de los dientes deciduos como material de injerto en defectos óseos en ratones.
BMP-2 and type I collagen preservation in human deciduous teeth after demineralization.	Bono N., Tarsini P., Candiani G.	Journal of Applied Biomaterials & Functional Materials.	2018	Estudio *in vitro.*	---	Estudio dirigido a averiguar la presencia de BMP-2 y colágeno en los tejidos dentarios después de su desmineralización.
Preservación de reborde en el sector posterior: Una revisión sistemática.	Ramos-Pilco E, Allasi Tejada G, Alarcón Palacios M.	Rev Estomatológica Hered.	2019	Revisión sistemática de literatura.	9 estudios incluidos.	Revisión sistemática de estudios sobre preservación alveolar en sector posterior.
Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study.	Schropp L, Wenzel A, Kostopoulos L, Karring T.	Int J Periodontics Restorative Dent.	2003	Estudio clínico prospectivo en seres humanos.	46 participantes.	Evaluación de los cambios dimensionales en los alveolos de premolares y molares a lo largo de un año después de la extracción.
A systematic review of postextractional alveolar hard and soft tissue dimensional changes in humans.	Tan WL, Wong TL, Wong MC, Lang NP.	Clin Oral Implants Res.	2012	Revisión sistemática de literatura.	20 estudios incluidos.	Revisión sistemática de literatura sobre los cambios dimensionales de los alveolos después de la exodoncia.
Comparative Alveolar Ridge Preservation Using Allogenous Tooth Graft versus Free-dried Bone Allograft: A Randomized, Controlled, Prospective, Clinical Pilot Study.	Joshi CP, D'Lima CB, Samat UC, Karde PA, Patil AG, Dani NH.	Contemporary clinical dentistry.	2017	Ensayo Clínico Aleatorizado.	15 participantes.	Compara la eficacia de aloinjertos de hueso liofilizado con aloinjertos de dentina y esmalte, a lo largo de 4 meses.

Surgical protocols for ridge preservation after tooth extraction. A systematic review.	Vignoletti F, Matesanz P, Rodrigo D, Figuero E, Martín C, Sanz M.	Clin Oral Implants Res.	2012	Revisión sistemática de literatura.	14 estudios incluidos.	Revisión sistemática de la literatura sobre los distintos protocolos de preservación alveolar.
Randomized and Controlled Clinical Trial of Bone Healing After Alveolar Ridge Preservation Using Xenografts and Allografts Versus Plasma Rich in Growth Factors.	Stumbras A, Januzis G, Gervickas A, Kubilius R, Juodzbalys G.	The Journal of oral implantology.	2020	Ensayo Clínico Aleatorizado.	40 participantes.	Compara entre ellos la eficacia en la preservación alveolar de materiales de xenoinjerto, aloinjerto y PRGF con grupo control.
Socket Preservation Using a (Dense) PTFE Barrier with or without Xenograft Material: A Randomized Clinical Trial.	Carvalho Formiga M, Dayube URC, Chiapetti CK, de Rossi Figueiredo D, Shibli JA.	Materials (Basel, Switzerland)	2019	Ensayo Clínico Aleatorizado.	13 participantes.	Compara radiográfica e histológicamente la preservación alveolar con membranas de PTFE con y sin utilizar xenoinjertos.
A study of the fate of the buccal wall of extraction sockets of teeth with prominent roots.	Nevins, M.; Camelo, M.; Paoli, S.; Friedland, B.; Schenk, R.K.; Benfenati, S.P.; Simion, M.; Tinti, C.; Wagenberg, B.	Int. J. Periodontics Restor. Dent.	2006	Ensayo Clínico Aleatorizado.	9 participantes.	Compara radiográficamente a los 6 meses el proceso de curación alveolar con Bio-Oss con el grupo control.
Ridge preservation with the use of Bio-Oss collagen: A 6-month study in the dog.	Araujo, M.G.; Lindhe, J.	Clin. Oral Implantol.	2009	Estudio prospectivo en animales.	5 perros.	Estudio sobre la colocación inmediata de implantes con Bio-Oss Collagen.
Ridge preservation with freeze-dried bone allograft and a collagen membrane compared to extraction alone for implant site development: A clinical and histologic study in humans.	Iasella, J.M.; Greenwell, H.; Miller, R.L.; Hill, M.; Drisko, C.; Bohra, A.A.; Scheetz, J.P.	J. Periodontol.	2003	Estudio clínico prospectivo en seres humanos.	24 participantes.	Estudio de comparación del proceso de preservación alveolar con aloinjertos y grupo control.
Transformation of fibroblasts by allogeneic and xenogeneic transplants of demineralized tooth and bone.	Huggins C, Wiseman S, Reddi AH.	The Journal of experimental medicine.	1970	Estudio prospectivo en animales.	Conejillos de India, ratones y ratas.	Estudio de los efectos de injertos de hueso y dientes desmineralizados de origen alo y xenogénicas en animales.
Analysis of the inorganic component of autogenous tooth bone graft material.	Kim YK, Kim SG, Oh JS, Jin SC, Son JS, Kim SY.	J Nanosci Nanotechnol.	2011	Estudio *in vitro.*	---	Análisis de los componentes inorgánicos del hueso autógeno utilizado como material de injerto.

Development of a novel bone grafting material using autogenous teeth.	Kim YK, Kim SG, Byeon JH, Lee HJ, Um IU, Lim SC.	Oral Surg Oral Med Oral Pathol Oral Radiol Endod.	2010	Estudio clínico prospectivo en seres humanos.	6 participantes.	Evaluación histomorfométrica de la eficacia de un material de injerto derivado de dientes autógenos.
Induction of cartilage and bone by dentin demineralized in citric acid.	Inoue T, Deporter DA, Melcher AH.	J Periodontal Res.	1986	Estudio prospectivo en animales.	30 ratones.	Investiga las propiedades osteogénicas de la dentina desmineralizada con ácido cítrico y con HCl.
Bone induction of human tooth and bone crushed by newly developed automatic mill.	Murata M, Akazawa T, Takahata M, Ito M, Tazaki J, Hino J.	J Ceram Soc Jpn.	2010	Bioensayo	---	Bioensayo sobre el funcionamiento de un nuevo aparato para moler hueso y dientes en biomateriales de injerto.
Radiological evaluation of human dentin autografts in Bangladesh.	Kabir MA, Murata M, Kusano K, Zakaria SM, Noor AM, Khuda F.	J Hard Tissue Biol.	2014	Estudio clínico prospectivo en seres humanos.	2 participantes.	Evaluación radiográfica e histológica de la eficacia de preservación alveolar con DDM en dos pacientes, a lo largo de un año.
Tooth bank system for bone regeneration-safety report.	Kim YK, Um IW, Murata M.	J Hard Tissue Biol.	2014	Revisión de datos.	---	Estudio sobre la seguridad y eficacia de los materiales de autoinjerto de origen dental, con particular enfoque en su almacenamiento en los “Bancos de dientes”.
Bone regeneration by demineralized dentin matrix in skull defects of rats.	Togari K, Miyazawa K, Yagihashi K, Tabuchi M, Maeda H, Kawai T.	J Hard Tissue Biol.	2011	Estudio prospectivo en animales.	120 ratones.	En este estudio DDM de origen bovino fue implantado en defectos óseos de ratones.
A bovine low molecular weight bone morphogenetic protein (BMP) fraction.	Urist MR and Lietze A.	Clin Orthop.	1982	Estudio prospectivo en animales.	Ratones y conejos.	Estudio prospectivo sobre la capacidad de los BMPs de inducir formación de hueso en defectos óseos de ratones y conejos.
Bone regeneration using dentin matrix depends on the degree of demineralization and particle size.	Koga T, Minamizato T, Kawai Y, Miura K, IT, Nakatani Y.	PLoS One.	2016	Estudio prospectivo en animales.	100 ratones.	Comparación de la eficacia de distintos tipos de dentina según su procesamiento y tamaño de partículas en defectos óseos de ratones.
Non-collagenous components of the organic matrix of rabbit incisor dentine.	Smith A, Leaver A.	Arch Oral Biol.	1979	Estudio *in vitro.*	---	Análisis de los componentes orgánicos de la matriz de dentina en dientes de conejos.

Dissolution of bio-active dentine matrix components by mineral trioxide aggregate.	Tomson PL, Grover LM, Lumley PJ, Sloan AJ, Smith AJ, Cooper PR.	J Dent.	2007	Estudio *in vitro*.	---	Estudio *in vitro* que compara la capacidad del MTA y de Ca(OH)2 para solubilizar las proteínas de la matriz de la dentina.
Processed bovine dentine as a bone substitute.	Moharamzadeh K, Freeman C, Blackwood K.	Br J Oral Maxillofac Surg.	2008	Estudio prospectivo en animales.	6 ratones.	Evaluación *in vivo* e *in vitro* de la biocompatibilidad dentinaria y de su osteogenicidad.
Properties of hydroxyapatite from bovine teeth.	Elkayar A, Elshazly Y, Assaad M.	Bone Tissue Regen Insights.	2009	Estudio *in vitro*.	---	Estudio *in vitro* sobre las propiedades de xenoinjertos bovinos.
Quantitation of growth factors IGF-I, SGF/IGF-II, and TGF-b in human dentin.	Finkelman RD, Mohan S, Jennings JC, Taylor AK, Jepsen S, Baylink DJ.	J Bone Miner Res.	1990	Estudio *in vitro*.	---	Bioensayo sobre la presencia de factores de crecimiento similares a los del hueso en la dentina.
The nature and functional significance of dentin extracellular matrix proteins.	Butler WT, Ritchie H.	Int J Dev Biol.	1995	Articulo científico.	---	Articulo científico sobre la composición orgánica de la dentina.
Reconstruction using an autograft containing tumour treated by liquid nitrogen.	Tsuchiya H, Wan SL, Sakayama K, Yamamoto N, Nishida H, Tomita K.	J Bone Joint Surg Br.	2005	Estudio clínico prospectivo en seres humanos.	28 participantes.	Estudio clínico que investiga un método para reconstruir lesiones tumorales con hueso autógeno.

5. DISCUSIÓN.

A lo largo de los últimos años, numerosos autores[42,43,44] se plantearon el problema de establecer la magnitud de perdida ósea que se produce después de una extracción.

Ya en los años ’80, y como consecuencia del nacimiento y la rapidísima difusión de las prótesis fijas, Seibert[5] y Allen[6] elaboraron separadamente dos clasificaciones de los defectos óseos; en el primer caso, Seibert basó su clasificación según el sentido, horizontal o vertical, de la reabsorción, mientras que Allen decidió introducir el concepto de severidad, categorizando los tipos de defectos según se extensión espacial en milímetros.

En 2003, Schropp et al.[42] analizaron los cambios tisulares ocurridos a lo largo de un año en el proceso alveolar de 46 pacientes, después de la remoción de un único diente, premolar o molar. Para este propósito utilizaron unos modelos de estudio y adicionalmente llevaron a cabo unos análisis radiográficos con el objetivo de determinar el tamaño de la reabsorción sufrida por los tejidos. Las mismas radiografías se convirtieron mediante un *software* en imágenes 3D. Los resultados mostraron que los mayores cambios se habían producido durante el primer año, al terminar el cual se registra una contracción de tejidos de hasta casi el 50%.

En 2012, Tan et al.[43] realizaron otra revisión sistemática con el mismo objetivo. En su estudio, los autores determinaron una contracción promedio de 3,79 ± 0,23 mm en la anchura de los alveolos, mientras que en sus altura se registró a los 6 meses una contracción de 1,24 ± 0,11 mm en el lado vestibular, de 0,84 ± 0,62 mm en el lado mesial y de 0,80 ± 0,71 mm en el lado distal. El porcentaje de reabsorción horizontal fue del 32% a los 3 meses y del 29-67% a los 6 meses, mientras que el de reabsorción vertical resultó ser, a los 6 meses, de un 11-22%. Los tejidos blandos sufrieron una reabsorción de 0,4-0,5 mm a los 6 meses. Los resultados obtenidos indican, al igual que en el estudio Schropp et al.[43], que el proceso de reabsorción se

divide en dos fases distintas: una primera de reabsorción rápida, dentro de los primeros tres meses, seguida por otra de reducción más lenta y gradual.

En 2019, E. Ramos-Pilco et al.[44] realizaron una revisión sistemática sobre un total de 435 casos de extracción de premolares y molares verificando que, a los 6 meses de la exodoncia, los estudios indicaban una pérdida ósea promedio horizontal por encima de 3,5 mm y vertical de hasta 1,3 mm. Se constató además una mayor reabsorción ósea en la pared vestibular que en la lingual. Como en el precedente estudio de Schropp et al.[42], los autores también constataron una perdida ósea más intensa en lado vestibular, concentrada particularmente durante los primeros tres meses.

Todos los tres estudios de E. Ramos-Pilco et al., Schropp et al. y Tan et al.[42,43,44] muestran que el proceso de reabsorción post- exodoncia afecta sobre todo a la pared vestibular del alveolo, y se articula en dos fases, una primera de reabsorción rápida, seguida por otra más lenta.

Con la introducción de las prótesis fijas en las últimas décadas, y con el consecuente nacimiento de la implantología, se hizo prioritario encontrar una forma de reducir lo más posible la reducción sufrida por la cresta alveolar posteriormente a una exodoncia. Se han propuesto, por lo tanto, distintos materiales de injerto a colocar en el alveolo para mantener sus dimensiones; fundamentalmente 4 categorías: injertos autógenos, aloinjertos, injertos aloplásticos y xenoinjertos. Entre los autores hubo mucho debate al respecto.

En 2021, Elfana A. et al. realizaron un ensayo clínico aleatorizado[36] que estudiaba la eficacia clínica de injertos autólogos de dentina y de hueso en cirugías de preservación alveolar. La muestra estaba compuesta por pacientes mayores de edad, no fumadores, en buen estado de salud y con una pérdida de hueso a nivel de la pared vestibular del alveolo inferior al 50%. Los participantes se dividieron en un grupo de casos (*autogenous whole-tooth group*, de aquí

en adelante AWTG), en el que fue utilizado hueso autólogo, y un grupo control (*autogenous demineralized dentin*, de aquí en adelante ADDG) en el que se utilizaron injertos de dentina. Cada grupo constaba de 10 miembros, cada uno de ellos con un solo diente a extraer (no molares).

En el grupo de casos, las partículas de AWTG se sumergieron en etanol 10 minutos para su desinfección y se lavaron luego dos veces en solución salina, mientras que en el grupo control todos los dientes extraídos se limpiaron cuidadosamente de cada residuo de ligamento periodontal, tejido conectivo, cemento, caries u obturaciones utilizando una fresa de turbina de grano fino; el conducto radicular y la cámara se eliminaron con limas endodónticas y, posteriormente, los dientes fueron molidos. Las partículas de ADDG fueron desmineralizadas sumergiéndolas en una solución de ácido clorhídrico 0,6 N por media hora. Luego, se lavaron dos veces en solución salina y se secaron con gasas estériles[36].

Los injertos fueron colocados en los alveolos y cubiertos con membranas colágenas reabsorbibles. Se realizaron CBCT al terminar la intervención y a los 6 meses, para establecer la magnitud de la reabsorción. También se realizaron biopsias y análisis histomorfométricos en los sitios interesados. En el grupo de casos se registró una reducción en anchura del 0,85 ± 0,38 mm, una reducción en altura por vestibular de 0,61 ± 0,20 mm y una reducción de altura en lingual de 0,66 ± 0,31 mm. En cambio, en el grupo control la reducción en anchura fue de 1,02 ± 0,45 mm, la reducción en altura por vestibular fue de 0,72 ± 0,27 mm y la en lingual de 0,56 ± 0,24 mm. No se registró ninguna reacción inflamatoria relevante. A nivel histomorfométrico, en el grupo de casos el volumen de hueso neoformado fue de 37.55% ± 8.94%, el de injerto residual de 17.05% ± 5.58% y el de tejido blando de 45.4% ± 4.06%, mientras que el grupo control el volumen de hueso neoformado fue del

48.4% ± 11.56%, el de injerto residual de 11.45% ± 4.13% y el de tejido blando del 40.15% ± 7.73%

Los resultados evidenciaron una eficacia similar de los grupos de injertos en la preservación alveolar a los 6 meses, demostrando los dos ser biocompatibles y osteoconductivos. A nivel histológico, todavía, el grupo de ADDG, es decir, el de la dentina, demostró incluso unas propiedades de osteogénesis, osteoinducción e integración con el hueso alveolar superiores al hueso autógeno[36].

Otros autores, Joshi C.P. et al.[45], llegan en 2017 a resultados similares, aunque utilizando aloinjertos en lugar de injertos autogenos: llevaron a cabo un estudio prospectivo aleatorizado para comparar la eficacia del aloinjerto de hueso liofiliado (FDBA), de aloinjertos de partículas de dentina (*"dentin allograft",* de aquí en adelante DA) y de aloinjertos de partículas del diente entero (*"whole tooth allograft",* de aquí en adelante WTA). Se seleccionaron en total 15 participantes que necesitaban de la extracción de por lo menos 4 dientes. Cada alveolo fue rellenado con WTA, DA y FDBA. El ultimo se dejó vacío. Posteriormente, los alveolos se cubrieron con una membrana. A los 4 meses se realizaron controles radiográficos (CBCT) y biopsias, aprovechando de las intervenciones para la colocación de implantes. En sentido vertical, se verificaron unos cambios de 0,36 ± 0,04 mm en el grupo de WTA, de 0,31 ± 0,07 mm en el grupo de DA y de 0,87 ± 0,07 mm en el grupo de FDBA. Los alveolos sin material de relleno sufrieron una reducción de 1,96 ± 0,24 mm. En sentido horizontal, el grupo de WTA sufrió una contracción de WTA de 0,49 ± 0,19 mm, el grupo de DA de 0,50 ± 0,29 mm, el de FDBA de 0,82 ± 0,50 mm y los alveolos sin material de relleno de 1,66 ± 0,97 mm.

Los datos obtenidos evidencian la necesidad de aplicar técnicas de preservación alveolar: hasta los materiales de injerto menos efectivos determinaron una reabsorción del hueso alveolar menor de la mitad que en los alveolos no tratados[45]. Al igual que el anterior estudio de Elfana et al.[36], se observó que los injertos de origen dental, tanto los de dentina (DA) como los de esmalte y dentina combinados (WTA) revelaron resultados superiores al hueso autógeno, aunque en este caso, y a diferencia del anterior, demostraron ser significativamente superior a este, mientras que en el anterior estudio la diferencia no fue tan significativa. El DA y el WTA, en cambio, se demostraron sustancialmente equivalentes. Los análisis histológicos confirmaron mayor osteogénesis en los sitios tratados con DA y WTA.

En 2012, Vignoletti el al.[46] realizaron una revisión sistemática sobre el mismo tema, utilizando distintos tipos de injertos, comparándolos entre ellos y con la curación espontanea del alveolo. Se utilizaron en los alveolos injertos de hueso autólogo, aloinjertos, xenoinjertos e injertos aloplásticos, cubriéndolos con membranas de origen autóloga o heteróloga. También, se colocaron en el alveolo factores de crecimiento o BMPs. Los participantes tratados con biomateriales constituyan el grupo de estudio, los otros el grupo control. Este último grupo mostró una disminución promedio en la altura del reborde de 1,47 mm mayor respecto al grupo de estudio, y una contracción promedio en la anchura de este de 1,83 mm superior, avalando así la validez y eficacia de las técnicas de preservación alveolar[46].

A diferencia de los anteriores estudios de Elfana A.[36] y Joshi C.P.[45] que evidenciaron una superioridad de los injertos de origen dental sobre los de origen ósea, y de ambos sobre los otros tipos de injertos, tanto de origen sintética como animal, esta investigación no encuentra diferencias significativas entre los diversos biomateriales. La conclusión que sugiere esta investigación es que el uso de membranas de colágeno y sobre todo el tipo de cirugía utilizada

(colgajo con sutura por primera intención) parece tener más importancia que el tipo de injerto elegido en el resultado clínico final[46].

En el estudio de Arturas Stumbras et al.[47] de 2020, aparte de xenoinjertos (*bovine bone mineral with collagen membrane*, de aquí en adelante BBM/CM), y aloinjertos (*freeze-dried bone allograft with collagen membran*, de aquí en adelante FDBA/CM), también se estudia el rendimiento de plasma rico en factores de crecimiento (PRGF). El estudio se lleva a cabo sobre 40 pacientes. A los 3 meses de realizar las extracciones, se llevaron a cabo biopsias y análisis histomorfométricos. El volumen de tejido óseo neoformado fue de 75,5% ± 16,3% en los alveolos tratados con PGRF, de 46,4% ± 15,2% en el grupo control, de 20,3% ± 21,9% en el grupo de BBM/CM y de 7,2% ± 8,6% en el grupo de FDBA/CM.

El grupo constituido por los solos factores de crecimiento registró los mejores resultados en términos de formación de nuevo hueso, seguido por el grupo control. Sorprendentemente, los xenoinjertos (hueso bovino) y los aloinjertos (hueso liofilizado) estimularon una formación de tejido mineralizado muy inferior incluso al grupo control. (20,3% y 7,2% respectivamente contra el 46% del grupo control) [47].

La validez de los xenoinjertos fue objeto de estudio también en 2019 en la investigación de Carvalho Formiga M. et al.[48], en la cual se observó el proceso de curación de los alveolos de 29 dientes extraídos (en 25 pacientes, en buen estado de salud y no fumadores). En el grupo de casos se utilizaron xenoinjertos y en el grupo control se dejaron los alveolos sanar normalmente; en ambos casos, los alveolos se cubrieron con membranas de politetrafluoroetileno. A los 4 meses se realizaron CBCT. El grupo de casos sufrió una reducción de 0,11 mm a nivel del tercio cervical, de 0,50 mm a nivel del tercio medio y de 0,14 mm a nivel del tercio apical. La pared vestibular, en cambio, aumentó de 0,91 mm y la

altura del alveolo de 0,35 mm. En el grupo control se verifico una reducción de 0,41 mm en la altura del alveolo, de 0,89 mm en el tercio cervical, y de 0,64 mm en el tercio medio, mientras que hubo un aumento de 0,46 mm el pared vestibular y de 0,09 mm en el tercio apical[48].

En resultado de este estudio, según el cual los injerto heterólogos serían más efectivos que el proceso curación espontanea del alveolo, contrasta con la posterior investigación de Arturas Stumbras et al.[47], en la cual los alveolos rellenados con xenoinjertos sufrieron una reabsorción aun mayor (incluso más del doble) que la del grupo control. En este caso, en cambio, los xenoinjertos permitieron una menor reabsorción de tejidos duros, en particular en los tercios medios y cervicales de los alveolos y en su altura[48].

Otros artículos de investigación y comparación se ocuparon de analizar las diferencias entre el uso de xenoinjertos y la curación espontanea del alveolo: los estudios de Nevins M. et al.[49] en 2006 o el de Araujo y Lindhe[50] en 2009, como en el caso anterior, dividieron su muestra de participantes en un grupo de casos (xenoinjertos) y un grupo control (coagulo de sangre en el alveolo) y, al cabo de unos meses, valoraron los cambios ocurridos con un CBCT, llegando a conclusiones parecidas a las de Formiga M. et al. [48], avalando así la eficacia de los xenoinjertos.

En una investigación realizada por Iasella et al.[51] y con los mismos parámetros, se evidenció que el grupo de alveolos sin materiales de injerto, solo con coagulo sanguíneo, presentaba al cabo de unos meses una cantidad de nuevo hueso mayor que los alveolos tratados con aloinjertos, si bien este último grupo registró mejores resultados en cuanto al volumen final de la cresta alveolar; este se explica por la presencia de materiales de injertos, que tardan meses en reabsorberse, mientras que en los alveolos dejados vacíos habrá solamente formación de nuevo hueso[51].

Los biomateriales hasta aquí analizados han dado una indiscutible contribución en las cirugías de preservación alveolar y en las de regeneración ósea en general, si bien no estén exentos de defectos. El hueso autólogo, considerado por su propiedades biológicas y químicas el "*Gold standard*", presenta, según evidenciaron diferentes autores[23,24,25] más de un inconveniente: entre ellos, se recuerda la morbilidad en el sitio donante y la limitada disponibilidad de material obtenible, además de la calidad variable según el lugar de obtención. Los injertos además, han demostrado estar sujetos a altas tasas de reabsorción, de hasta el 50% según el sitio donante[26,27,28]. Además, la necesidad de una cirugía previa de obtención del injerto alarga mucho los tiempos quirúrgicos.

Los otros tipos de material de injerto también presentan inconvenientes: los aloinjertos, por ejemplo, podrían tener un comportamiento infeccioso y antigénico, llevando a una posible incompatibilidad inmunológica si no tratados adecuadamente[10], mientras que los xenoinjertos han demostrado, según algunos estudios, escasa predictibilidad a nivel clínico[15,16].

Por todas estas razones, la atención de muchos autores se ha movido hacia una nueva clase de injertos libres de estos inconvenientes: la dentina autóloga.

En 2016, Tabatabaei, F. S. et al.[30] realizan una revisión sistemática sobre los distintos métodos de preparación dentinaria y su eficacia en la preservación alveolar. En el estudio se destacan las principales técnicas propuestas en la literatura hasta hoy. Se establecen 4 procedimientos principales: **preparación dentinaria por desmineralización de la matriz**, **preparación dentinaria por extracción de las proteínas no colágenas** (*non collagenous proteins*, de aquí en adelante NCPs), **preparación dentinaria por eliminación de la matriz orgánica** y por último el uso de la **dentina sin cambio significativos**.

La primera, y más difusa, es la preparación de la dentina por desmineralización de su matriz. Esta técnica fue elaborada por primera vez por Reddi et al.[52] ya en 1970, y es de las más antiguas propuestas. Todavía se emplea hoy en día con algunas mejoras. Posteriormente muchos autores contribuyeron en la elaboración de un procedimiento viable y eficaz para obtener este material[30].

Conseguir desmineralizar la matriz de la dentina es un proceso complejo que requiere múltiples fases. Con el paso de los años se han propuesto numerosas variantes, diferenciándose cada una en las técnicas y materiales empleados. La DDM se puede presentar en forma sólida y en polvo. La forma en polvo contiene normalmente de un 5 a un 10% de contenido mineral mientras que la sólida lleva de un 10 a un 30%[53].

Además, la DDM presentan en su superficie unos microporos del diámetro de 1,0 y 3,0 μm. Estos pequeños huecos es lo que queda de los túbulos dentinarios[54] y a pesar de ser demasiado pequeños para permitir la colonización y proliferación de células en su interior, resultan útiles al proceso de regeneración ósea ya que permiten el paso de células fundamentales para la nutrición y proliferación de los odontoblastos. Mas allá de esto, otorgan una mayor aspereza a la superficie, lo cual aumenta la capacidad de absorción de la dentina.

El tipo de preparación propuesta por Reddi et al.[52] en 1970 es uno de los métodos más antiguos elaborados para desmineralizar la dentina, y se sigue empleando con algunas modificaciones. Esta técnica requiere del rápido procesamiento de los dientes después de su extracción. Así se ilustró la preparación en el artículo publicado por Reddi: en primer lugar, se remueve la pulpa por medio de un hilo metálico, y se sumerge el diente en una solución de HCl 0,5 N (1 cc/mg) a temperatura ambiente 1 hora. Posteriormente, el diente se retira del líquido, se lava en agua destilada, se fragmenta en minúsculas partículas que se colocan en un

baño de HCl 0,5 N dos horas. Posteriormente, los fragmentos se sumergen 5 horas en una solución de agua saturada con fenol y etanol al 70%. Las muestras así obtenidas se congelan con nitrógeno líquido (N_2) y se reducen a partículas del tamaño de 70-420 μm, por medio de un mortero. El polvo obtenido se hidrata con etanol y éter. El tiempo total de procesamiento no llega a las 8 horas. Una vez realizados todos los pasos, el polvo de DDM se seca a 37°C. El material, ahora listo para su uso clínico, fue implantado en defectos subcutáneos del abdomen o del muslo de distintos animales (ratones y conejillas de india). Pasadas unas semanas, se estudió la evolución y el desarrollo del injerto: su colocación había sido bien tolerada por todos los animales participantes al experimento[52].

En todas las especias hubo formación de cartílago y hueso, demostrando así por primera vez, la capacidad osteoinductora de las partículas de dentina desmineralizada[52].

Si bien este procedimiento se basa en la desmineralización de la dentina mediante HCl, en la comunidad científica y entre los autores se propusieron otras sustancias para conseguir tal resultado.

Por ejemplo, un estudio de 1986 de Inoue et al.[55] examinaron el efecto de dos muestras de dentina tratadas respectivamente con HCl y con HNO_3, para ver cuál de las dos tuviese mayor capacidad osteogénica. Se observó una formación de cartílago sensiblemente mayor en la superficie de la muestra tratada con HCl en comparación a la tratada con HNO_3[55].

En cambio, en dos estudios[56,57] de 2010 y 2014, se demostró una análoga eficacia de ambas sustancias en la desmineralización de la matriz dentinaria.

A confirmación de esta tesis, en 2014 un estudio de Kim et al.[58] comprobó que el HCl a la concentración de 0,6 N permitía eliminar la gran parte de la fase mineral de la matriz, manteniéndose solo un muy bajo porcentaje de minerales. Las fibras colágenas de tipo I y los

NCPs se conservaron en su gran mayoría, proveyendo un andamiaje rico en factores de crecimiento con propiedades de osteoconducción y osteoinducción.

Tampoco hay acuerdo entre los distintos autores sobre el procedimiento a realizar y el tamaño de las partículas, variando estas de unas pocas decenas de μm hasta incluso 1000 μm.

En 2011 Togari et al.[59] proponen utilizar como injerto partículas de dentina de 250-500 μm de diámetro, subrayando su alto potencial osteinductivo. El estudio se realizó sobre aproximadamente 120 ratones divididos en grupo de casos y de control. Los injertos de dentina desmineralizada se obtuvieron según el método indicado por Urist et al. en su estudio[60]: después de ser extraídos, se removió la pulpa y los tejidos blandos circundantes. A continuación, los dientes se congelaron a -80° C un día, después se sumergieron en HCl a la concentración de 0,6 N 7 días. Posteriormente, los dientes se lavaron en agua destilada y se bañaron 24 horas en una combinación de cloroformo y metanol para eliminar los lípidos. El último paso consistió en la liofilización de los dientes procesados. La dentina desmineralizada se pulverizó en partículas de diámetro incluido entre 250 y 500 μm. Los ratones fueron entonces sometidos a cirugías para crear defectos óseos de unos 3-4 mm a nivel del hueso parietal, en los que se aplicaron 10 mg de DDM. En el grupo control este se dejó vacío. Los controles se llevaron a cabo a las 1, 2, 4, 6 y 8 semanas mediante biopsias y análisis histomorfométricos. El resultado del estudio reveló una formación de tejido osteoide ya a partir de la segunda semana de la colocación del injerto, y a la cuarta se empezó a formar tejido óseo. A la semana 8, el defecto entero resultaba cubierto y rellenado por tejido óseo. En la misma semana se constató además el grupo de injertos presentaba volumen promedio de 2,5 veces mayor respecto al grupo control. En cuanto a la superficie ósea (calcificada) del injerto, se observó que ésta resultaba ser considerablemente más extendida en el grupo de

injertos que en el de controles, confirmando así la capacidad osteoinductora de estas partículas[59].

El mismo estudio destaca que, según datos de su laboratorio, los BMPs demostraron conservar su bioactividad por más de 10 años, incluso si conservados a temperatura ambiente. La conservación y el almacenamiento a temperaturas bajo cero podría mantener sud propiedades biológicas por un tiempo virtualmente ilimitado[59].

Este hecho, si confirmado, podría abrir nuevos horizontes en el campo de la regeneración ósea: dientes extraídos a lo largo de la vida por distintas razones podrían ser almacenados en condiciones oportunas por décadas hasta que el paciente los vaya a necesitar en algún tipo de cirugía.

El mismo dato es confirmado en una investigación de 2018 de Minetti et al.[39], un estudio en vivo sobre un paciente al que se realizó preservación alveolar utilizando dientes temporales conservados en condiciones normales por más de 15 años, con éxito.

Hace unos pocos años, en 2016, Koga et al.[61] analizaron el comportamiento de partículas de distintos tamaños (200, 500 y 1000 μm). Cada uno de estos 3 grupos fue dividido a su vez en otros 3 grupos, según su grado de mineralización: dentina totalmente desmineralizada (*undemineralized dentin*, de aquí en adelante UDD), dentina parcialmente desmineralizada (*partially demineralized dentin matrix*, de aquí en adelante PDDM) y dentina completamente desmineralizada (*completely demineralized dentin matrix*, de aquí en adelante CDDM). A las semanas 4 y 8 se observó el grado de regeneración ósea con el auxilio de micro-CT, análisis histológicos, e incluso se realizaron cultivos de los osteoblastos de las muestras de UDD y DDM para analizar el grado de adhesión de las colonias celulares al tejido[61].

Los resultados indicaron que la muestra de CDDM se había en su gran mayoría reabsorbido. Las muestras de UDD y CDDM produjeron ambos escasa formación de hueso, mientras que la de PDDM ocasionó mayor crecimiento de hueso, en particular en el subgrupo de partículas de 1000 μm de diámetro. El análisis al microscopio electrónico, además, mostró la presencia de osteoblastos adheridos a la muestra de DDM, pero no a la de UDD[61].

Otra técnica propuesta por los autores consiste en preparar la dentina mediante la extracción de los NCPs de su matriz. Se trata, junto con la preparación por desmineralización de la matriz, de unos de los protocolos más antiguos elaborados; se basa en la extracción de las NCPs de la matriz dentinaria, y su posterior uso en el defecto óseo a preservar. Elaborados por Smith et al.[62] ya a final de los '70, hoy en día esta técnica se sigue utilizando, con algunas modificaciones.

Distintas sustancias han sido utilizadas para extraer los NCPs: entre ellas, la principal es el EDTA al 10%. Se utilizaron también otras sustancias, como el cloruro de guanidinio ($CH_5N_3 \cdot HCl$), el hidróxido de calcio (HCl) y el MTA, en distintas combinaciones. El EDTA se ha demostrado, según el estudio de Tomson P.L. et al., la sustancia con los mejores resultados clínicos[63].

Respecto a la tercera técnica propuesta, o sea la preparación de dentina mediante eliminación de su matriz orgánica, hay escasos estudios[64,65]: de hecho, las proteínas de la matriz orgánica resultan tener un papel muy importante en los procesos de adhesión, proliferación, migración y diferenciación de las células. La denaturación de esta mediante eliminación de la matriz orgánica no parece ser un proceso beneficioso a la hora de generar nuevo hueso.

Sin embargo dos investigaciones realizadas en 2008 por Moharamzadeh et al.[64] y en 2013 por Elkayar et al.[65] se han ocupado de estudiar esta técnica, llegando a resultados positivos; en el

primer estudio[64] se llegó a eliminar la matriz hirviendo la dentina en agua durante 2 horas, luego 2 horas en isopropanol y secándola al final a 100°C.

En la segunda investigación[65] la dentina se hirvió en agua 90 minutos, luego se sometió a un proceso de calcinación en ambiente húmedo a 735 °C y por último a uno de sinterización a 1150 °C, obteniendo al final partículas de 45 μm.

En ambos casos, la dentina así tratada resultó presentar buena biocompatibilidad y se demostró capaz de generar nuevo hueso[64,65]. Sin embargo, el no presentar un método *in vitro* para evaluar las propiedades de la dentina limita la validez científica de estos dos estudios.

Por otro lado, algunos autores intentaron utilizar las partículas de dentina como material de injerto sin aplicarles cambios significativos[66,67,68].

En los estudios dirigidos a investigar la solidez de las técnicas de preparación dentinaria, la muestra analizada se suele dividir en un grupo control, al que se le aplica dentina sin tratar, y en un grupo de casos a los que se administra dentina tratada según el protocolo a investigar. Los resultados, en general, muestran como los distintos procesos de modificación de la dentina (entre los cuales el principal es la desmineralización) mejoran significativamente las propiedades de esta a la hora de preservar defectos del hueso como un alveolo post-extracción[66,67]. Cabe todavía destacar que, hasta en el ámbito de la dentina sin tratar, los distintos procesos dirigidos a esterilizarla y/o almacenarla tienen repercusión en cuanto a su éxito clínico: parece ser, en efecto, que el almacenaje en nitrógeno líquido no modifica negativamente el comportamiento de esta, mientras que la esterilización en autoclave empeora significativamente su rendimiento[68].

Un tema a parte es el representado por los dientes deciduos: una serie de investigaciones[39,40,41], a partir de 2015, se ocupó de evaluar por primera vez las propiedades

clínicas de las partículas de esmalte y dentina obtenidas a partir de dientes deciduos. Si su viabilidad como material de injerto fuese confirmada, se aumentarían exponencialmente las posibilidades en cuanto a preservación ósea con dentina. Los resultados de estos estudios fueron prometedores: en el estudio en vivo de 2015, Park et al.[40] llegaron a la conclusión que la estructura y las propiedades microbiológicas de los dientes deciduos, si correctamente desmineralizados, los hacen aptos al uso como materiales de injerto.

En 2018, Bono et al.[41] también afirmaron que los dientes deciduos presentan capacidades osteogénicas, y representan un buen material de injerto en las intervenciones de preservación alveolar y regeneración ósea, demostrando sustancial acuerdo con la anterior investigación de Park.

El mismo año, Minetti et al.[39] realizaron un estudio en vivo utilizando partículas de dentina y esmalte desmineralizadas provenientes de dientes deciduos como material de injerto. El sujeto fue una paciente de 26 años que precisaba de las extracciones de 31 y 41. El plan de tratamiento incluya extraer ambos dientes, realizar preservación alveolar y, al final, rehabilitar de la zona con dos implantes. Para preservar el alveolo fue imposible utilizar los dientes extraídos: al ser incisivos inferiores, además endodonciados, la cantidad de dentina utilizable era ampliamente insuficiente. Por tanto se decidió utilizar unos dientes deciduos de la paciente, que ella había guardado en una caja de plástico durante los últimos 15 años. Después de realizar las extracciones, se seleccionaron unos dientes deciduos (sin caries), que fueron lavados, fragmentados, molidos y por fin desmineralizados con un especifico aparato. Se obtuvieron 1,5 gr de materiales en partículas de 0,4-0,8 mm de diámetro, tanto de esmalte como de dentina, y se colocó luego el material en el alveolo. Cinco meses después, al colocar los implantes y se realizó una biopsia para evaluar el grado de conversión del injerto en hueso neoformado. Los análisis histológicos realizados mostraron un 47,22% de hueso residual, un

28,55% de hueso vital y tan solo un 18,68% de volumen de injerto: resulta así que la gran mayoría del volumen de injerto se ha convertido en hueso, demostrando una sustancial integración del material con el hueso alveolar[39] y corroborando la tesis de los anteriores estudios de Bono et al.[41] y Park et al.[40]

6. CONCLUSIONES.

1. La reabsorción del hueso tras una exodoncia al cabo de una año se sitúa en torno al 50%, afectando en particular a la pared vestibular del alveolo, siendo considerablemente más intensa que en la pared lingual/palatina.

2. Los estudios analizados convienen en indicar en el hueso autógeno el mejor material de preservación alveolar, debido a que presenta las tres propiedades de osteogénesis, osteoconducción e osteoinducción, y a pesar de sus problemas de morbilidad en el sitio donante y de limitada disponibilidad. Los otros tipos de injerto estudiados, menos eficaces, también presentan inconvenientes: posible infecciosidad y antigenicidad (aloinjertos), escasa predictibilidad clínica (xenoinjertos).

3. De las distintas técnicas analizadas, la desmineralización de la matriz dentinaria ha resultado ser la más prometedora en la preservación alveolar. Las otras técnicas se descartan por presentar menor eficacia clínica o bien por la escasez de estudios sobre el tema.

7. RESPONSABILIDAD.

Al derivar de dientes extraídos, la dentina representa una alternativa rentable, natural, biocompatible, además de ser clínicamente superior a los injertos actuales. En lugar de considerarlos como desechos biomédicos, se podrían almacenar los dientes extraídos para utilizarlos cuando oportuno; incluso se podría imaginar la creación de “Bancos” de dientes (y en algunos países ya existen) donde recolectar y almacenar dientes, procesarlos y luego emplearlos.

Este permitiría disminuir los gastos económicos relativos a la adquisición de otros tipos de biomateriales, en particular los de origen sintético (aloplásticos) y los de origen animal (heterólogos), ya que el coste del empleo de la dentina autóloga es prácticamente nulo, con una evidente ventaja tanto para el profesional como para el paciente.

Además, tendría un impacto ecológico positivo al eliminar la necesidad de producir injertos de naturaleza sintética, por lo tanto contaminantes, como los aloplásticos.

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9. ANEXOS.

A CEPHALOMETRIC STUDY OF THE CLINICAL REST POSITION OF THE MANDIBLE

PART II. THE VARIABILITY IN THE RATE OF BONE LOSS FOLLOWING THE REMOVAL OF OCCLUSAL CONTACTS

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CLINICALLY, THE PROBLEM OF rest position of the mandible in the edentulous patient resolves itself to two basic questions: (1) Is the rest position always the same? (2) If there can be a decrease in resting vertical dimension following the removal of occlusal contacts, can we restore this lost vertical dimension when we construct dentures? The fact that there was an average closure of 3 mm. in 22 out of 42 patients (as seen in Part I[1]) does *not* answer the question as to whether we can restore this lost vertical dimension with impunity. It is often stated that if the present resting vertical dimension is exceeded by dentures, rapid resorption of the residual bone always occurs due to the constancy of muscle length and the dominance of muscle over bone. Let us first review neuromuscular physiology from the viewpoint of the clinician.

A CLINICAL APPROACH TO MUSCLE PHYSIOLOGY

The very nature of human striated muscle implies constantly changing activity under both voluntary and reflex control within certain physiologic limits. If the clinician consults the standard texts of physiology, he is likely to be confused by the detailed analysis of the muscle fiber and the simple reflex arc with the result that he may fail to get an over-all broad concept of the dynamic character of the complex neuromuscular system. The clinician can receive much help from texts of "physical medicine" and "muscle exercise" which discuss muscles in a more clinical fashion. In particular, Kraus[2] presents a clear, logical, *clinical* approach to the "pathophysiology" of muscles.

As pointed out in Part I, general body posture is under the influence of many factors, both physiologic and pathologic. It is apparent that, as body posture changes, either the length or the tone of the muscles involved, or both, must change and that, as one group of muscles shortens, the antagonists lengthen. Moreover, it is evident that a state of balance between the antagonists can occur at an infinite variety of muscle lengths and tones within certain physiologic limits.

Perhaps a more dramatic example of change in muscle length occurs during and after pregnancy. As the products of conception grow, the abdominal muscles

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Dimensional ridge alterations following tooth extraction. An experimental study in the dog

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Abstract

Objective: To study dimensional alterations of the alveolar ridge that occurred following tooth extraction as well as processes of bone modelling and remodelling associated with such change.

Material and Methods: Twelve mongrel dogs were included in the study. In both quadrants of the mandible incisions were made in the crevice region of the 3rd and 4th premolars. Minute buccal and lingual full thickness flaps were elevated. The four premolars were hemi-sected. The distal roots were removed. The extraction sites were covered with the mobilized gingival tissue. The extractions of the roots and the sacrifice of the dogs were staggered in such a manner that all dogs contributed with sockets representing 1, 2, 4 and 8 weeks of healing. The animals were sacrificed and tissue blocks containing the extraction socket were dissected, decalcified in EDTA, embedded in paraffin and cut in the buccal–lingual plane. The sections were stained in haematoxyline–eosine and examined in the microscope.

Results: It was demonstrated that marked dimensional alterations occurred during the first 8 weeks following the extraction of mandibular premolars. Thus, in this interval there was a marked osteoclastic activity resulting in resorption of the crestal region of both the buccal and the lingual bone wall. The reduction of the height of the walls was more pronounced at the buccal than at the lingual aspect of the extraction socket. The height reduction was accompanied by a ''horizontal'' bone loss that was caused by osteoclasts present in lacunae on the surface of both the buccal and the lingual bone wall.

Conclusions: The resorption of the buccal/lingual walls of the extraction site occurred in two overlapping phases. During phase 1, the bundle bone was resorbed and replaced with woven bone. Since the crest of the buccal bone wall was comprised solely of bundle this modelling resulted in substantial vertical reduction of the buccal crest. Phase 2 included resorption that occurred from the outer surfaces of both bone walls. The reason for this additional bone loss is presently not understood.

Key words: bundle bone; modelling; remodelling; wound healing

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The alveolar process is a tooth dependent tissue that develops in conjunction with the eruption of the teeth. Further, the volume as well as the shape of the alveolar process is determined by the form of the teeth, their axis of eruption and eventual inclination (Schroeder 1986). Subsequent to the removal of all teeth in the adult individual, the alveolar processes will undergo atrophy (e.g. Atwood 1957, Hedegård 1962, Tallgren 1972). The amount of hard tissue reduction varied considerably between subjects as reported by e.g. Atwood (1962), Carlsson & Persson (1967) and Tallgren (1972).

Clinical and/or radiographic studies by e.g. Johnson (1963, 1969), Pietrokovski & Massler (1967), Lekovic et al. (1997, 1998), Camargo et al. (2000), Schropp et al. (2003) have demonstrated that marked alterations of the height and width of the alveolar ridge will occur following single or multiple tooth extractions. The healing process following tooth removal apparently resulted in more pronounced resorption on the buccal than on the lingual/palatal aspects of the ridge. Pietrokovski & Massler (1967) studied the amount of

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Dynamics of bone tissue formation in tooth extraction sites

An experimental study in dogs

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Abstract

Objectives: The aim of the present experiment was to study events involved in the healing of marginal, central and apical compartments of an extraction socket, from the formation of a blood clot, to bone tissue formation and remodeling of the newly formed hard tissue.

Material and Methods: Nine mongrel dogs were used for the experiment. The fourth mandibular premolars were selected for study and were divided into one mesial and one distal portion. The distal root was removed and the socket with surrounding soft and mineralized tissue was denoted ''experimental unit''. The dogs were killed 1, 3, 7, 14, 30, 60, 90, 120 and 180 days after the root extractions. Biopsies including the experimental units were demineralized in EDTA, dehydrated in ethanol and embedded in paraffin. Serial sections 7 μm thick were cut in a mesio-distal plane. From each biopsy, three sections representing the central part of the socket were selected for histological examination. Morphometric measurements were performed to determine the volume occupied by different types of tissues in the marginal, central and apical compartments of the extraction socket at different intervals.

Results: During the first 3 days of healing, a blood clot was found to occupy most of the extraction site. After seven days this clot was in part replaced with a provisional matrix (PCT). On day 14, the tissue of the socket was comprised of PM and woven bone. On day 30, mineralized bone occupied 88% of the socket volume. This tissue had decreased to 15% on day 180. The portion occupied by bone marrow(BM) in the day 60 specimens was about 75%, but had increased to 85% on day 180.

Conclusion: The healing of an extraction socket involved a series of events including the formation of a coagulum that was replaced by (i) a provisional connective tissue matrix, (ii) woven bone, and (iii) lamellar bone and BM. During the healing process a hard tissue bridge – cortical bone – formed, which ''closed'' the socket.

Key words: bone healing; extraction sockets; tooth extraction; socket healing; bone formation

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The healing of an extraction socket following tooth removal was studied in different animal models (e.g. Schram 1929, Claflin 1936, Simpson 1960, Kuboki et al. 1988, Lin et al. 1994). The experiments demonstrated that during the process of healing a series of events occurred, such as (i) formation and maturation of a blood clot, (ii) infiltration of fibroblast to replace the coagulum, and eventually (iii) establishment of a provisional matrix (PCT) that allowed for bone tissue formation. Unfortunately, most of the studies referred to were of comparatively short duration and, thus, included limited information related to later phases of socket healing including the process of remodeling of the newly formed bone tissue in various parts of the alveolus.

The formation of soft and hard tissue following tooth extraction was also studied in specimens obtained from humans (e.g. Mangos 1941, Christopher 1942, Amler 1969). The frequently cited study by Amler (1969) – ''The time sequence of tissue regeneration in human extraction wounds'' – reported on new tissue formation in fresh extraction sockets in human volunteers. In this study, following the removal of a tooth, socket healing was monitored and soft tissue biopsies were harvested from the extraction sites after varying intervals; from 48 h to 32 days. Since the tissue sampled was not demineralized prior to sectioning, only events that preceded hard tissue formation could have been analyzed. From his observations, Amler (1969) concluded that a blood clot formed within the socket soon after the removal of a tooth. This clot was replaced first by a granulation tissue (GT) and subsequently by an osteoid. The illustrations, published by Amler (1969), however, described only tissues from the marginal portions of the socket. It must be anticipated, therefore,

PRESERVING THE SOCKET DIMENSIONS WITH BONE GRAFTING IN SINGLE SITES: AN ESTHETIC SURGICAL APPROACH WHEN PLANNING DELAYED IMPLANT PLACEMENT

Tassos Irinakis, DDS, MSc; Moe Tabesh, DDS

Recent advancements in barrier membranes, bone grafting substitutes, and surgical techniques have led to a predictable arsenal of treatment methods for clinicians who practice implant dentistry. The contemporary clinician is supplied with proven knowledge, substantiated materials, and instrument inventory that allows implant placement in cases that used to be reserved for the specialist in the past because of their complexity. Nowadays, postextraction alveolar ridge maintenance can be a predictable procedure and can certainly aid the clinician in preventing ridge collapse, thereby allowing for implant placement in a position that satisfies esthetics and function. Extraction socket maintenance for future implant therapy does not rule out immediate implant placement but rather provides an additional option when treatment planning implant patients. This article will focus on the concept of extraction socket preservation using regenerative materials. It will describe a technique suggested by the authors to resist bone resorption and soft tissue shrinkage following tooth extraction.

Key Words: socket, extraction, socket preservation, ridge preservation, bone grafting, Implants

INTRODUCTION

Different etiologies may be associated with tooth loss. Such examples are endodontic pathology (root fractures, root perforations); periodontal pathology (combined endodontic-periodontic lesions, periodontal disease); advanced caries lesions; and facial injuries. Alveolar bone loss can also occur as a result of iatrogenic trauma from aggressive maneuvering while extracting teeth or as a result of natural postextraction socket healing. Whatever the reason for tooth extraction, postextraction socket healing commonly results in deformities of the alveolar ridge.[1] In most cases, the extractions are performed without a thought as to what may happen to the underlying ridge. Therefore, the practitioner may just wait to see where the healing patterns lead prior to deciding on the choice of restoration, underestimating the likelihood that the residual ridge might heal in an unesthetic fashion. The severity of this problem becomes even more apparent if one considers that, in the United States alone, more than 20 million teeth are extracted on an annual basis by dental practitioners.[2]

Because the healing patterns of human sockets are unpredictable (with likely detrimental effects to the

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Improved Technique for Localized Ridge Augmentation*

A Report of 21 Cases

Edward P. Allen,† Craig S. Gainza, Gregory G. Farthing and Dewey A. Newbold

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TOPOGRAPHICAL ABERRATIONS IN A RESIDUAL EDENTULOUS ridge often prevent establishment of a satisfactory pontic/ridge relationship. An improved technique is described for predictable augmentation of localized alveolar-ridge deficiencies. Results are reported from 21 cases involving 26 sites. All 14 sites using fibrous connective tissue grafts demonstrated shrinkage, although an improvement in residual ridge contour was obtained. Hydroxylapatite implant material was placed in 12 sites with shrinkage seen in only two sites. Advantages, requirements for success and technical considerations of the improved technique are discussed.

Proper pontic-residual ridge relationship is a critical factor in fixed prosthodontics. A properly constructed pontic must satisfy demanding requirements of function, esthetics and cleansability. Topographical aberrations in the residual edentulous ridge often prevent the establishment of an ideal pontic-to-ridge relationship, and in such cases residual ridge surgery may be indicated.[1] A ridge that is excessive in its dimensions may be reduced by appropriate hard and soft tissue resective procedures. A much more difficult situation exists when the remaining alveolar ridge is markedly deficient. Until recent years, little could be done surgically to alter the deficient ridge, and restorative dentists were forced to compromise pontic design in ways that in many cases were only marginally acceptable from a functional and/or esthetic standpoint. The resulting restoration was often a disappointment to both the patient and therapist despite the most conscientious efforts.

Causes of alveolar ridge deformities include developmental defects, advanced periodontal disease, traumatic injury and surgical trauma. The eccentrically placed maxillary incisors with their extremely thin facial and thick palatal plates are common sites for ridge deficiencies. The thin facial plate predisposes to fracture upon extraction or trauma. Subsequent healing often results in ridge deficiency, scar formation and compromised prosthetics.

In a modification of Seibert's original classification,[2] different types of ridge deformities may be described as follows:

Type A—Apico-coronal loss of ridge contour.

Type B—Buccolingual loss of ridge contour.

Type C—Combined loss of ridge contour in both apico-coronal and buccolingual dimensions.

The ridge deformity may be further described by assessing the depth of the defect relative to the adjacent ridge:

Mild—less than 3 mm.

Moderate—3 to 6 mm.

Severe—greater than 6 mm.

Recently, there have been reports describing surgical procedures for reconstruction of deformed, partially edentulous ridges. Abrams[3] described a de-epithelialized connective tissue pedicle or roll technique. The roll technique is most useful in restoring defects in the apico-coronal dimension but requires sufficient soft tissue thickness directly over and palatal to the residual ridge crest. A technique using fibrous connective tissue grafts was originally reported by Langer and Calagna[4,5] and later by Garber and Rosenberg,[6] and has been used successfully to restore moderate defects in the buccolingual dimension. Seibert[2,7,8] described a full thickness onlay grafting technique for augmenting moderate to severe ridge defects. In one case, he described the implementation of hydroxylapatite (Durapatite®) when onlay grafting failed to correct satisfactorily a severe defect. Cohen[9] recently described augmentation of a single site using hydroxylapatite (Calcitite®). However, placement of the initial incision directly over the defect site resulted in an open wound exposing the implant particles, consequently delaying healing and jeopardizing the final result.

Durapatite is a nonresorbable polycrystalline form of hydroxylapatite that is well tolerated by hard and soft tissues and produces neither an immune nor inflam-

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UNIVERSIDAD COMPLUTENSE DE MADRID

FACULTAD DE ODONTOLOGÍA

Departamento de Medicina y Cirugía Bucofacial

UTILIZACIÓN DE MATERIAL DENTARIO AUTÓLOGO COMO INJERTO EN EL ALVEOLO POST-EXTRACCIÓN

TRABAJO FIN DE MASTER

MASTER EN CIENCIAS ODONTOLÓGICAS

Alejandra del Canto Díaz

Bajo la dirección del Prof. Dr.

José Mª Martínez González

Effect(s) of the Demineralization Process on the Osteoinductivity of Demineralized Bone Matrix

Min Zhang, Ralph M. Powers, Jr.,† and Lloyd Wolfinbarger, Jr.*†*

THE RELATIONSHIPS BETWEEN RESIDUAL calcium levels and particle size of ground demineralized bone matrix and its osteoinductive potential were investigated using in vitro and in vivo assays. The effects of variable residual calcium levels, variable particle sizes, and donor age and gender were studied using a tissue culture-based bioassay (in vitro) as well as an athymic mouse (in vivo) bioassay. The osteoinductive potential of the bone-derived biomaterial was assessed by measuring the degree of new bone formation (change in percent calcium content after 4 weeks of implantation) in the in vivo assay and levels of alkaline phosphatase activity associated with cultures of human periosteal cells (HPO cells) in the in vitro assay, respectively. Slightly demineralized bone matrix and overly demineralized bone matrix possessed a degree of osteoinductive potential whereas bone demineralized to levels of approximately 2% residual calcium provided for maximum osteoinductive potential in both assay systems. The osteoinductive potential of ground demineralized bone varied relative to the particle size such that DBM particles ranging from 500 to 710 microns provided for the highest level of calcium deposition (increase of 8.1 weight percent calcium) after 4 weeks of implantation in muscle pouches of an athymic mouse, whereas explanted particles less than 250 microns showed the lowest level of calcium deposition (increase of only 2.8 weight percent calcium). In the donor age and gender study, DBM from different donors were divided into 5 age groups for both female and male donor derived bone: less than 20, 21 to 30, 31 to 40, 41 to 50, and 51 to 60 year old age groups. This study indicated that DBM from female donors in the 31 to 40 years old age group and male donors in the 41 to 50 year age group possess the highest osteoinductive potential, whereas DBM derived from donor bone from both female and male donors in the 51 to 60 year age group presented the lowest osteoinductive potential. DBM derived from male and female donors did not in general show significant differences in osteoinductive potential. *J Periodontol 1997;68:1085–1092.*

Key Words: Biological assay; bone regeneration; bone matrix; alkaline phosphatase; osteogenesis; periodontal diseases/physiopathology.

As early as 1889, Senn[1] reported using demineralized bovine bone as a vehicle for delivery of antiseptics (iodoform) in patients with osteomyelitis. In the twentieth century Leriche and Policard,[2] LaCroix,[3] Levander,[4] Urist,[5] and Huggins et al.,[6] as pioneers, studied induced bone formation. The first unequivocal demonstration of matrix induced bone formation was by Urist[5] in 1965 in a report describing specific preparations of allogeneic bone matrix implanted in muscle.

Due to its remarkable regenerative ability, bone is one of the most frequently transplanted tissues in humans and is routinely used for the repair of skeletal defects caused by trauma, neoplasia, and infection. Three mechanisms may contribute to the deposition of bone after bone grafting: osteogenesis, osteoinduction, and osteoconduction. Osteogenesis is the formation of new bone from bone-forming cells (osteoblasts) that are transplanted as a viable cellular component in autogenous bone grafts. Osteoinduction is the formation of new bone by recipient mesenchymal cells that differentiate into bone-forming cells under the stimulation of matrix and associated protein factors present in demineralized bone. Osteoconduction is a process in which host bone-forming cells infil-

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Utilization of type I collagen gel, demineralized bone matrix, and bone morphogenetic protein-2 to enhance autologous bone lumbar spinal fusion

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Autologous bone grafts are currently considered "gold standard" material for achieving long-term spinal arthrodesis. The present study was performed to determine whether demineralized bone matrix (DBM), type I collagen gels, or bone morphogenetic protein-2 (BMP-2) can improve autologous bone spinal fusions. Using a unilateral decompression–contralateral fusion technique in dogs, each of these materials was added to an autologous bone graft. Volumetric analysis, histological analysis, and biomechanical testing were performed to assess the effectiveness of each material. The DBM had an inhibitory effect on solid bone fusion of the spine, whereas the type I collagen gels improved the bony interface between the graft and the host spine. The BMP-2 strongly enhanced the amount of bone deposition at the fusion site and increased the number of intervertebral levels that were solidly fused. This study strongly supports the use of BMP-2 as an additive to autologous bone grafts in spine stabilization.

Key Words • spinal fusion • bone morphogenetic protein • collagen • demineralized bone matrix

Spinal fusion continues to play a significant role in both neurological and orthopedic surgery in the treatment of numerous pathological conditions of the spine including trauma, tumors, congenital anomalies, and degenerative disease. Although internal fixation that is supplemented with instrumentation, such as Harrington rods, Luque rings, and Steffi plates, is useful in facilitating short-term spinal stability, bone fusion is always required for long-term stability. The ideal spinal fusion technique creates a strong, healthy bone mass between the vertebrae with a high rate of fusion, needs little technical expertise, and has a low complication rate. It has been well established in both clinical and laboratory studies that autologous bone is the "gold standard" grafting material for achieving arthrodesis in the spine. Obtaining an autologous bone graft from the iliac crest is now a standard procedure, but it is also associated with risks of infection, bleeding, and increased postoperative pain.[29,42] To avoid donor-site morbidity, allografts, xenografts, and synthetic grafts have been studied experimentally, but there is a risk of transmission of infectious agents and none of these graft materials is superior to autologous bone alone.[37]

During the last 10 years, the cellular mechanisms that regulate bone formation have been extensively studied.[19,21,38,39] Osteoinductive growth factors such as the bone morphogenetic proteins (BMPs) have been shown to induce bone formation through endochondral mechanisms, leading to their potential use in fusions of the spine and fractured long bones.[11,39] Manipulation of the support proteins in the extracellular space around a fusion site may also improve bone fusion. For example, isotonic, neutral pH gels of purified type I collagen have been shown to provide a matrix onto which osteoblasts freely migrate, leading to enhanced healing of critical size defects in the rat skull.[30] The aim of the present study was to determine whether isotonic, neutral pH type I collagen gel, demineralized bone matrix (DBM) (an excellent source of bone growth factors), and recombinant human (rh)BMP-2 can be used to improve the rate and strength of autologous bone fusions in the decompressed canine lumbar spine.

Materials and Methods

Forty adult female beagles were included in this study. We followed the method for lumbar decompression and fusion used by the University of Virginia Health Sciences Center for the treatment of spinal stenosis. This method consists of a unilateral bone decompression of laminae, facets, and pedicles with undercutting of the spinous processes, followed by a contralateral autologous bone fusion. All dogs received a unilateral decompression. In addition, Group I (10 dogs) received the usual contralateral bone fusion; Group II (seven dogs), a contralateral fusion using autologous bone and DBM; Group III (10 dogs), a contralateral fusion using autolo-

A Quantitative Assessment of Osteoinductivity of Human Demineralized Bone Matrix

Min Zhang, Ralph M. Powers, Jr.,† and Lloyd Wolfinbarger, Jr.*†*

DEMINERALIZED BONE MATRIX (DBM) is widely used in the repair of pathologies associated with skeletal defects and periodontal diseases. The present study was directed at establishing in vivo and in vitro models for a quantitative assessment of the osteoinductivity of DBM before clinical use. Athymic mice were used in an in vivo assay to overcome the species limitations (for human DBM) found in xenogeneic animal models. Calcium contents of explants, as an indicator of new bone formation, were assayed and expressed as a change in the weight percent calcium in the explant as compared to the weight percent of calcium in the implanted material. A total of 82 mice (2 implants per mouse) were used in this study. Significant amounts of new bone were induced in this animal model in response to implantation of DBM. Muscular implantation was found to be more osteoinductive (increases of 10.0 ± 0.4 calcium weight percent of explant) than subcutaneous implantation (increases of 1.62 ± 0.27 calcium weight percent of explant) and new bone formation in muscular implantation sites of athymic mice mimics endochondral bone formation. Between weeks 1 to 4, the weight of explanted materials did not significantly differ from the weight of the implanted material; however, by week 5 the explant weight began to increase. Calcium deposition over the 5 weeks of implantation increased in a nearly linear fashion. Consequently week 4 was chosen as the optimum time for explantation in the in vivo assay in that sufficient calcium levels had been achieved without a significant increase in explant dry weight. Aliquots of 10, 20, 30, and 40 mg per implantation site were used in dose response studies in the in vivo bioassay. Dose response curves with DBM exhibited maximal activity at the 20 mg DBM implant dose in the in vivo bioassay. An in vitro bioassay was also developed where human periosteal (HPO) cells were chosen because osteoprogenitor cells found in bone repair typically come from periosteal tissue. Alkaline phosphatase (ALP) activity in confluent cell cultures of HPO cells exposed to DBM, as an indicator of osteoblast induction, reached its highest level on day 5 of DBM treatment. Aliquots of 2, 5, 10, 20, 30, and 40 mg DBM per flask were chosen in dose response studies using the in vitro bioassay. These dose response studies with DBM revealed that quantities approximating 5 to 10 mg DBM in the in vitro model provided for maximal levels of ALP in cell extracts. A linear correlation ($R^2 = 0.7397$) was demonstrated between the in vivo calcium remineralization assay and the in vitro ALP assay of osteoinductivity of DBM, suggesting that the in vitro assay can be used to quantitatively assess the osteoinductive potential of DBM where production and distribution of clinically usable DBM dictates rapid analysis. *J Periodontol 1997;68:1076–1084.*

Key Words: Biological assay; bone mineralization; models; biological; calcium/analysis; bone matrix; periodontal diseases/physiopathology.

The process of bone induction after the implantation of demineralized bone matrix has been studied extensively in animal models.[1–3] Basically two kinds of implantation sites have been used. One approach involved the implantation of demineralized bone in intramuscular sites[2,4] and subcutaneous sites.[5,6] Implanted demineralized bone matrix evokes ectopic bone formation via the endochondral

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Medical Hypotheses

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Does Xenogeneic Demineralized Bone Matrix Have Clinical Utility as a Bone Graft Substitute?

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Abstract — Autologous bone harvested from the iliac crest is a commonly used grafting material for a number of surgical procedures; however, there is documented morbidity associated with secondary site harvesting. Because demineralized bone matrix (DBM) is inherently osteoinductive (i.e., it facilitates differentiation of uncommitted connective tissue cells into bone-forming cells), it has potential appeal as a bone-graft substitute. Allogeneic DBM usage has intrinsic shortcomings related to procuring, processing and characterizing bone from a human donor pool. Xenogeneic bone represents an unlimited supply of available material if it can be processed to render it safe for transplantation to the human host. It is hypothesized that reported immunogenicity and non-viability of xenogeneic DBM results from lipids and plasma proteins not removed during typical demineralization processes. The authors propose a rigorous examination of this hypothesis, followed by several pivotal studies to determine the effectiveness of xenogeneic DBM.

Clinical usage and pitfalls of bone grafts

The use of bone grafts is conventional practice in orthopaedics, neurosurgery and dentistry, as well as in plastic/reconstructive surgery and this utilization has been growing in frequency over the past two decades. With the exception of blood, bone is the most frequently transplanted tissue with an estimated 500 000 bone grafts used in the United States annually. Common orthopedic uses of bone grafts, for example, include the management of non-unions and acute long bone fractures, joint reconstruction and to facilitate fusion of vertebral motion segments in treating a variety of spinal disorders (1). Currently, the most clinically acceptable grafting material is autologous bone (i.e., bone harvested from one's own body). So-called 'autografts' are often obtained from a secondary operative site such as the iliac crest. However, surgical use of autografts is not without pitfalls. First, the available supply of transplantable tissue is often insufficient for large defects, particularly in children. Lack and quality of sufficient iliac crest material may likewise affect elderly individuals where underlying osteopenia makes autograft usage problematic. Second, attendant morbidity associated with secondary operative procedures is high. Complications include infections, pelvic instability, sensory loss, hematoma, and pelvic fracture (2–5). In a literature synthesis of 47 studies of lumbar spinal fusion, chronic pain at the bone graft donor site (9%)

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Ethical Considerations in Allograft Tissue Transplantation

A Surgeon's Perspective

Richard Nicholas, MD

Methods for procurement, processing and distribution of allograft tissues have changed rapidly and many of the advances have resulted in widespread use of allograft tissues for reconstruction. However, unlike other types of orthopaedic implants, these human graft tissues are not simple commodities delivered to the surgeon or operating room in prepackaged sterile containers, but rather are more akin to gifts from a donor to a patient in need. As such, ethical behavior and responsible stewardship on the part of each surgeon and each of those involved throughout the allograft enterprise is required. Surgeons using donated tissues should be aware of the advances and changes within the field and the ethical considerations surrounding human tissue transplantation. The following remarks focus on the generosity of donors and their families and the subsequent responsibilities for the medical community, in particular, the surgeons who use these grafts.

Few procedures in the field of orthopaedics are more basic than bone grafting. Almost from the beginning of the specialty, many procedures have been developed that use autologous bone. Although previously limited in use, donated human bone and soft tissue grafts are increasingly used as surgeons find expanded indications for these allograft tissues. Ranging from large segmental allografts, used in tumor and joint revision reconstructions, to processed powders and specialized tissues, the number of implanted allograft tissues is growing yearly. In spine surgery alone, orthopaedists do thousands of procedures every year that use a wide variety of allografts.

Improved availability of donated human tissues may be one of the main reasons behind the increased use of allografts. Much has changed since the establishment of the first major bone banking program, the United States Navy Tissue Bank in Bethesda, Maryland.[3] Current processing methods no longer resemble those of the previous "bone banks" where excess bone (such as a femoral head removed at the time of hip arthroplasty) was wrapped, frozen, and stored for later use. Instead, a complex industry has developed that requires the collaboration and cooperation of diverse groups and organizations to support today's allografting practices. In some cases, for-profit companies and commercialization now provide surgeons with highly processed tissues required to do state-of-the-art surgical procedures. Such business practices risk commoditization of the graft forms, making a product out of human tissue. The increased availability of allograft tissue, often ready for implantation right out of the package, means that many orthopaedists have become far removed from the processes of retrieving, preparing, and distributing tissues. Although considerable scientific and clinical literature exists related to allograft technology and clinical utility, very little material has been published regarding the social or ethical issues surrounding tissue donation and transplantation. Despite the rapid and at times remarkable advances in this field, we must remember that the availability of any human tissue remains completely dependent on the willingness of individuals to donate. The ethical principles underlying donation and the corresponding responsibilities of those implanting human tissue remain central to the continued success of this clinical practice. I will discuss the concept of responsible stewardship. In this respect, the surgeon serves as the steward of the donation, considered as a gift, as it makes its way from a donor to its recipient. I argue that the surgeon has the ethical responsibility to recognize the nature of the donation, to use these tissues appropriately, and to support and promote tissue donation to patients, peers and medical institutions continually.

Advances in Allograft Procurement and Banking Practices

Tissue procurement and processing practices have become complex, highly regulated, and often integrated services.

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PRESERVACIÓN DE ALVEOLOS POSTEXODONCIA MEDIANTE EL USO DE DIFERENTES MATERIALES DE INJERTO.

REVISIÓN DE LA LITERATURA.

LEONARDO VARGAS

CÓDIGO: 500500

ESPECIALIDAD EN PERIODONCIA

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ALVEOLAR RIDGE SOCKETS PRESERVATION WITH BONE GRAFTING – REVIEW

UTRZYMANIE WYSOKOŚCI GRZBIETU WYROSTKA ZĘBODOŁOWEGO Z WYKORZYSTANIEM MATERIAŁÓW PRZESZCZEPOWYCH KOŚCI – PRZEGLĄD PIŚMIENNICTWA

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Streszczenie

Wstęp: Kość wyrostka zębodołowego odgrywa kluczową rolę w zapewnieniu utrzymania zębów, które są zakotwiczone w kości za pomocą włókien desmodontalnych. Postępująca resorpcja kości zachodzi w wyniku działania czynników anatomicznych, biologicznych i mechanicznych. Mechaniczna stymulacja kości zębodołowej podczas żucia jest decydująca z punktu widzenia utrzymania zębów i jakości otaczającej je tkanki kostnej. Ekstrakcja zęba prowadzi do typowego ubytku wysokości i szerokości kości grzbietu wyrostka zębodołowego zmniejszając możliwość umiejscowienia w nim śruby implantu. Jeśli ekstrakcja zęba jest konieczna, uraz powinien być zminimalizowany przez zastosowanie odpowiedniej procedury. Podczas zabiegu powinno się także zwrócić szczególną uwagę na zachowanie kości. Z danych z piśmiennictwa wynika, że wczesna utrata kości może być istotnie zredukowana poprzez zastosowanie materiałów wszczepowych. Zabezpieczenie kości zębodołowej wymaga zrozumienia procesu gojenia rany poekstrakcyjnej i wiedzy na temat biologicznych właściwości dostępnych materiałów wszczepowych. Materiały augmentacyjne mogą, a nawet muszą zagwarantować optymalne protetyczne zastąpienie utraconych tkanek. Sukces lub niepowodzenie zabiegu augmentacji zależy od rewaskularyzacji i remodelingu przeszczepu kostnego w żywym organizmie. W przeciwieństwie do widocznych i trójwymiarowych zmian, pojęcie remodelingu oznacza wewnętrzną przemianę kości, która jest złożonym procesem, gdzie resorpcja przez osteoklasty i tworzenie tkanki przez osteoblasty jest w większej lub mniejszej równowadze. W celu odtworzenia ubytku kości zębodołowej i utrzymania dogodnych warunków dla implantacji stosowanych jest wiele substytutów kości, takich jak przeszczepy własnej tkanki, wszczepy allogeniczne, ksenogeniczne, biomateriały syntetyczne i czynniki stymulujące kość. Aby zapobiec konieczności pobierania autoprzeszczepu, a przez to wyeliminować dodatkowe zabiegi chirurgiczne i związane z nimi ryzyko powikłań, do augmentacji stosuje się materiały kościozastępcze.

Cel: Zaprezentowanie przeglądu literatury dotyczącej biomateriałów stosowanych poekstrakcyjnie dla utrzymania

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Dimensional changes of the ridge contour after socket preservation and buccal overbuilding: an animal study

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Abstract

Objectives: The aim of the study was to volumetrically assess alterations of the ridge contour after socket preservation and buccal overbuilding.

Material and Methods: In five beagle dogs, four extraction sites were subjected to one of the following treatments:

Tx 1: The socket was filled with BioOss Collagen® and covered with a free gingival autograft from the palate (SP).

Tx 2: The buccal bone plate was forced into a buccal direction using a manual bone spreader and SP was performed.

Tx 3: The buccal bone plate was forced into a buccal direction using a manual bone spreader; SP was performed.

Tx 4: The socket was filled with BioOss Collagen and a combined free gingival/connective tissue graft was used to cover the socket and for buccal tissue augmentation.

Impressions were obtained at baseline, 2 weeks and 4 months post-operatively. Casts were optically scanned and superimposed in one common coordinate system. Using digital image analysis, the volumetric differences per area among the different treatment time points and among the treatment groups were calculated.

Results: Four months after tooth extraction, no statistically significant differences with regard to the buccal volume per area could be assessed among the treatment groups.

Conclusion: Overbuilding the buccal aspect in combination with socket preservation is not a suitable technique to compensate for the alterations after tooth extraction.

Key words: extraction socket; socket preservation; volumetric evaluation

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Introduction

Tooth extraction is followed by marked dimensional alterations of the alveolar ridge contour (Schropp et al. 2005, Fickl et al. 2008c). A previous clinical study reported that approximately 50% of the original alveolar bone width was reduced within the first 12 months after tooth removal (Schropp et al. 2005). Volumetric alterations of the alveolar ridge can be unfavourable for future endosseous implant placement and implant aesthetics. Therefore, socket preservation has been advocated at the time of tooth extraction to compensate for the postoperative volumetric alterations. Various methods have been described for socket preservation after tooth extraction. Besides techniques using occlusive membranes (Lekovic et al. 1997, 1998, Iasella et al. 2003) grafting extraction sockets with bone substitutes (Artzi & Nemcovsky 1998, Becker et al. 1998, Artzi et al. 2000, Carmagnola et al. 2003, Jung et al. 2004, Nevins et al. 2006) has been reported in the literature. It was recently

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Hard tissue alterations after socket preservation with additional buccal overbuilding: a study in the beagle dog

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Abstract

Objectives: The aim of this study was to histometrically assess alterations of the ridge following socket preservation alone and socket preservation with additional buccal overbuilding.

Material and Methods: In five beagle dogs four extraction sites were randomly subjected to one of the following treatments:

Tx 1: The socket was filled with BioOss Collagen® and covered with a free gingival graft from the palate.

Tx 2: The buccal bone plate was augmented using the GBR-technique, the socket was filled with BioOss Collagen® and covered with a free gingival graft.

Tx 3: The buccal bone plate was forced into a buccal direction using a manual bone spreader. The socket was filled with BioOss Collagen® and covered with a free gingival graft from the palate.

Tx 4: The socket was filled with BioOss Collagen® and a combined free gingival/connective tissue graft was used to cover the socket and for buccal tissue augmentation.

For each experimental site, two histological sections were subjected to histometric analysis and evaluated for (i) vertical bone dimensions and (ii) horizontal bone dimensions.

Results: All treatment groups showed horizontal and vertical bone loss. The mean vertical bone loss of the buccal bone plate was significantly lower in Tx 4 than in the other groups, while no statistical significant differences could be detected among the groups in the horizontal dimension.

Conclusion: Overbuilding the buccal aspect in combination with socket preservation does not seem to be a suitable technique to compensate for the alterations after tooth extraction.

Key words: bone substitute; extraction socket; GBR; socket preservation

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Tooth extraction is followed by dimensional changes of the alveolar ridge contour (Amler et al. 1960, Pietrokovski & Massler 1967, Schropp et al. 2003, Araújo & Lindhe 2005, Fickl et al. 2008c). The resorption of the ridge is more pronounced on the buccal than on the lingual aspect of the extraction socket (Pietrokovski & Massler 1967, Araújo & Lindhe 2005).

Socket preservation at time of tooth extraction has been advocated to minimize horizontal ridge resorption and facilitate ideal implant placement and thus an aesthetic site reconstruction. Different approaches have been developed to preserve or improve the ridge contour following tooth extraction, including the use of immediate implants (Paolantonio et al. 2001, Botticelli et al. 2004, Araújo et al. 2005), or occlusive membranes with or without graft materials (Lekovic et al. 1997, 1998, Iasella et al. 2003). However, using these techniques with a reported loss of horizontal ridge dimensions between − 1.17 and − 1.73 mm, the original ridge contours cannot be preserved (Lekovic et al. 1997, 1998, Iasella et al. 2003).

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Review paper

Biodegradation and Bioresorption of Calcium Phosphate Ceramics

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Abstract: The use of several calcium phosphate (Ca-P) materials for bone repair, augmentation, substitution and as coatings on metal implants has gained clinical acceptance in many dental and medical applications. These Ca-P materials may be of synthetic or natural origin, available in different physical forms (dense or macroporous, particles or blocks) and are used in bulk as coatings for metallic and non-metallic substrates or as components in composites, cements and bioactive glasses. Biodegradation or bioresorption of calcium phosphate materials implies cell-mediated degradation *in vitro* or *in vivo*. Cellular activity during biodegradation or bioresorption occurs in acid media, thus the factors affecting the solubility or the extent of dissolution (which in turn depends on the physicochemical properties) of the Ca-P materials are important. Enrichment of the microenvironment due to the release of calcium and phosphate ions from the dissolving Ca-P materials affects the proliferation and activities of the cells. The increase in the concentrations of the calcium and phosphate ions promotes the formation of carbonate apatite which are similar to the bone apatite. The purpose of this invited paper is to discuss the processes of biodegradation or bioresorption of Ca-P materials in terms of the physico-chemical properties of these materials and the phenomena involved including the formation of carbonate apatite on the surfaces and in the vicinity of these materials. This phenomenon appears to be related to the bioactivity of the material and the ability of such materials to directly attach to bone and to form a uniquely strong material–bone interface.

INTRODUCTION

The use of some Ca-P materials for bone substitution, augmentation and repair has gained clinical acceptance in many areas of orthopedics and dentistry. Dental applications include fillers for periodontal bony defects, alveolar ridge augmentation, immediate tooth root replacement, coatings for dental metal implants and maxillofacial reconstruction.[4,9,26,36,41,42,50,61,79,89,91,112–114,137,141,151–154,162,171,176,187,194] Medical applications include ear implants, spine fusion, repair of bony defects, and coatings for orthopedic metal implants.[1,2,32,37,59,64,73,78,80,81,87,114,160,165,173,185–187,190] Ca-P materials differ in composition from each other, reflecting the differences in their origin (e.g. natural or synthetic) and methods of preparation (Table 1; Figs 1 and 2), and can be prepared in different physical forms, e.g. dense, microporous and/or macroporous or particles or blocks (Fig. 3). These materials can be used in bulk or as coatings on metallic[25,37,39,46,93,107,114] or polymeric substrates;[120,178] or admixed with other inorganic materials, e.g. gypsum, alumina,[2,13,168] glass,[59,97,102,195] or polymeric[2,16,114,119,191] materials to form composites. Experimental materials include calcium phosphate cements, CPC,[20,79,127,168] apatite with CO_3 or F.[5,94–96,105,112]

Biodegradation is the process caused by the action of living systems (e.g. microorganisms, cells) when a material breaks down into its simpler components; reduces the complexity of a chemical compound or wears away by erosion (Webster's dictionary, paraphrased). Resorption of bone

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CALCIUM SULFATE– AND CALCIUM PHOSPHATE–BASED BONE SUBSTITUTES

Mimicry of the Mineral Phase of Bone

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Each year in the United States, 6.2 million fractures occur. Of these, 5% to 10% exhibit delayed healing or nonunion. Autogenous bone graft from the iliac crest or local sources has been the material of choice for the treatment of significant bone loss, delayed unions, and nonunions. Autogenous bone grafting, however, has been limited by the finite amount of bone available and the possibility of significant donor site morbidity, which can approach 30%. These two limitations of autogenous bone grafting have prompted the development of materials to replace or reduce the need for autograft bone.

As knowledge of the material, chemical, and biologic properties of living bone increases, clinicians become increasingly able to design and develop materials that mimic the properties of bone graft. Although most, if not all, of the materials introduced into the market thus far have been osteoconductive, the osteogenic nature of cancellous autograft sets the gold standard that clinicians strive to replicate. The ideal bone-graft substitute is (1) osteogenic, (2) biocompatible, (3) bioabsorbable, (4) able to provide structural support, (5) easy to use clinically, and (6) cost-effective. Practically, however, depending on where it is used, one or more of these properties may be more desirable than the others. For instance, the requirements for a material used to fill a bony defect at a metaphyseal site is much different biologically and mechanically from a material used in the treatment of a bony nonunion. In the former case, a purely osteoconductive material in concert with internal or external fixation may suffice to provide a transient scaffold on which the patient's natural healing process can deposit bone. Treatment of nonunion, however, requires stimulation of bone growth beyond that of simple osteoconduction.

To evaluate critically the compounds that are being rapidly introduced into the market, it is essential to understand the structure, composition, and behavior of living bone. Bone is a composite material that comprises organic and inorganic components. The inorganic phase, comprising 60% to 70% of the total dry weight, is composed of apatitic calcium phosphate containing carbonate and small amounts of sodium, magnesium, and trace components. The main constituent of the organic phase is collagen I, with cellular elements composing the remainder of the organic phase.[3]

The structural integrity of bone, especially its compressive strength, directly depends on

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Case Series

Radiologic and Histomorphometric Evaluation of Maxillary Sinus Grafting with Alloplastic Graft Materials

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Background: *Sinus lifting procedures are widely used to obtain adequate bony support for implant placement at the atrophic maxillae. The aim of this study was to compare various sinus lifting and grafting techniques and materials.*

Methods: *Nine maxillae were treated with delayed and 46 maxillae with immediate implant placement techniques. A total of 104 implants were inserted. Panoramic radiographs were obtained prior to, after, and 6 to 8 months after surgery. Computed tomographies were also taken before and after surgery. The height of new bone was compared. Biopsy specimens were obtained during delayed implant placement and analyzed histomorphologically.*

Results: *There were no statistically significant differences between the panoramic radiographs for delayed and immediately placed implants, or between the graft materials. We observed correlations between the panoramic radiographs and computerized tomographies.*

Conclusion: *Both delayed and immediate placement of implants can be used safely for sinus lifting. There were no statistically significant differences between the various graft materials.* J Periodontol 2003;74:909-915.

KEY WORDS

Dental implants, immediate; maxilla, atrophic/surgery; maxilla, atrophic/therapy; sinus lift.

Osseointegrated oral implants are widely used to restore total or partial edentulism.[1-3] Implant placement in the posterior maxilla is often complicated due to the insufficient bone volume caused by atrophy of the maxillae and pneumatization of the maxillary sinus.[4] Onlay or inlay grafting procedures have been developed to increase the dimensions of the bone.[5,6] The sinus lifting and grafting technique is a well-known method to obtain sufficient bone levels for implant placement. Maxillary sinus floor augmentation and grafting with various materials prior to implant placement in cases of atrophied posterior maxillae have been frequently used.[7-9] The sinus lift procedure uses an access window through the lateral wall of the maxillary sinus for bone graft insertion between the sinus membrane (Schneiderian membrane) and the floor of the sinus.[9-11] The grafts consist of either autogenous bone[12] and/or heterogeneous materials. Previously, autogenous grafts were widely used. With the development of various allogenic, alloplastic, and xenogenic graft materials, however, autogenous techniques have been used less frequently, as the harvesting procedure requires additional surgical procedures at the donor sites, which may lead to morbidity.[10] The procedure is termed a 1-stage or immediate technique when the graft materials and implants are placed at the same appointment. In a 2-stage or delayed technique implant placement is postponed for 6 to 8 months to allow healing of the graft material. In the immediate technique, the implants can be inserted simultaneously if primary stabilization is achieved with a sufficient level of bone height (>4 mm).[13-15] Delayed or 2-stage surgery is used when primary stabilization is not possible during sinus floor elevation and grafting.[10,13-15] A third technique, the indirect osteotome technique, has also been evaluated.[10]

Bovine hydroxyapatite§ is a bovine deproteinized cancellous bone with a structure similar to human bone.[3] The bone-conductive properties of bovine hydroxyapatite have been demonstrated previously.[16-19] Bovine dehydrated cancellous bone is used in periodontal and oral surgeries. β tricalcium phosphate is a bioabsorbable grafting material.[20]

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An evaluation of two configurations of tricalcium phosphate for treating craniotomies*

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Biodegradable beta-tricalcium phosphate disks (TCP) of two configurations were inserted into 15-mm-diameter craniotomy wounds and nontreated control sites were evaluated in 60 rabbits. There were no adverse tissue reactions and no apparent difference in the clinical appearance of the 12- and 24-week implanted disks. By 36 weeks and continuing to 48 weeks, the omnidirectional TCP (OTCP) implants were degrading more rapidly than the unidirectional TCP (UTCP) implants, with degradation progressing centripetally and replacement by woven bone and maturing lamellar bone. Host–implant interface of both TCP configurations was a bone bond without interposed soft tissue. TCP disks may be clinically useful for craniotomy repair.

Regeneration of bone of the facial skeleton lost as a consequence of trauma, disease, or resective surgery has been a goal sought by oral and maxillofacial surgeons. Although many materials have been used for osseous wound repair, no agent currently available provides the surgeon with a predictable level of bone regeneration. Autogenous grafts and allogeneic implants are the substances most commonly used by surgeons to treat bone defects; unfortunately, these materials have a failure rate ranging from 13–30%.[1] Ceramics and polymer alloplastic materials have been reviewed as possible alternatives to the traditionally used autogenous and allogeneic bone preparations.[2,3] To the best of our knowledge, there have been no studies that evaluated TCP in the form of disks for repairing nonhealing, 15-mm skull defects for a period of 48 weeks. It was the purpose of this study, therefore, to determine if disk forms of unidirectional and omnidirectional, biodegradable tricalcium phosphate (100% beta phase) could be used for treating craniotomies.

*The views of the authors do not purport to reflect the position of the Department of the Army or the Department of Defense. (Para. 4-3, AR 360-5).

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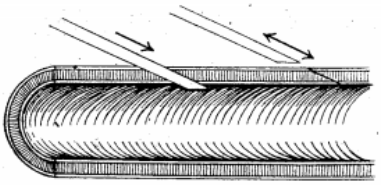
sheath on a tape. Minimal disturbance helps to avoid the local spasm which appears occasionally even under spinal analgesia.

Arteriogram.—Diodone ('Per-Abrodil,' Bayer) 50% has been used, warmed to body temperature. The syringe is a 10 c.cm. Record with an eccentric nozzle, carrying a no. 19 needle. Before the injection is made, all instruments and towel clips are removed so they will not appear on the plate. The tube is brought into correct position. The needle is then passed into the artery, bevel downwards and parallel to its wall, to prevent leakage of blood during its passage and provide a long valvular tunnel which will be rapidly closed by intra-arterial pressure when the needle is withdrawn (see figure). When blood appears in, or is aspirated into, the syringe, the injection is rapidly completed (less than 5 sec.), the syringe being firmly steadied with the left forefinger and thumb to prevent displacement of the needle's point, and the exposure is made when the injection is almost complete. The needle is then withdrawn, and a moist gauze swab pressed on the vessel at the site of puncture. Pressure is maintained until the film has been developed; by this time oozing from the puncture has stopped.



Method of inserting needle so as to prevent leakage of blood and leave valvular track on its withdrawal.

Closure.—If the plate gives the required information, the small wound is closed by silkworm sutures. If the lesion has not been demonstrated, a film may be placed more distally and the arteriogram repeated.

Complications.—Hæmatoma has not been encountered. On one occasion, as a consequence of inaccurate placement of the needle, the medium was injected into the soft tissues, where its position was verified by X ray; there was no untoward reaction and all radiographic trace of the diodone had disappeared in 24 hours. On one occasion the artery went into spasm at the site of puncture, but the injection was made successfully. According to Wagner (1944), a clot may form in the artery at the site of puncture, but this has not been suspected clinically in our series. Systemic reactions have also been recorded by Wagner, such as "flushing of the skin with a feeling of warmth, erythematous eruptions, nausea, vomiting, cyanosis, respiratory distress and fall in blood-pressure"; none such has occurred in this centre.

Convalescence.—If there is no other contra-indication, the patient may be out of bed in 48 hours.

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CANCELLOUS CHIP BONE-GRAFTS
REPORT ON 75 CASES

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EARLY in 1941 it became necessary to make good the loss of part of the frontal bone in a child aged 11 years. At that time a considerable experience in the use of massive cancellous grafts from the ilium pointed to the probability that this type of bone survives from the beginning. The two most important facts underlying this belief are first, the rapidity with which structural adaptation occurs, so that a new cortex is well marked on radiographic investigation in 8–12 weeks, and second, the very high tolerance to infection which these grafts possess as compared with that of the more usual compact graft from the tibia. Both of these characteristics appear to argue an early vascularisation of the graft, followed by cellular activity of the transplant. At the same time, it had been found that in children, even if the difficulty of obtaining sufficient iliac bone before fusion of the secondary epiphysis is not insurmountable, that part of the graft which had been nearest to the epiphyseal line tends to be absorbed This is thought to be due to an insufficient blood-supply being immediately available to ensure the survival of this recently laid down bone, which presumably has greater metabolic requirements than its more adult counterpart.

On biological grounds, therefore, it was thought that fragmentation of the graft might be expected to provide a much greater surface area through which the transplanted bone cells would become accessible, first to serum and secondly to the ingress of newly formed capillaries, and that the chances of their survival would thereby be enhanced. Once survival is ensured, fusion of the fragments can be expected to be rapid.

Accordingly, a section of cancellous tissue from the ilium was cut into fragments and inserted through a small incision in the frontal region to fill the cranial defect. The bone chips were applied so that they overlapped both the exposed bony margins of the defect and each other. No endeavour was made to produce a continuous surface; rather were spaces of some millimetres left between adjoining fragments to permit the permeation of blood, though care was taken to create a smooth general contour. The chips were arranged in at least two layers, and defects between those in the outer layer did not correspond with gaps between those beneath them. The wound was closed without drainage, and in 10 days the whole mass was clinically sound and firmly united with the cranium. Over a period of months no absorption was seen; in fact, the condition now is indistinguishable from that seen at the time of discharge over 3 years ago.

This experience appeared to confirm expectations, and completely altered one's outlook on the whole technique and rationale of bone-grafting, so from that time the principle of fragmentation of cancellous bone has been applied in other areas. Seventy-five consecutive cases are here reported.

SOURCE OF BONE

In all cases the graft is derived from the ilium. This bone is chosen for its relatively high cellular content and for its porosity. The fragmentation is designed to increase the surface area of the transplant and thus to create optimal conditions for survival of the greatest number of bone cells. The advantage of increased simplicity of operative technique, although important, is secondary.

The ilium is exposed by an incision about 3 in. long, and its crest and outer plate are freed from their muscular and aponeurotic attachments. Occasionally this process is continued on to the inner aspect. A block of bone of sufficient bulk is then removed with an osteotome, and its cortical covering is discarded. The remaining cancellous mass is divided into chips of various sizes, usually about $1 \times 0{\cdot}5 \times 0{\cdot}2$ cm. Irregular shapes are often useful, but it is undesirable to make the chips too small or excessive condensation is likely to occur.

GRAFTS FOR THE RESTORATION OF CONTOUR

Cancellous chips have been used in thirty-four cases for the restoration of contour in the frontal, supra-orbital, malar, zygomatic and mental regions. Cranial defects are included in this group, partly because they are often associated with loss of prominence of the eyebrow region, and partly because their margins are static, so that no problems of fixation arise.

The basic technique is always much the same. A small skin incision is deepened to the appropriate level, and undermining is carried out to expose the area to be grafted. In cranial defects the margins of the gap are denuded of periosteum with a raspatory to provide a strip of bare bone to which the chips may adhere, but no other shaping or freshening is carried out. In losses of, say, the superior maxilla, a complete bony foundation is probably not available, and in these cases the exposure of two or three bony areas to act as fixation points is sufficient because the graft depends for its survival on blood-supply and not on contact with existing bone. The correct contour is obtained by simply building up chips to the requisite levels. Fixation by pressure bandage for four to six days completes the process.

There have been no untoward sequelæ, and consequently the appearance of these grafts after varying intervals has not been seen. In one case, however, a

CLINICAL ORAL IMPLANTS RESEARCH

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Ridge preservation after tooth extraction

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Conflicts of interest:
The authors declare no potential conflicts.

Key words: bone substitutes, GBR, implant dentistry, membrane, ridge preservation, tooth extraction

Abstract

Background: Following tooth extraction, the alveolar ridge will undergo dimensional changes. This change may complicate the subsequent restorative procedure when oral implants are chosen. "Alveolar ridge preservation" has been assessed in various studies.

Aim: To evaluate the more recent studies on this topic and to explore new insights under this topic.

Material and methods: Animal studies and clinical studies have addressed different techniques.

Results and conclusions: Implants placed into the fresh extraction sockets do not prevent the resorption of the alveolar bone. Simultaneous guided bone regeneration could partially resolve alveolar bone resorption. The use of root-formed implants does not preserve alveolar ridges. Moreover, various bone substitutes have been tested: magnesium-enriched hydroxyapatite, human demineralized bone matrix, and deproteinized bovine bone mineral have been shown to be effective in ridge preservation. Applying the guided bone regeneration principle using bone substitutes together with a collagen membrane has shown clear effects on preserving alveolar ridge height as well as ridge width. Soft tissue grafts or primary closure did not show beneficial effect on preserving the alveolar bone.

Following tooth extraction, the alveolar ridge will undergo structural changes. These changes in extraction sockets were amply demonstrated with histological observations in dog studies (Cardaropoli et al. 2003). At day 1 after extraction, the socket was occupied by a coagulum; this coagulum was comprised mainly of erythrocytes and platelets that were trapped in a fibrous matrix. Immediately adjacent to the hard tissue wall was the "bundle bone", and principal fibers from periodontal ligament (Sharpey's fibers) could be found invested in the bundle bone. These were also in direct contact with the coagulum. At day 3, the coagulum had been replaced by a richly vascularized granulation tissue. At day 7, newly formed blood vessels were evident in the primary matrix. Various types of leukocytes and collagen fibers had taken the place of the residual periodontal ligament as well as the granulation tissue. At day 14, most of the bundle bone had disappeared, and instead, adjacent to the newly formed blood vessels, "woven bone" started extending from the old bone of the socket walls toward the center of the socket. At day 30, woven bone underwent resorption, suggesting that the remodeling process had begun. At day 60, hard tissue bridges separated the marginal mucosa from the socket, and bone marrow replaced woven bone at the center of the previous socket. At day 90, woven bone was replaced by lamellar bone. At days 120 and 180, most of the woven bone had been replaced by lamellar bone.

The role of bundle bone in the dimensional change in the alveolar ridge was investigated in several dog studies (Araùjo & Lindhe 2005; Araùjo et al. 2005) At 1 week after extraction (Araùjo & Lindhe 2005), the buccal bony crest was 0.3 mm coronal to the lingual bony crest, but at 2 weeks after extraction, the buccal crest became 0.3 mm apical to the lingual crest. This relative distance was increased to 0.9 and 1.9 mm at 4 and 8 weeks after extraction, respectively. It was also observed that the crestal region of the buccal bone wall was made up exclusively of bundle bone, whereas the corresponding region of the lingual bone was made of a combination of bundle bone and lamellar bone. Obviously, the function of bundle bone is to anchor the tooth in the alveolar bone through the invested periodontal ligament. As the tooth is extracted, the bundle bone will lose its function, and subsequently, will resorb. This may explain the more pronounced resorption of the buccal than the lingual bony crest.

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Current Concepts Review

Autogenous Bone Graft: Donor Sites and Techniques

Chad Myeroff, MD, and Michael Archdeacon, MD, MSE

Investigation performed at the University of Cincinnati College of Medicine, Cincinnati, Ohio

- Autogenous cancellous bone graft provides an osteoconductive, osteoinductive, and osteogenic substrate for filling bone voids and augmenting fracture-healing.
- The iliac crest remains the most frequently used site for bone-graft harvest, but the proximal part of the tibia, distal end of the radius, distal aspect of the tibia, and greater trochanter are alternative donor sites that are particularly useful for bone-grafting in the ipsilateral extremity.
- The most common complication associated with the harvest of autogenous bone graft is pain at the donor site, with less frequent complications including nerve injury, hematoma, infection, and fracture at the donor site.
- Induced membranes is a method that uses a temporary polymethylmethacrylate cement spacer to create a bone-graft-friendly environment to facilitate graft incorporation, even in large segmental defects.

Autogenous bone graft remains a reliable treatment option when structural stability is required, bone voids exist, or bone-healing augmentation is desired. Cortical autografts provide a structurally sound osteoconductive medium with minimal osteoinductive and osteogenic properties. Cancellous autografts provide a highly osteoconductive, osteoinductive, and osteogenic substrate while corticocancellous grafts provide some benefits of both. The iliac crest remains the most common donor site for autogenous bone graft, providing sufficient quantities of cortical and cancellous bone for most clinical settings, but with donor-site morbidity. Alternative donor sites include the proximal part of the tibia, distal end of the radius, distal aspect of the tibia, and greater trochanter. A novel technique uses a reamer-irrigator-aspirator (RIA; Synthes, West Chester, Pennsylvania) to harvest intramedullary bone graft. Bone graft harvested from any site can be combined with the so-called induced membrane in more complex bone void settings.

Use of Levels of Evidence in the Assessment of Scientific Information

The literature summarized in this article is evaluated with use of the Levels of Evidence ratings for studies addressing clinical care[1]. These levels are summarized with use of Grades of Recommendation (see Appendix) previously published in *The Journal of Bone and Joint Surgery* (American Volume)[2]. Grade-A recommendations are based on consistent Level-I studies. Grade-B recommendations are based on consistent Level-II or III evidence. Grade-C recommendations represent either conflicting evidence or are based on Level-IV or V evidence. A grade of I indicates that there is insufficient evidence to make a treatment recommendation.

Clinical Relevance

Each year 200,000 bone-graft procedures are performed in the United States[3]. Indications for bone-grafting include delayed union or nonunion, malunion, arthrodesis, limb salvage, and

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Complications following autologous bone graft harvesting from the iliac crest and using the RIA: A systematic review

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ABSTRACT

Bone grafting is a commonly performed surgical procedure to augment bone regeneration in a variety of cases in orthopaedic and maxillofacial surgery. Autologous bone graft remains to be the 'gold standard' and the iliac crest to be the most common harvesting site. The intramedullary canal of long bones represents another potential site for large volume of autologous bone graft harvesting and is recently being used as an alternative donor site. However, harvesting of autologous bone graft is associated with morbidity and a number of complications. The aim of this systematic review was to collect and summarise the existing data on reported complications after harvesting autologous bone from the iliac crest (anterior and posterior) and the long bone intramedullary canal using the RIA device. We searched the PubMed Medline and Ovid Medline databases, from January 1990 to October 2010, to retrieve all relevant articles. A total of 92 articles (6682 patients) were included in the analysis. Overall, the complication rate following RIA was 6% (14 complications in 233 patients) and 19.37% after iliac crest bone graft harvesting (1249 complications in 6449 patients). The rate of each of the reported complications was assessed and, when the donor site was properly documented, comparison within the anterior and posterior iliac crest donor sites was performed. Although the difference of the overall morbidity rates between the two harvesting sites was not statistically significant ($p = 0.71$); the rates of certain complications were found to significantly differ when anterior or posterior iliac crest was used. The rates of infection ($p = 0.016$), haematoma formation ($p = 0.002$), fracture ($p = 0.017$), and hyperthrophic scar ($p = 0.017$) were significantly higher when the donor site was the anterior iliac crest compared to the posterior iliac crest; whereas the rates of chronic donor site pain ($p = 0.004$) and sensory disturbances ($p = 0.003$) were significantly lower. The incidence of bone graft harvesting related complications can be reduced further if certain principles are followed depending on the performed harvesting methods; but overall the use of RIA device as harvesting method seems a promising alternative with a low complication rate.

Introduction

Autologous bone is considered to be the "gold standard" bone grafting material as it combines all properties required in a bone graft material: osteoinduction (BMPs and other growth factors), osteogenesis (osteoprogenitor cells) and osteoconduction (scaffold).[1] It is widely used in a number of orthopaedic and oral and maxillofacial procedures for augmentation and acceleration of bone regeneration (fusion, non-union, fracture and osteotomy healing) or restoration of bony defects (traumatic, congenital, following tumour or infection). Harvested from the patient itself, autologous bone is histocompatible and nonimmunogenic, thus reducing to the minimum immunoreactions and transmission of infections.

Iliac crest bone graft (ICBG) is by far the most commonly used autologous bone graft compared to other alternative donor sites, such as the proximal tibia, distal femur, fibula, ribs and distal radius. It can be harvested from the anterior or the posterior iliac crest. Its main advantages include the availability of a fair bone quantity of bone graft (cancellous, cortico-cancellous or vascularised) with progenitor cells and growth factors, and structural support when tricortical graft is used.[1,2] Although iliac crest bone harvesting is a frequently performed surgical procedure with relatively easy access, its complications have been well documented in the literature with a wide range of morbidity rate and a number of various complications, including

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Article

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Site Selection and Pain Outcome After Autologous Bone Graft Harvest

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Abstract

Background: In foot and ankle surgery, there are multiple sites used for autologous bone graft, including the proximal (PT) or distal tibia (DT), calcaneus (C), and iliac crest (ICBG). There has been no comparison between these anatomic areas and the potential for acute or persistent pain at 1 year. The purpose of this study was to prospectively compare patient-reported outcomes of acute and persistent pain at 1 year after surgery to determine if harvest site selection made a difference.

Methods: As part of a clinical trial examining ankle and hindfoot fusion rates with autograft compared with synthetic graft, the autologous bone graft harvest sites were assessed with visual analog pain outcome scores at 3, 24, 36, and 52 weeks after surgery. Patients with a score of 20+ defined clinically significant pain. Four harvest sites were compared: ICBG, PT, DT, and C. Fisher exact test was used to compare the graft site pain between locations.

Results: Twelve percent of subjects reported clinically significant pain at 24 weeks and 8.5% at 52 weeks postoperatively. Each lower extremity harvest site (C, DT, PT) showed higher rates of clinically significant graft harvest site pain than the ICBG at 52 weeks.

Conclusions: Autologous bone graft harvest carried a risk of persistent pain at up to 1 year (weeks 24-52) in 18% of patients. Lower-extremity bone graft sites had the greatest risk for persistent pain at 1 year.

Level of Evidence: Level II, prospective comparative study.

Keywords: bone graft pain, foot and ankle autologous graft

Autologous bone graft is routinely used to enhance bone healing in various musculoskeletal conditions including comminuted fractures, fusions, and nonunions. Specifically, there are numerous peer-reviewed publications using autologous bone graft to supplement bone healing in foot and ankle fusion surgery. Autologous bone graft provides an effective scaffold for new bone formation (osteoconductive) and contains appropriate growth factors and cells to potentiate new bone formation (osteoinductive). Autologous bone graft eliminates the risk of disease transmission or immunogenic reactions from an allographic bone source.[4,7] It is generally accepted, however, that harvesting autologous bone graft does come with other increased risks to the patient. Gupta et al[2] conducted a literature review of the clinical complications of iliac crest bone grafting. The authors noted an overall complication rate of 31% among the 1020 patients included in the analysis. One of the potential risks includes acute and/or chronic pain lasting 1 year after surgery at the harvest site. Gupta et al[2] found that donor site pain in excess of 24 months occurred in 27% of patients. More recently, a prospective clinical study on the pain and morbidity of the iliac crest bone graft was conducted in 104 patients.[3] At 52 weeks, 16.5% of patients reported more severe pain at the iliac crest harvest site as compared with the primary operative site.

Although these studies examined the pain associated with iliac crest bone graft, the sites used for bone graft in foot and ankle surgery commonly include other lower-extremity locations such as the proximal tibia, distal tibia, and calcaneus. There is limited literature examining these sites for bone graft complications. Schmidt and Townsend[5] reviewed the salient clinical literature on the complication rates of harvesting proximal tibia bone graft. The study included 1137 patients demonstrating an overall complication rate of 5.5%. Several of the complications were severe,

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The TIME Technique: A New Method for Localized Alveolar Ridge Augmentation Prior to Placement of Dental Implants

Thomas von Arx, Dr Med Dent/Nicolas Hardt, Prof Dr Med, Dr Med Dent/Beat Wallkamm, Dr Med Dent

Sufficient bone volume is still considered the most important prerequisite for the osseointegration of dental implants. The TIME technique (autogenous bone grafting combined with stabilization using a titanium mesh) for localized alveolar ridge augmentation was evaluated in 20 patients who had insufficient bone volumes for the primary placement of dental implants. Different clinical recordings were evaluated at TIME stage 1 (augmentation surgery) and at TIME stage 2 (reentry surgery with mesh removal and simultaneous dental implant placement). In most patients, single- or extended-tooth gaps (up to four units) were augmented with autogenous bone harvested from the chin or retromolar area. With the exception of temporary disturbances of tooth sensibility, no morbidity at the donor sites was observed. In one patient, the stabilizing titanium micromesh had to be removed prematurely because of graft infection. At the reentry surgery, the bone grafts were found to be completely incorporated in 75% of the patients. In 15% of the patients, only minimal graft resorption was observed (less than 10% of the graft volume). Subsequently, 28 implants could be placed in 19 patients. The stabilizing titanium mesh was best suited for vertical ridge augmentations. Another feature of the mesh was the excellent tissue compatibility, with little clinical or histologic inflammation, even when the mesh had become exposed.
(Int J Oral Maxillofac Implants 1996;11:387-394)

Key words: autogenous bone grafting, clinical study, localized alveolar ridge augmentation, titanium micromesh

Placement of endosseous dental implants has become a widely used treatment modality in dental medicine. The long-term success of dental implants depends on several factors that can be attributed to the following four treatment phases: *(1)* placement of implant (surgical phase), *(2)* osseointegration of implant (biologic phase), *(3)* loading of implant (prosthetic phase), and *(4)* hygiene of implant (maintenance phase). Inadequate bone volumes at implant recipient sites often adversely affect the surgical and biologic treatment phases. Moreover, prosthetic treatment of a malpositioned dental implant may be compromised. Where an atrophied alveolar ridge profile exists, dental implants often have axis inclinations to the buccal aspect in the maxilla and to the lingual aspect in the mandible. As a

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Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges

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The aim of this study was to analyse the clinical outcome of two different surgical methods for the reconstruction of narrow edentulous ridges before implant installation: guided bone regeneration with e-PTFE membranes and autologous bone chips or grafting of autologous bone blocks without e-PTFE membranes. Thirty partially edentulous patients, presenting insufficient bone width (less than 4 mm) in the edentulous sites for installation of screw-type titanium implants, were selected and assigned to two different treatment modalities. Fifteen patients (group 1) were treated by means of guided bone regeneration with e-PTFE membranes supported by stainless steel screws and autologous bone chips taken from intraoral sites. Fifteen patients (group 2) were treated by means of autologous bone blocks taken from intraoral or extraoral sites (anterior iliac crest and calvaria) and stabilized with titanium microscrews. Six to 8 months later, during re-entry for implant insertion, the gain of ridge width obtained was measured. In group 1 the average amount of bone gain was 2.7 mm, whereas in group 2 the value was 4.0 mm. Five to 6 months after implant placement prosthetic rehabilitation was started. The mean follow-up after prosthetic load has been 22.4 months. Success rates of implants according to Albrektsson criteria has been 93.3% in group 1, and 90.9% in group 2. Although a statistical comparison between the two treatment modalities may not be feasible, due to the bias resulting from the choice of treatment by the clinician and from the differences in donor sites and defect extension, some considerations can be made: 1) both methods are a reliable means for the correction of narrow edentulous ridges; 2) both techniques necessitate overcorrection of the defect because of interposition of connective tissue beneath the membrane in the first group and bone resorption in the second one; 3) the use of semipermeable barriers increases the costs of the surgical procedure, as compared to bone grafting without membranes; 4) guided bone regeneration presents a higher risk of infection because of wound dehiscence and membrane exposure. Therefore, in case of wide edentulous areas, reconstruction of narrow ridges should be performed with bone blocks without membranes.

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Key words: guided bone regeneration – bone grafts – atrophic jaws

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In the last few years, rehabilitation of edentulous patients by means of osseointegrated implants has become a predictable treatment modality, provided that adequate residual bone volume is present. In particular, clinical experience has shown that a bone wall of at least 1 mm should be present on the facial and oral aspects of the implant, to achieve reliable long-term results (Albrektsson et al, 1986; Shulman 1988; Lekholm & Zarb 1995).

In Cawood & Howell class IV patients (Ca-

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Horizontal bone-augmentation procedures in implant dentistry: prosthetically guided regeneration

Matteo Chiapasco & Paolo Casentini

Experimental and clinical studies show osseointegration to be highly predictable, and dental implants currently represent a reliable means for restoring dental function in partially and completely edentulous patients (1, 16, 32). Although surgical and prosthetic procedures are well consolidated as a result of more than 30 years of clinical experience, treatment planning in oral implantology has, in recent years, undergone tremendous evolution. Implants were originally used in restoring fully edentulous patients based on the concept of 'surgically and anatomically driven implant placement'. Implant placement was primarily determined by the location of available bone, and the main goal was to allow adequate bone anchorage to provide a functionally efficient prosthetic rehabilitation. Following this concept, because osseointegration was the primary outcome of surgery, prosthetic rehabilitation did not fulfill the esthetic ideal. In these cases, dental restorations were often implant-supported overdentures or fixed implant-supported prostheses with distal cantilevers (Toronto bridge concept) and it was possible to compensate for inadequate implant position using acrylic flanges (9, 59).

As oral implants have also been used for the rehabilitation of partially dentate patients, esthetic outcomes have become more important because implant-supported partial prostheses have to integrate with the adjacent natural dentition, both from a functional and an esthetic point of view (6). A good esthetic result can be achieved only if the implant is placed in a carefully planned position, as determined by the prosthetic needs. Therefore, the concept of 'restoration-driven implant placement' has been introduced to optimize both function and esthetics (44). As correct implant position is vital in order to achieve a good esthetic result (14, 15), optimal conditions of the alveolar bone, in terms of adequate volume, as well as optimal conditions of the surrounding soft tissues, are key prerequisites to obtain a good clinical outcome. When these conditions are lacking, because of hard- and soft-tissue deficiencies (for instance, following atrophy, sequelae of periodontal disease, traumas or congenital malformations), the bone volume and/or the surrounding soft tissues (keratinized mucosa) must be augmented.

A host of bone-augmentation techniques, such guided bone regeneration (11, 48, 57, 74), bone-grafting techniques (10, 23, 29, 41, 51, 53, 60), and alveolar bone expansion (3, 31, 72), have been proposed and different systematic reviews have been published to evaluate the outcome of various bone- and soft-tissue augmentation procedures (2, 7, 27, 34, 56, 64). The aim of this article is to present a rational, evidence-based and prosthetically driven approach for the treatment of edentulous ridges affected by horizontal defects, using augmentation procedures and dental implants. A diagnostic protocol, a classification of bone defects and the main augmentation techniques will be described in detail. The selection criteria for different surgical techniques for different classes of bone defects will also be discussed.

Diagnosis and treatment planning for partially dentate patients with compromised alveolar ridges, following a prosthetically driven diagnostic protocol

As the rehabilitation (with implant-supported prostheses) of partially dentate patients affected by horizontal

The Biology of Bone Graft Repair

HANS BURCHARDT, PH.D.*

Cancellous and cortical autografts histologically have three differences: (1) cancellous grafts are revascularized more rapidly and completely than cortical grafts; (2) creeping substitution of cancellous bone initially involves an appositional bone formation phase, followed by a resorptive phase, whereas cortical grafts undergo a reverse creeping substitution process; (3) cancellous grafts tend to repair completely with time, whereas cortical grafts remain as admixtures of necrotic and viable bone. Physiologic skeletal metabolic factors influence the rate, amount, and completeness of bone repair and graft incorporation. The mechanical strengths of cancellous and cortical grafts are correlated with their respective repair processes: cancellous grafts tend to be strengthened first, whereas cortical grafts are weakened. Bone allografts are influenced by the same immunologic factors as other tissue grafts. Fresh bone allografts may be rejected by the host's immune system. The histoincompatibility antigens of bone allografts are presumably the proteins or glycoproteins on cell surfaces. The matrix proteins may or may not elicit graft rejection. The rejection of a bone allograft is considered to be a cellular rather than a humoral response, although the humoral component may play a part. The degree of the host response to an allograft may be related to the antigen concentration and total dose. The rejection of a bone allograft is histologically expressed by the disruption of vessels, an inflammatory process including lymphocytes, fibrous encapsulation, peripheral graft resorption, callus bridging, nonunions, and fatigue fractures.

For at least 65 years bone grafting has been used to fuse joints and to repair skeletal defects. Unfortunately, nonunion or fatigue failure still occurs as frequently as in the past, with one recent report indicating a greater than 50% failure rate for large segmental autografts.[55]

An additional problem of bone grafting is the availability and acquisition of the appropriate material. Hence, autogenous materials are obtained with certain costs to the patient, including (1) additional surgical incisions; (2) increased postoperative morbidity; (3) weakened donor bone sites; and (4) potential serious complications from any of the previous conditions. The alternative to autografting, *e.g.*, allografting, has achieved moderate success. Long-term follow-up data reveal a high incidence of delayed union, nonunion, fatigue fractures, and, occasionally, complete resorption of the graft material. Similarly, synthetic implants can be easily manufactured to specification, but these materials are susceptible to wear, tear, and fixation, especially since they can not be incorporated into the skeleton.[4,39,94]

The author describes the biology of bone graft repair by presenting (1) general information on the microscopy and correlative biomechanics of autograft repair; (2) biologic aspects of allograft repair; and (3) alternatives when autogenous bone is insufficient.

MORPHOLOGY AND BIOMECHANICS OF BONE GRAFT REPAIR

TERMINOLOGY

The process of incorporation is a function of the recipient bed and depends on close contact with the donor tissue, time se-

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Society For Biomaterials

Review Article

Different methods of dentin processing for application in bone tissue engineering: A systematic review

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Abstract: Dentin has become an interesting potential biomaterial for tissue engineering of oral hard tissues. It can be used as a scaffold or as a source of growth factors in bone tissue engineering. Different forms of dentin have been studied for their potential use as bone substitutes. Here, we systematically review different methods of dentin preparation and the efficacy of processed dentin in bone tissue engineering. An electronic search was carried out in PubMed and Scopus databases for articles published from 2000 to 2016. Studies on dentin preparation for application in bone tissue engineering were selected. The initial search yielded a total of 1045 articles, of which 37 were finally selected. Review of studies showed that demineralization was the most commonly used dentin preparation process for use in tissue engineering. Dentin extract, dentin particles (tooth ash), freeze-dried dentin, and denatured dentin are others method of dentin preparation. Based on our literature review, we can conclude that preparation procedure and the size and shape of dentin particles play an important role in its osteoinductive and osteoconductive properties. Standardization of these methods is important to draw a conclusion in this regard. © 2016 Wiley Periodicals, Inc. J Biomed Mater Res Part A: 104A: 2616–2627, 2016.

Key Words: dentin, biomaterial, bone substitute, tissue engineering, regeneration

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INTRODUCTION

Despite great advances in dentistry, oral and dental diseases remain a major dilemma worldwide. Oral and dental treatments are often performed using synthetic materials with properties different from those of natural tissues and thus, they eventually fail even under ideal conditions. Tissue engineering is a novel concept in regenerative medicine and dentistry. Using a combination of stem cells, scaffolds and growth factors, tissue engineering offers promising results for regeneration of the injured or lost tissues.[1] Dentin is a suitable biomaterial for use in tissue engineering since it can serve both as a scaffold and a rich source of growth factors. Dentin is a calcified connective tissue and its properties highly depend on its mineralized extra-cellular matrix. This tissue is composed of 50% minerals, 30% organic compounds, and 20% water. However, distribution of these components is variable in different parts and different types of dentin.[2,3] Organic dentin matrix contains macromolecules characteristic of many connective tissues. Also, this matrix contains compounds specific for mineralized tissues.[4] The matrix is synthesized by odontoblasts and is a rich source of growth factors and bioactive molecules required for dentinogenesis, which are released in presence of bacterial acids or some dental materials in case of caries or restorative treatments and cause regeneration and repair of dentin.[5–15] Dentinal matrix compounds released by ethylenediaminetetraacetic acid (EDTA) etchants have shown significant morphogenetic activities and caused induction of dentinogenesis *in vivo*.[16] Dentin organic matrix includes non-collagenous (NCPs) and collagenous proteins, proteoglycans, glycoproteins, and lipids. Collagens are the most abundant dentin extracellular matrix proteins (90%), which are mainly composed of type I collagen as in bone. Dentin collagen forms a compact and crosslinked scaffold in which, mineral crystals deposit[17,18] and contains several growth factors such as transforming growth factor-β (TGF-β1), insulin-like growth factor (IGF), bone morphogenetic proteins (BMPs) as well as some angiogenic growth factors.[19–21] These growth factors are released secondary to processes such as caries progression, which result in dentin dissolution and stimulate reparative dentinogenesis.[22] The family of TGF-β has been identified in human dentin, pulp cells and odontoblasts and its

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BONE INDUCTION BY DECALCIFIED DENTINE IMPLANTED INTO ORAL, OSSEOUS AND MUSCLE TISSUES

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Summary—The fate of implants of decalcified dentine was compared with that of decalcified bone, tendon and muscle in three different sites: muscle pouch, drill-hole in mandible, and extracted tooth socket. Within the implants of dentine and bone matrix in areas undergoing resorption by collagenolytic mesenchymal cells and sprouting capillaries, a consistently reproducible induction system was set up for osteogenesis. Similarly prepared tendon and muscle implants did not induce osteogenesis. Except that the new bone developed from the interaction of hypertrophied mesenchymal cells with extracellular substances in the matrix of dentine and bone, and that a film of cement substance generally separates the old and new tissue, the local physical-chemical reactions are obscure. Transfer of ^{3}H-glycine does not appear to occur locally between the old dentine matrix and ingrowing new cells of the host.

RECENT experimental investigations demonstrate that when implants of lyophilized, decalcified bone matrix are resorbed, collagenolytic mesenchymal cells enter into an induction system for new bone formation (URIST, 1965). Other materials, such as undecalcified, allogeneic (homogenous) devitalized bone, frozen bone, processed xenogeneic (heterogenous) bone, deproteinized bone, or hydroxyapatite crystals, are also resorbed by mesenchymal cells but rarely produce new bone. KRÖMER (1962), SCHAEFFER and PACKER (1962) and others they cite, reviewed a large literature on implants of a wide variety of materials in bone and tooth extraction defects. Almost every conceivable kind of material, except decalcified dentine, seems to have been tested in either extraskeletal, or mandibular, or tooth socket defects, If decalcified dentine had been tested, heteroinduction (induction of formation of one tissue, bone, by the matrix of another, dentine) probably would have been noted previously by both experimental and clinical investigators. Recently, homeoinduction (induction of bone by bone matrix) has been affirmed by experimental work on decalcified bone matrix implants in rats, mice guinea pigs, rabbits and human beings. According to URIST (1965), VAN DE PUTTE and URIST (1965), and URIST *et al.* (1967), an acid-insoluble macromolecular complex is mobilized from organic matrix of lyophilized bone and dentine to promote cell interactions which induce mesenchymal cells to differentiate into bone cells. The cell origins and the cytochemical reactions are obscure. The object of the present communication is to describe bone induction by decalcified dentine in implants in the jawbone, and to compare the process with implants in muscle pouches in the anterior abdominal wall.

Human Dentin-matrix-derived Bone Morphogenetic Protein

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Bone morphogenetic protein (BMP) was extracted from human dentin matrix with 4 mol/L guanidine-HCl and was purified by liquid chromatography. SDS-PAGE and IEF showed that the purified BMP was homogeneous and induced new bone formation *in situ* after three weeks when implanted into muscle pouches in Wistar rats. The molecular weight of BMP was estimated to be about 20.0 kDa by SDS-PAGE, and the pI value was 8.8 by IEF. Amino acid analysis suggested that BMP is a protein containing 191 amino acids. A partial amino acid sequence was obtained from the final purified BMP. Dentin-matrix-derived BMP is probably not identical to, but is similar to, bone-matrix-derived BMP, though both types of BMP have the same action *in vivo*.

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Introduction.

Bone morphogenetic protein (BMP) has been extensively studied for possible clinical applications since Urist (1965) experimented with bone induction in demineralized bone. After it was found that BMP could be dissolved by 4 mol/L guanidine-HCl (Takaoka *et al.*, 1980; Hanamura *et al.*, 1980) and 6 mol/L urea (Urist *et al.*, 1982), its isolation and purification have progressed rapidly. Studies have revealed that BMP exists in the bone matrix (Sampath and Reddi, 1983; Muthukumaran *et al.*, 1985), in osteosarcoma tissue (Takaoka *et al.*, 1980; Bauer and Urist, 1981), in the dentin matrix (Butler *et al.*, 1977; Conover and Urist, 1979; Kawai and Urist, 1989), and in wound tissue after tooth extraction (Bessho *et al.*, 1990). It acts on immature mesenchymal-type cells to initiate bone induction through endochondral bone differentiation. Moreover, several studies have reported the isolation of bone-inducing factors. Sampath *et al.* (1987) and Luyten *et al.* (1989) isolated a 22-kDa protein called osteogenin. Bentz *et al.* (1989) isolated a 22-28-kDa protein called osteo-inductive factor (OIF). However, it remains to be clarified whether the identified proteins have the reported biological activity. Using an *in vivo* model similar to that of Sampath *et al.* (1987), Wozney *et al.* (1988) reported the cloning and recombinant expression of several molecules that induce cartilage, but not bone formation.

In this study, BMP was extracted and purified from human dentin matrix. The amino acid composition and partial amino acid sequence of the BMP were determined.

Materials and methods.

Preparation of treated dentin.—Specimens (about 2 kg) were obtained from human vital teeth immediately after extraction. They were prepared as follows: The enamel, cementum, pulp, and caries were mechanically removed, and the remaining dentin was washed in cold distilled water. The washed dentin was then frozen in liquid nitrogen and crushed in a Wiley mill (Ikemoto Scientific Technology, Tokyo, Japan) to a particle size of 1 mm^3. This was then washed in distilled water, defatted in chloroform:methanol (1:1) for 12 h, and demineralized in 0.5 mol/L HCl for 72 h at 4°C. The demineralized specimen was re-defatted in chloroform:methanol (1:1) for six h, treated with 2.0 mol/L $CaCl_2$ for 24 h, with 0.5 mol/L EDTA (pH 7.4) for four h, with 8.0 mol/L LiCl for 24 h, and finally re-washed in distilled water at 4°C.

Dissociative extraction.—The treated specimen was chemically extracted with 20 volumes of 4 mol/L guanidine-HCl (pH 5.2) for 96 h at 4°C. This extract was centrifuged (10,000 g, 30 min, 4°C), and the supernatant was concentrated (1:5) by ultrafiltration (Diaflo membrane YM-10; 10,000 molecular weight cut-off, Amicon, Ireland). Three volumes of chilled ethanol (−20°C) were added to the concentrated fraction, and the mixture was left standing for 12 h at 4°C. It was then separated by centrifugation (10,000 g, 30 min, 4°C) into an ethanol-supernatant fraction and an ethanol-precipitate fraction. The ethanol-precipitate fraction was lightly washed in distilled water, and dialyzed (Spectrapor membrane tubing; 8000-molecular-weight cut-off; Spectrum, Los Angeles, CA) against 10 volumes of distilled water at 4°C for 72 h until precipitation was complete. The distilled water was changed every 12 h. The dialyzed specimen was centrifuged (70,000 g, 30 min, 4°C) for separation into water-soluble and water-insoluble fractions, lyophilized, and weighed.

Fractionation by liquid chromatography.—The water-insoluble fraction was dissolved in 4 mol/L guanidine-HCl at pH 5.2 (25 mg/5 mL) and analyzed (flow rate, 20 mL/h) in a Sephacryl S-200 column (2.6 × 100 cm, Pharmacia, Sweden) that had been prepared and equilibrated with the same solution. The active fraction obtained by Sephacryl S-200 chromatography was dissolved in 6 mol/L urea/50 mmol/L Tris-HCl at pH 9.5 (5 mg/mL) containing 10 mmol/L NaCl and was applied to a MONO Q HR 5/5 column (5.0 × 50 mm, Pharmacia, Sweden) that had been prepared and equilibrated with the same solution. Analysis was performed at a flow rate of 0.5 mL/min with a NaCl concentration gradient of 10 mmol/

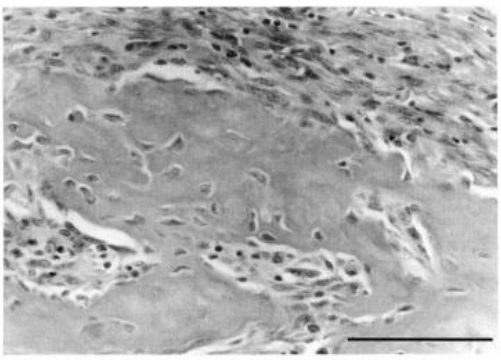

Fig. 1—Photomicrograph of bone induced in the calf muscle pouch of a Wistar rat. Bar = 100 μm.

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Bone Induction in Excavation Chambers in Matrix of Decalcified Dentin

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EXPERIMENTS by Charles B. Huggins and his associates,[1] and many others during the past thirty years,[2-11] demonstrate that whole toothbuds and parts of toothbuds possess the capacity to grow and develop in areas of the body other than the jawbone, even in the form of explants in tissue culture. The toothbud not only continues its characteristic development, but also exhibits the capacity to induce undifferentiated connective tissues to form bone. To explain these observations, Hoffman[12] postulates that the enamel organ and its derivative, Hertwig's epithelial root sheath, stimulates connective tissue cells to differentiate into bone cells, while Zussman[13] contends that odontoblasts which had previously participated in dentin formation can produce bone even when not in contact with oral tissues. Except that the new bone originates from proliferating living cells in both the transplanted tooth and in the host bed, present knowledge of the local physiology of cellular differentiation of bone tissue is meager. If bone develops from an embryonic induction system in postfetal life, the mechanism is comparable to that of induction by living cartilage cells, as described by Urist and McLean[14] in 1952. However, new evidence, recently contributed by Urist[15] and van de Putte and Urist,[16] demonstrates that bone induction can be instituted by a cell-free matrix of dead, decalcified bone. The investigations presented in this communication are designed to determine whether decalcified dentin can induce osteogenesis. While the matrix of dentin is different in structure, it is similar in chemical composition to the matrix of bone and may induce bone formation just as consistently as bone matrix.

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Materials and Methods

A total of 520 samples of decalcified first-molar rat toothbuds, suckling rat dentin, mature rat dentin, mature human dentin, and mature rabbit dentin were implanted in 162 rats and 24 rabbits, as listed in Table 1. Host animals consisted of Lewis inbred-strain female rats, 12 weeks old, and New Zealand male rabbits, 8 to 10 weeks old. The animals were killed at intervals between 1 and 12 weeks after the operation.

The toothbuds were dissected out by the technique described by Lefkowitz and Mardfin.[17] Mature rat and rabbit dentin was obtained from incisors and molars by cutting off the roots, removing the pulp, and decalcifying the remnant in 0.6N HCl, or in 0.5M edetic acid (EDTA) solutions, at pH 7.4. Human dentin was isolated by mechanically grinding away the root cementum and by cutting off pieces of root dentin by means of a bone-cutting forceps. The rats were anesthetized under open-drop ether anesthesia. The rabbits were anesthetized by intramuscular injection of propiopromazine HCl (Tranvet), 0.1 cc/kg, and intravenous injection of a combination of chloral hydrate, propylene glycol, magnesium sulfate, sodium pentobarbital (Equi-thesin), 0.5 to 1 cc/kg. Using aseptic technique, the specimens were either implanted immediately following decal-

RECYCLED DENTIN ROOT MATRIX FOR A CARRIER OF RECOMBINANT HUMAN BONE MORPHOGENETIC PROTEIN

Masao Ike, DDS
Marshall R. Urist, MD

KEY WORDS

Recycled root matrix
Bone morphogenetic protein (BMP)
Recombinant human bone morphogenetic protein (rhBMP-2)

Dysfunctional teeth, donated by community dental clinics, were recycled for research on bone morphogenetic protein (BMP) in health and disease. The crown remnants were trimmed away, and the roots were washed in 70% alcohol, demineralized, lyophilized, and prepared in one of two forms: (1) human partially demineralized root dentin matrix (PDM) or (2) autolysed, antigen-extracted root matrix (AAAD), including attached cementum. Composites of either PDM or antigen-extracted, autolysed, delipidized allogenic dentin matrix (AAAM) and recombinant human bone morphogenetic protein (rhBMP-2) were implanted in either normal or athymic mice. The percentage of muscle replaced by heterotopic bone was estimated by computer-assisted random point analysis. Implants of PDM and AAAD made from dysfunctional teeth exhibited little or no endogenous BMP activity and failed to induce new bone formation. Composites of 1 µg of rhBMP-2 per 70 mg of PDM carrier induced 61% replacement of muscle by bone formation; 1 µg of rhBMP-2 in 70 mg of AAAM matrix induced 78% replacement of muscle mass by bone; 2 or 5 µg of rhBMP-2 and 70 mg of AAAM carrier induced 100% replacement of thigh muscle mass by bone. In athymic mice, the areas of new bone were only slightly greater than those in normal mice. These observations suggest that root dentin prepared from extracted teeth may be recycled for use as a carrier of rhBMP-2 because it induces new bone formation in the periodontium.

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INTRODUCTION

Dentin matrix is osteoinductive and rich in bone morphogenetic protein (BMP).[1-3] BMP is a low molecular weight hydrophobic glycoprotein found in the organic matrix of both bone and dentin. BMP has the same physicochemical characteristics in dentin as in bone.[4-7] Classified as a local hormone, or morphogen, BMP forms a concentration gradient pattern leading cell development along a pathway of bone in orthotopic and heterotopic sites.[8-15]

Bone BMP[16] and dentin BMP[7] are assayed by implantation in heterotopic

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CASE REPORT Open Access

Alveolar ridge preservation with autologous particulated dentin—a case series

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Abstract

Introduction: Ridge preservation can be performed with autologous bone, alloplastic bone substitute material or a combination of both. Dentin is similar to bone in its chemical composition. In its use as bone substitute material, it undergoes a remodelling process and transforms to bone. The presented case report introduces a technique in which the extraction socket is augmented with autologous, particulated dentin.

Material and methods: The fractured, non-savable mesial incisor of the upper jaw was carefully extracted in axial direction. After the extraction, the tooth was cleared from remaining periodontal tissue. The vital pulp tissue or a root canal filling, enamel and cementum were also removed. Following the particulation of the remaining dentin in a bone mill, the dentin particles were immediately filled orthotope into the alveolar socket. The soft tissue closure was performed with a free gingival graft of the palate.

Results: After an observation period of 4 months, an implant was placed in the augmented area, which osseointegrated successfully and could be restored prosthodontically in the following. The results of this method showed a functional and aesthetic success.

Conclusion: The pre-implantological, autologous ridge preservation with dentin could be performed successfully. For the establishment of dentin as augmentation material for jaw augmentation procedures, a prospective, clinical trial is now necessary.

Keywords: Alveolar ridge preservation, Particulated dentin, Autologous augmentation, Bone augmentation, Bone substitute

Background

Subsequent to tooth extraction, a resorption of the host bone as defined by atrophy of the alveolar ridge can be observed. Sutton et al. classified the different degrees of alveolar ridge atrophy [32]. Bone resorption especially occurs in the frontal and premolar area of the jaw in the region of the thin buccal lamella. This may lead to a change in contour [11, 28]. Physiological reason for this atrophy is the periodontal ligament blending into the bone. Overall, a total clinically relevant loss of bone height of approximately 2–5 mm in the first 6 months can be observed in the vertical dimension [10, 20]. After 12 months, the alveolar ridge may lose up to 50% of its width. With regard to dental implants, this implicates that an implant insertion in a sufficient bone bed will often not be possible. In order to prevent this bone atrophy, different methods of alveolar ridge preservation have been described. The augmentation of extraction sockets with deproteinized bovine bone is clinically well established and has analysed in various studies [17, 18, 31]. Systematic reviews showed a preservation of the bone contour for this method [6, 15].

Today, clinical techniques like the socket-shield technique are performed [9]. Applying this technique, a vestibular slice of the tooth root is left in the alveolar socket during tooth extraction. The reason is to prevent the resorption of the vestibular bony lamella. Studies show the osseointegration of implants having been inserted in such areas, thus indicating the biocompatibility of autologous tooth material [8, 13, 16]. The application of autologous dentin as a bone

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ORIGINAL RESEARCH

CLINICAL ORAL IMPLANTS RESEARCH WILEY

Alveolar ridge preservation using autogenous whole-tooth versus demineralized dentin grafts: A randomized controlled clinical trial

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Abstract

Objective: The objective of this randomized controlled trial was to evaluate the radiographic changes and histologic healing following alveolar ridge preservation (ARP) using autogenous whole tooth (AWTG), test group, versus autogenous demineralized dentin graft (ADDG), control group.

Material and methods: Twenty non-molar teeth indicated for extraction were randomized into two groups (n = 10/group). Extracted teeth were prepared into AWTG or ADDG (0.6N HCl; 30 min), inserted into extraction sockets and covered by collagen membranes. Cone-beam computed tomography (CBCT) scans at baseline and six months were compared to assess ridge-dimensional changes. At six months, bone biopsies of engrafted sites were harvested and analyzed histomorphometrically.

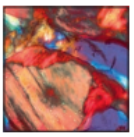
Results: All sites healed uneventfully. Reduction was 0.85 ± 0.38 mm and 1.02 ± 0.45 mm in ridge width, 0.61 ± 0.20 mm and 0.72 ± 0.27 mm in buccal and 0.66 ± 0.31 mm and 0.56 ± 0.24 mm in lingual ridge height for the AWTG and ADDG group, respectively ($p > .05$). Histologically, no inflammatory reactions were noticeable and all samples showed new bone formation. Qualitatively, graft-bone amalgamations were more pronounced in ADDG samples. Histomorphometrically, new bone, graft remnants and soft tissue occupied 37.55% ± 8.94%, 17.05% ± 5.58% and 45.4% ± 4.06% of the areas in the AWTG group and 48.4% ± 11.56%, 11.45% ± 4.13% and 40.15% ± 7.73% in the ADDG group of the examined areas, respectively ($p > .05$).

Conclusions: AWTG and ADDG are similarly effective in ARP. Yet, histologically ADDG seems to demonstrate better graft remodeling, integration and osteoinductive properties.

KEYWORDS

alveolar ridge preservation, autogenous, extraction, randomized controlled clinical trial, tooth-bone graft

Healing Dynamics Following Alveolar Ridge Preservation with Autologous Tooth Structure



Ziv Mazor, DMD[1]
Robert A. Horowitz, DDS[2]
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The objective of this clinical study was to assess the outcomes of autologous tooth structure in alveolar ridge preservation procedures. Extraction sites were grafted with autologous tooth structure prepared from the extracted teeth, and histologic samples were obtained at varying intervals to allow observation of bone-healing dynamics over time. Grafted areas were occupied by dentin particles that had begun to connect via bridges of woven bone at 3 months posthealing, and vital bone was in direct contact with residual particles with no inflammatory infiltrate. Further clinical investigation is warranted on the comparative effectiveness of autologous tooth structure against established bone-substitute biomaterials.
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Alveolar ridge preservation procedures that aim to limit postextraction ridge resorption have become mainstream dental procedures.[1] Nearly all available types of bone grafts and bone substitute biomaterials have been proposed for this indication and tested clinically.[1,2] Various types of allografts, xenografts, and alloplastic biomaterials have been recommended as viable alternatives to the use of autogenous grafts for ridge preservation due to the morbidity associated with the latter.[2] Nonetheless, an alternate source of autogenous mineralized tissue has been investigated for this indication: autologous dentin and cementum.[3–5]

This nonimmunogenic approach includes other benefits, such as immediate availability of the extracted tooth. This concept is not novel. The first approaches to using autologous tooth structure as a bone substitute date back to the late 1960s.[6] Bone induction has been shown after grafting with decalcified dentin implanted into oral, osseous, and muscle tissues.[6,7] In particular, Yeomans and Urist reported that the use of either decalcified dentin or bone as socket grafts demonstrated osteoinductive properties as compared to tendon or muscle grafts.[6] This research area was forgotten for nearly half a century until the recent interest in optimal extraction site

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ORIGINAL ARTICLE

Combining autologous particulate dentin, L-PRF, and fibrinogen to create a matrix for predictable ridge preservation: a pilot clinical study

Catherine Andrade[1] · Joaquin Camino[1] · Mauricio Nally[1] · Marc Quirynen[2] · Benjamín Martínez[3] · Nelson Pinto[1,2]

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Abstract

Objectives The aim of this study was to describe the histological and clinical outcome of "**d**entin block" (a mixture of autologous particulate dentin, leukocyte- and platelet-rich fibrin (L-PRF), and liquid fibrinogen) in alveolar ridge preservation.

Material and methods **Ten** extraction sockets were grafted with "**d**entin **b**lock," a mixture of particulate autologous dentin with chopped leukocyte-platelet-rich fibrin (L-PRF) membranes at a 1:1 ratio, and liquid fibrinogen as a binder. **Two** grafted sites were followed at 4 and 5 months, and 6 sites at 6 months. Biopsies were taken from the core of the grafted site for histologic and histomorphometric analysis.

Results All patients completed the study without any adverse event. The vertical and horizontal dimensions of the alveolar ridge were preserved or even increased after 4, 5, or 6 months and remained stable after 6 months of the implant placement. The histological examination revealed a median relative percentage of bone, dentin, and connective tissue of 57.0, 0.9, and 39.3%, respectively. A comparison of samples at different time points (4, 5, and 6 months) showed a progressive increase in the proportion of bone with a decrease in the proportion of dentin. The bone was compact with normal osteocytes and moderate osteoblastic activity. In **4 out of** 10 samples, no dentin was observed; in the other samples, it represented 1–5% (with geometric fragments).

Conclusions Dentin block showed to be a suitable bone substitute in an alveolar ridges preservation model.

Clinical relevance The promising results of dentin block as a bone substitute in alveolar ridge preservation could have an important clinical impact considering this biomaterial brings together the regenerative potential of three autologous products with excellent biological and clinical behavior, low risk of adverse effects, and feasible acquisition.

Keywords Bone substitute · Bone regeneration · Dentin · Dentin block · GBR · Ridge preservation

Introduction

The alveolar process is prone to major resorption in a vertical and horizontal dimension after tooth extraction [1, 2], primarily due to the loss of bundle bone. This may jeopardize future implant therapy [3], which requires an adequate three-dimensional osseous volume of the alveolar ridge, accompanied by good soft tissue architecture to provide an optimal esthetic, phonetic, and long-term functional result [4].

Various surgical techniques have been proposed to compensate for this resorption. Alveolar ridge preservation (ARP) techniques are widely used to compensate for this resorption. The application of grafting biomaterials into a fresh extraction socket has been thoroughly investigated in both animal and clinical studies [5–7]. These materials are used because they can possess one or more of these biological properties: osteogenesis, osteoinduction, and/or osteoconduction [8]. A systematic review from Vignoletti and co-workers [9] revealed that there are no clear guidelines on which biomaterial to select for this purpose. A recent meta-

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AUTOLOGOUS TOOTH GRAFT: A HISTOLOGICAL COMPARISON BETWEEN DENTIN MIXED WITH XENOGRAFT AND DENTIN ALONE GRAFTS IN SOCKET PRESERVATION

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The aim of this study is to compare the histological results after socket preservation between dentin mixed with xenograft and dentin alone in tooth graft procedure. Six patients were included in this prospective case series study and treated in three clinical centers using standardized clinical procedures. This clinical trial enrolled patients with three walls post-extractive defects requiring the restoration of bone dimension and shape in mandibular zone. The patients were divided in two groups: extracted teeth alone (first group) and extracted teeth mixed with equal quantity of xenograft (second group). The extracted tooth was cleaned and processed by a recently introduced automated device, that allows fragmentation and partial demineralization of the tooth matrix and used as graft material. The graft obtained in this way, was inserted at the time of the extraction. A covering membrane was used to protect the graft. Implants were placed after 4 months of healing. Bone biopsies of the all grafted sites were taken at the time of implant surgery, for histological analysis. Descriptive statistics was used to synthesize the results, using mean values and standard deviations. Six patients (5 women, mean age at surgery 50.3±12.1 years) were treated and after 4 months of healing both groups, grafts height appeared stable. No signs of infection were present. Bone biopsy were taken in all grafted sites (3 with group one and 3 with group two). The histologic analysis revealed no inflammatory or infective reaction against both groups. The histomorphometry results between the two groups are different. The first group show an amount of new bone greater than the second group (+85.29%) and minor quantity of residual graft (-83.59%). The dentin alone shows a larger amount of new bone.

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Demineralized deciduous tooth as a source of bone graft material: its biological and physicochemical characteristics

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BMP-2 and type I collagen preservation in human deciduous teeth after demineralization

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Abstract

Background: Great interest has recently been focused on tooth and tooth derivatives as suitable substrates for the treatment of alveolar bone defects. Here, we propose the use of demineralized baby teeth (BT) as potential grafting materials for bone augmentation procedures.

Methods: Particles of human BT (Ø < 1 mm) were demineralized by means of a chemical/thermal treatment. Demineralized BT particles were thoroughly characterized by scanning electron microscopy/energy dispersive X-ray analyses to evaluate the effects of the demineralization on BT topography and mineral phase composition, and by enzyme-linked immunosorbent assays (ELISA) to quantify collagen and bone morphogenetic protein-2 (BMP-2) protein contents. The response of SAOS-2 cells to exogenous BMP-2 stimulation was evaluated to identify the minimum BMP-2 concentration able to induce osteodifferentiation in vitro (alkaline phosphatase (ALP) activity).

Results: The demineralization treatment led to a dramatic decrease in relative Ca and P content (%) of ≈75% with respect to the native BT particles, while preserving native protein conformation and activity. Interestingly, the demineralization process led to a rise in the bioavailability of BMP-2 in BT particles, as compared to the untreated counterparts. The BMP-2 content found in demineralized BT was also proved to be very effective in enhancing ALP activity, thus in the osteodifferentiation of SAOS-2 cells in vitro, as confirmed by cell experiments performed upon exogenously added BMP-2.

Conclusions: In this study we demonstrate that the BMP-2 content found in demineralized BT is very effective in inducing cell osteodifferentiation, and strengthens the idea that BTs are very attractive bioactive materials for bone-grafting procedures.

Keywords

Baby teeth, demineralization, BMP-2, collagen

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Introduction

Over recent years, the field of biomaterials has made significant progress in the search for functional and bioactive materials for bone repair procedures and regeneration. Current clinical approaches for bone defect treatments involve the grafting of autologous (autograft), homologous (allograft), and heterologous (xenograft) bone.[1] Among them, autografts are considered the gold standard because they are biocompatible and non-immunogenic, and they contain every essential component to trigger osteoinduction, osteogenesis, and osteoconduction. As an autologous bone transplant involves the harvesting of bone from the patient's body, however, it relies on a relatively

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Bone Healing and Soft Tissue Contour Changes Following Single-Tooth Extraction: A Clinical and Radiographic 12-Month Prospective Study

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Preservation of alveolar bone volume following tooth extraction facilitates subsequent placement of dental implants and leads to an improved esthetic and functional prosthodontic result. The aim of the present study was to assess bone formation in the alveolus and the contour changes of the alveolar process following tooth extraction. The tissue changes after removal of a premolar or molar in 46 patients were evaluated in a 12-month period by means of measurements on study casts, linear radiographic analyses, and subtraction radiography. The results demonstrated that major changes of an extraction site occurred during 1 year after tooth extraction. (Int J Periodontics Restorative Dent 2003;23:313–323.)

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Sufficient alveolar bone volume and favorable architecture of the alveolar ridge are essential to obtain ideal functional and esthetic prosthetic reconstruction following implant therapy.[1] Knowledge about the healing process at extraction sites, including contour changes caused by bone resorption and remodeling, is essential. Loss of alveolar bone may occur prior to tooth extraction because of periodontal disease, periapical pathology, or trauma to teeth and bone. Damage of the bone tissues during tooth extraction procedures may also result in bone loss. Finally, alveolar bone atrophy after tooth extraction is a well-known phenomenon.[2,3]

Histologic investigations in animals[4] and humans[5,6] have described the healing of extraction sockets. The gross morphologic changes of the alveolar processes after loss of teeth have been evaluated by cephalometric analyses[2,7,8] and measurements on study casts.[9,10] The resorption of the alveolar process after tooth extraction in the maxilla or mandible is significantly larger at the buccal aspect than at

CLINICAL ORAL IMPLANTS RESEARCH

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A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans

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Conflicts of interest
The authors declare no conflict of interest.

Key words: alveolar bone, dimensional change, extraction, hard tissue, human, removal of teeth, resorption, soft tissue, systematic review

Abstract

Background: Removal of teeth results in both horizontal and vertical changes of hard and soft tissue dimensions. The magnitude of these changes is important for decision-making and comprehensive treatment planning, with provisions for possible solutions to expected complications during prosthetic rehabilitation.

Objectives: To review all English dental literature to assess the magnitude of dimensional changes of both the hard and soft tissues of the alveolar ridge up to 12 months following tooth extraction in humans.

Methods: An electronic MEDLINE and CENTRAL search complemented by manual searching was conducted to identify randomized controlled clinical trials and prospective cohort studies on hard and soft tissue dimensional changes after tooth extraction. Only studies reporting on undisturbed post-extraction dimensional changes relative to a fixed reference point over a clearly stated time period were included. Assessment of the identified studies and data extraction was performed independently by two reviewers. Data collected were reported by descriptive methods. Weighted means and percentages of the dimensional changes over time were calculated where appropriate.

Results: The search provided 3954 titles and 238 abstracts. Full text analysis was performed for 104 articles resulting in 20 studies that met the inclusion criteria. In human hard tissue, horizontal dimensional reduction (3.79 ± 0.23 mm) was more than vertical reduction (1.24 ± 0.11 mm on buccal, 0.84 ± 0.62 mm on mesial and 0.80 ± 0.71 mm on distal sites) at 6 months. Percentage vertical dimensional change was 11–22% at 6 months. Percentage horizontal dimensional change was 32% at 3 months, and 29–63% at 6–7 months. Soft tissue changes demonstrated 0.4–0.5 mm gain of thickness at 6 months on the buccal and lingual aspects. Horizontal dimensional changes of hard and soft tissue (loss of 0.1–6.1 mm) was more substantial than vertical change (loss 0.9 mm to gain 0.4 mm) during observation periods of up to 12 months, when study casts were utilized as a means of documenting the changes.

Conclusions: Human re-entry studies showed horizontal bone loss of 29–63% and vertical bone loss of 11–22% after 6 months following tooth extraction. These studies demonstrated rapid reductions in the first 3–6 months that was followed by gradual reductions in dimensions thereafter.

The periodontium is an important structure that supports the tooth and is affected by any changes that the tooth may undergo, including eruption and extraction (Cohn 1966; Pietrokovski & Massler 1967, 1971). The alveolar process is a tooth-dependent tissue; the shape and volume of the alveolar process is influenced by tooth form, as well as the direction of eruption of the tooth (Marks 1995; Marks & Schroeder 1996), and the presence or absence of teeth (Tallgren 1972). Similarly, gingival tissues undergo changes together with eruption and eventual exfoliation or extraction of the tooth. Subsequent to removal of a tooth, the periodontium undergoes atrophy (Cohn 1966; Schropp et al. 2003), with the complete loss of attachment apparatus including cementum, periodontal ligament fibres and bundle bone (Araujo & Lindhe 2005).

Tooth extraction is one of the most widely performed dental procedures. In general, post-extraction healing of both the hard and soft tissues proceeds uneventfully. However, the removal of a tooth will generally result in some alveolar bone loss, as well as structural

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Preservación de reborde en el sector posterior: Una revisión sistemática

Ridge preservation in posterior sites: A systematic review.

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RESUMEN

Objetivo: Evaluar mediante una revisión sistemática los cambios dimensionales producidos después de una extracción dental en el sector posterior empleando técnicas de preservación de reborde alveolar y cicatrización convencional. ***Material y métodos:*** Dos revisores independientes y calibrados realizaron una búsqueda electrónica de ensayos clínicos aleatorizados publicados hasta diciembre del 2018 en Pubmed y Cochrane la cual fue complementada con una búsqueda manual en las revistas de mayor impacto en Periodoncia e Implantología según el ISI Web of Science. La evaluación del riesgo de sesgo en los estudios incluidos fue realizada siguiendo el manual de Cochrane para intervenciones de revisiones sistemáticas Versión 5.1.0. ***Resultados:*** Un total de 435 piezas posteriores, entre premolares y molares, fueron evaluadas en los estudios incluidos a partir de los 3 meses post extracción. Se obtuvo valores estadísticamente significativos para el grupo que realizó la preservación de reborde (pérdida ósea vertical desde -0,25 hasta -1,53 mm y a nivel horizontal desde -0,91 hasta -2,87 mm) en comparación al grupo control (pérdida ósea vertical desde -0,71 hasta -3,1 mm y a nivel horizontal desde -2,26 hasta -3,96 mm). El biomaterial más utilizado fue el xenoinjerto más membrana de colágeno. Los estudios incluidos manifestaron un bajo riesgo de sesgo. ***Conclusiones:*** La preservación de reborde en sitios posteriores es recomendada porque conduce a mantener los tejidos duros y blandos, reduce la neumatización sinusal y minimiza la reabsorción del hueso crestal simplificando así los procedimientos para una buena posición tridimensional del implante.

PALABRAS CLAVE: Implantes dentales; extracción dental; diente molar; proceso alveolar; reabsorción ósea; revisión sistemática.

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Original Article

Comparative Alveolar Ridge Preservation Using Allogenous Tooth Graft versus Free-dried Bone Allograft: A Randomized, Controlled, Prospective, Clinical Pilot Study

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Abstract

Background: For the first time in India, allografts from human extracted teeth were prepared. A randomized, prospective, clinicoradiographical, histological study was conducted to evaluate their efficacy in comparison with freeze-dried bone allograft (FDBA) in alveolar ridge preservation. **Materials and Methods:** Graft preparation: with written consent, teeth were collected from three donors (full mouth extraction cases). Once donors' serums were tested negative for HIV, HBV, HCV, and Venereal disease research laboratory (VDRL), mineralized whole tooth allograft (WTA) and dentin allograft (DA) were prepared using the standard protocol of Tissue Bank at Tata Memorial Hospital, Mumbai, India. **Study Design:** In this randomized controlled trial, 15 patients undergoing extraction of at least four teeth were selected. In each patient after atraumatic extractions, one socket was grafted with WTA, second with DA, third with FDBA, and fourth was left ungrafted (control site). All the sites were covered with chorion membrane. To estimate three-dimensional alveolar crest changes, cone beam computed tomography scans were taken immediately after grafting and 4 months postoperatively. Bone biopsies using 3 mm trephine bur were obtained from four patients at the time of implant placement and evaluated histologically. **Results:** Clinically uneventful healing was observed at all sites. Compared to other sites, WTA and DA consistently showed superior results demonstrating least reduction in alveolar crest height and width which was statistically significant ($P < 0.05$). Between WTA and DA sites, there was no statistically significant difference. Histological analysis also confirmed more new bone formation at WTA and DA sites. **Conclusions:** Rather than disposing extracted human teeth as a biomedical waste (common practice), they can be collected from suitable systemically healthy donors. With the help of tissue bank, they can be processed into an allograft, serving as an excellent alternative to conventional allografts.

Keywords: *Allografts, bone graft(s), bone regeneration, imaging, ridge preservation*

Introduction

Bone grafts have been used for decades in reconstruction and regeneration of alveolar bone defects formed by traumatic extractions, periodontal or endodontic origin. However, complete preservation and reconstructions of alveolar ridge to its original dimensions still seem to be a distant goal. Autogenous bone graft being osteoinductive, osteoconductive, and osteoproliferative is considered a gold standard.[1] However, most of time its quantity is inadequate due to limited availability of donor site. Thus to suffice the required quantity of bone graft material, numerous alternatives are investigated for bone regeneration over the years.

Dentin and bone have similarities in terms of structural and biochemical properties. This led an idea of using dentin as a bone graft material..[2] Demineralized dentin matrix (DDM) has been shown to possess osteogenic capacity.[3] Use of autogenous dentin graft was developed and clinically applied from 2003 onward.[4] It has shown promising clinical and histological results as an alternative to autogenous bone graft. However, it still has its own sets of limitations such as:

1. Patient may not accept his/her own tooth as it is diseased and has to be extracted
2. Quantity is dependent on the number of teeth indicated for extraction, and quality of graft depends on the nature of extracted teeth
3. Chairside graft preparation is tedious as well as time consuming.

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CLINICAL ORAL IMPLANTS RESEARCH

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Surgical protocols for ridge preservation after tooth extraction. A systematic review

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Key words: bone grafts, bone regeneration, bone substitutes, dental implants, ridge preservation, systematic review, tooth extraction

Abstract

Objective: This systematic review aims to evaluate the scientific evidence on the efficacy in the surgical protocols designed for preserving the alveolar ridge after tooth extraction and to evaluate how these techniques affect the placement of dental implants and the final implant supported restoration.

Material and methods: A thorough search in MEDLINE-PubMed, Embase and the Cochrane Central Register of controlled trials (CENTRAL) was conducted up to February 2011. Randomized clinical trials and prospective cohort studies with a follow-up of at least 3 months reporting changes on both the hard and soft tissues (height and/or width) of the alveolar process (mm or %) after tooth extraction were considered for inclusion.

Results: The screening of titles and abstracts resulted in 14 publications meeting the eligibility criteria. Data from nine of these 14 studies could be grouped in the meta-analyses. Results from the meta-analyses showed a statistically significant greater ridge reduction in bone height for control groups as compared to test groups (weighted mean differences, WMD = −1.47 mm; 95% CI [−1.982, −0.953]; $P < 0.001$; heterogeneity: $I^2 = 13.1\%$; χ^2 *P*-value = 0.314) and a significant greater reduction in bone width for control groups compared to the test groups (WMD = −1.830 mm; 95% CI [−2.947, −0.732]; $P = 0.001$; heterogeneity: $I^2 = 0\%$; χ^2 *P*-value = 0.837). Subgroup analysis was based on the surgical protocol used for the socket preservation (flapless/flapped, barrier membrane/no membrane, primary intention healing/no primary healing) and on the measurement method utilized to evaluate morphological changes. Meta-regression analyses demonstrated a statistically significant difference favoring the flapped subgroup in terms of bone width (meta-regression; slope = 2.26; 95% IC [1.01; 3.51]; $P = 0.003$).

Conclusions: The potential benefit of socket preservation therapies was demonstrated resulting in significantly less vertical and horizontal contraction of the alveolar bone crest. The scientific evidence does not provide clear guidelines in regards to the type of biomaterial, or surgical procedure, although a significant positive effect of the flapped surgery was observed. There are no data available to draw conclusions on the consequences of such benefits on the long-term outcomes of implant therapy.

The alveolar processes in the jaws are tooth-dependent structures that will undergo significant structural changes whenever the teeth are lost. The dynamics and magnitude of these changes have been investigated in the dog model (Kuboki et al. 1988; Devlin et al. 1997; Cardaropoli et al. 2003; Araujo & Lindhe 2005; van Kesteren et al. 2010) as well as in humans (Amler et al. 1960; Evian et al. 1982; Devlin & Sloan 2002; Trombelli et al. 2008). These investigations have identified the key processes of tissue modelling and remodelling after tooth extraction that eventually lead to a reduction on the overall ridge dimensions with significant changes in both the buccal and lingual bone crests.

The amount of vertical and horizontal resorption of the socket walls has been investigated with different methods, ranging from studying and measuring cast models (Pietrokovski & Massler 1967; Johnson 1969; Schropp et al. 2003), to radiographic analysis

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Randomized and Controlled Clinical Trial of Bone Healing After Alveolar Ridge Preservation Using Xenografts and Allografts Versus Plasma Rich in Growth Factors

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The aim of this study was to compare bone regeneration in the anterior maxilla between bone substitutes and autologous platelet concentrate in alveolar ridge preservation. Forty patients requiring tooth extraction in the anterior maxilla were randomly allocated to the following 4 treatment modalities: spontaneous healing (control), natural bovine bone mineral covered with resorbable native collagen membrane (BBM/CM), freeze-dried bone allograft covered with resorbable native collagen membrane (FDBA/CM), and plasma rich in growth factors (PRGF) alone. Bone biopsies and histomorphometrical analysis were performed after 3 months of healing. The following parameters were assessed: newly formed mineralized tissue, newly formed nonmineralized tissue, and residual bone-grafting material (if applicable). Statistical analysis was performed to provide descriptive analysis and to compare the parameters of the bone regeneration between the study groups. Histomorphometrical analysis revealed the highest new mineralized tissue formation in the PRGF group. Statistically significant differences in new mineralized tissue formation were found between control/PRGF (46.4% ± 15.2% vs 75.5% ± 16.3%), control/(BBM/CM) (46.4% ± 15.2% vs 20.3% ± 21.9%), control/(FDBA/CM) (46.4% ± 15.2% vs 7.2% ± 8.6%), PRGF/(BBM/CM) (75.5% ± 16.3% vs 20.3% ± 21.9%), and PRGF/(FDBA/CM) (75.5% ± 16.3% vs 7.2% ± 8.6%) groups. The new mineralized tissue formation was in the following order: PRGF > control > BBM > FDBA. Alveolar ridge preservation in the esthetic zone with PRGF was the most effective for bone regeneration of the alveolar ridge.

Key Words: tooth extraction, bone regeneration, alveolar ridge preservation, platelet-rich plasma, PRGF

INTRODUCTION

The implant is currently accepted as the preferred treatment option for tooth replacement, and long-term success after implant therapy requires maintaining a sufficient amount of alveolar bone volume. More recently, dental implantology has shifted from implant placement in a fully healed bone to treatment protocols that reduce overall treatment time, such as immediate implant placement.[1] In their systematic review, Tan et al[2] assessed postextraction alveolar ridge dimensional changes.[2] In that review, different studies showed that vertical hard-tissue resorption was 11%–22% with horizontal bone loss of 29%–63%, whereby two-thirds of the tissue was lost during the first 3 months after tooth extraction.[3–6] Bone resorption is greater on the buccal bone plate and results in the palatal/lingual shift of the alveolar crest, especially in the thin periodontal biotype.[7] The more pronounced resorption of the buccal alveolar plate could be related to its lower thickness and the fact that it is composed mostly of bundle bone.[8–10] Bundle bone is a tooth-dependent structure and is lost after tooth removal. Thus, several alveolar ridge-preservation techniques have been proposed for preserving the alveolar ridge dimensions.[3,4] Both alveolar ridge preservation and the quality of regenerated bone are factors that may affect the long-term success of implant-supported rehabilitation.[11] Although the dimensions of alveolar bone are important for a proper 3-dimensional position of the implant, the quantity of newly regenerated bone is related to successful osseointegration and long-term stability of dental implants.[11,12]

Many different bone-grafting materials have been proposed for alveolar ridge preservation.[13–15] Jung et al[16] suggested a clinical decision tree for alveolar ridge preservation in the esthetic zone and proposed preservation of the extraction socket in clinical cases with more than 50% of the buccal bone present. Meanwhile, in cases of severe bone loss (more than 50%), researchers have suggested performing a guided bone-regeneration procedure. With regard to the definition of terms, there are 2 different approaches to maintaining the alveolar ridge profile: maintaining alveolar ridge dimensions (socket preservation) and increasing the ridge volume (guided bone regeneration).[17] Although there are many studies investigating postextraction dimensional changes of

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materials

MDPI

Article

Socket Preservation Using a (Dense) PTFE Barrier with or without Xenograft Material: A Randomized Clinical Trial

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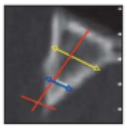
Abstract: When alveolar preservation procedures are not performed after tooth extraction, aesthetic and functional impairment could occur. Guided bone regeneration using polytetrafluoroethylene (PTFE) membranes has proven to be a simple alternative treatment that results in good maintenance of the alveolar bone for mediate/late implant placement. Therefore, this study compared the effect of alveolar preservation with the use of dense PTFE membranes, with and without xenograft material by Computerized tomography-based body composition (CTBC) analysis, after four months of the socket preservation procedure. A total of 29 teeth indicated for extraction. In the test group, the sockets were filled with bone graft biomaterial and subsequently coated with a dense PTFE membrane. In the control group, the sockets were filled with the blood clots and subsequently coated with a dense PTFE membrane. The results we found on the changes of the bone width and height after the procedures were: buccal plate: control group 0.46 mm, test group 0.91 mm; alveolar height: control group −0.41 mm, test group 0.35 mm; cervical third: control group −0.89 mm, test group −0.11 mm; middle third: control group −0.64, test group −0.50; and apical third: control group 0.09 mm, test group −0.14 mm. The use of a xenograft in conjunction with d-PTFE membranes proved to be superior to the use of the same membrane and blood clot only in regions of the crest, middle third, and alveolar height.

Keywords: biomaterials; guided bone regeneration; socket preservation

1. Introduction

Socket preservation after tooth extraction is a constant challenge for clinicians, given the importance of maintaining sufficient bone height and thickness to assist in oral rehabilitation, with or without implants. The natural bone remodeling that occurs after an extraction leads to cosmetic and functional defects, and these defects can be so severe that the placement of implants or conventional dentures can be difficult, or even impossible, without the use of some type of grafting procedure [1,2]. This socket resorption refers to the remodeling that occurs after tooth extraction, and it may result in up to 50% bone resorption, with the magnitude of horizontal resorption usually being more pronounced than the vertical resorption [3]. Socket preservation by any procedure, performed at the time of extraction for the purpose of minimizing resorption of the bone crest and buccal plate and maximizing bone formation in the alveoli, is very important. This principle, called osteopromotion, can be very successful irrespective of the cause of tooth loss [4]. On the other hand, the principles of osteoconductivity provide the space and framework for cell substrate and biochemical events to enable bone formation to occur [5].

A Study of the Fate of the Buccal Wall of Extraction Sockets of Teeth with Prominent Roots



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The objective of this investigation was to determine the fate of thin buccal bone encasing the prominent roots of maxillary anterior teeth following extraction. Resorption of the buccal plate compromises the morphology of the localized edentulous ridge and makes it challenging to place an implant in the optimal position for prosthetic restoration. In addition, the use of Bio-Oss as a bone filler to maintain the form of the edentulous ridge was evaluated. Nine patients were selected for the extraction of 36 maxillary anterior teeth. Nineteen extraction sockets received Bio-Oss, and seventeen sockets received no osteogenic material. All sites were completely covered with soft tissue at the conclusion of surgery. Computerized tomographic scans were made immediately following extraction and then at 30 to 90 days after healing so as to assess the fate of the buccal plates and resultant form of the edentulous sites. The results were assessed by an independent radiologist, with a crest width of 6 mm regarded as sufficient to place an implant. Those sockets treated with Bio-Oss demonstrated a loss of less than 20% of the buccal plate in 15 of 19 test sites (79%). In contrast, 12 of 17 control sockets (71%) demonstrated a loss of more than 20% of the buccal plate. In conclusion, the Bio-Oss test sites outperformed the control sites by a significant margin. No investigator was able to predict which site would be successful without the grafting material even though all were experienced clinicians. This leads to the conclusion that a patient has a significant benefit from receiving grafting materials at the time of extraction. (Int J Periodontics Restorative Dent 2006;26:19–29.)

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The application of osseointegrated implants in the anterior maxilla has created pointed interest in obtaining an optimal esthetic result. A prominent root position is almost always accompanied by a thin, frail buccal plate that may be damaged during tooth removal, resulting in a deformed edentulous ridge whose bone morphology would require augmentation to place an implant in an optimal position for prosthetic restoration (Fig 1a). The shift in paradigm from the fixed partial denture to the implant has placed new emphasis on management of the extraction wound.

Alveolar ridge resorption following tooth removal is a physiologically undesirable and possibly avoidable phenomenon[1] (Figs 1b and 1c). Significant knowledge exists of the healing process of extraction wounds, including contour changes caused[2] by bone resorption and the cascade of histologic events in both animals and humans.[3–5] The resorption of the alveolar process following tooth extraction in both jaws is significantly greater on the buccal aspect than the lingual or palatal, so that the reduction in width of the maxillary alveolar ridge is greater than the loss of height.[6–8] The significant loss of tissue contour takes place

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Ridge preservation with the use of Bio-Oss® collagen: A 6-month study in the dog

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Key words: biomaterial, extraction socket, grafting, ridge preservation

Abstract

Background: In previous short-term studies, it was observed that while the placement of biomaterial in alveolar sockets may promote bone formation and ridge preservation, the graft may in fact also delay healing.

Aim: The objective of the present experiment was to evaluate the more long-term effect on hard tissue formation and the amount of ridge augmentation that can occur by the placement of a xenogeneic graft in extraction sockets of dogs.

Material and methods: Five beagle dogs were used. The third mandibular premolars were hemi-sected. The distal roots were carefully removed. A graft consisting of Bio-Oss® collagen was placed in one socket while the contra-lateral site was left without grafting. After 6 months of healing, the dogs were euthanized and biopsies were sampled. From each experimental site, four ground sections – two from the mesial root and two from the healed socket – were prepared, stained and examined under a microscope.

Results: The placement of Bio-Oss® collagen in the fresh extraction socket served as a scaffold for tissue modeling but did not enhance new bone formation. In comparison with the non-grafted sites, the dimension of the alveolar process as well as the profile of the ridge was better preserved in Bio-Oss®-grafted sites.

Conclusion: The placement of a biomaterial in an extraction socket may modify modeling and counteract marginal ridge contraction that occurs following tooth removal.

During healing following tooth extraction, the edentulous site will undergo a marked change (Amler 1969; Cardaropoli et al. 2003; Schropp et al. 2003; Araújo & Lindhe 2005). The walls of the socket will be reduced, and the change of the buccal wall will be more pronounced than that of its lingual/palatal counterpart (Pietrokovski & Massler 1967; Araújo & Lindhe 2005). In addition, the space previously occupied by the root of the tooth and its periodontal ligament will be replaced mainly by the bone marrow (Cardaropoli et al. 2003; Araújo & Lindhe 2005).

It was proposed that the placement of implants in a fresh extraction socket could offset tissue change following tooth loss (Paolantonio et al. 2001). Recent studies in humans and experiments in dogs were unable to document the validity of this hypothesis (e.g. Botticelli et al. 2004, 2006; Araújo et al. 2005).

Various graft materials including autogenous, allogenous, xenogeneic and alloplastic bone graft were used in attempts to preserve the alveolar ridge following tooth extraction (Diès et al. 1996; Becker et al. 1998; Artzi et al. 2000; Froum et al. 2002, 2004; Carmagnola et al. 2003; Iasella et al.

Ridge Preservation with Freeze-Dried Bone Allograft and a Collagen Membrane Compared to Extraction Alone for Implant Site Development: A Clinical and Histologic Study in Humans

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Background: Tooth extraction typically leads to loss of ridge width and height. The primary aim of this 6-month randomized, controlled, blinded, clinical study was to determine whether ridge preservation would prevent post-extraction resorptive changes as assessed by clinical and histologic parameters.

Methods: Twenty-four patients, 10 males and 14 females, aged 28 to 76 (mean 51.5 ± 13.6), requiring a non-molar extraction and delayed implant placement were randomly selected to receive either extraction alone (EXT) or ridge preservation (RP) using tetracycline hydrated freeze-dried bone allograft (FDBA) and a collagen membrane. A replaced flap, which did not completely cover the sockets, was used. Following extraction, horizontal and vertical ridge dimensions were determined using a modified digital caliper and an acrylic stent, respectively. Prior to implant placement, a 2.7 × 6.0 mm trephine core was obtained and preserved in formalin for histologic analysis.

Results: The width of the RP group decreased from 9.2 ± 1.2 mm to 8.0 ± 1.4 mm ($P<0.05$), while the width of the EXT group decreased from 9.1 ± 1.0 mm to 6.4 ± 2.2 mm ($P<0.05$), a difference of 1.6 mm. Both the EXT and RP groups lost ridge width, although an improved result was obtained in the RP group. Most of the resorption occurred from the buccal; maxillary sites lost more width than mandibular sites. The vertical change for the RP group was a gain of 1.3 ± 2.0 mm versus a loss of 0.9 ± 1.6 mm for the EXT group ($P<0.05$), a height difference of 2.2 mm. Histologic analysis revealed more bone in the RP group: about 65 ± 10% versus 54 ± 12% in the EXT group. The RP group included both vital bone (28%) and non-vital (37%) FDBA fragments.

Conclusions: Ridge preservation using FDBA and a collagen membrane improved ridge height and width dimensions when compared to extraction alone. These dimensions may be more suitable for implant placement, especially in areas where loss of ridge height would compromise the esthetic result. The quantity of bone observed on histologic analysis was slightly greater in preservation sites, although these sites included both vital and non-vital bone. The most predictable maintenance of ridge width, height, and position was achieved when a ridge preservation procedure was employed. *J Periodontol 2003;74:990-999.*

KEY WORDS

Alveolar ridge; bone resorption/prevention and control; clinical trials, controlled; clinical trials, randomized; collagen/therapeutic use; follow-up studies; membranes, barrier; tooth extraction/adverse effects.

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TRANSFORMATION OF FIBROBLASTS BY ALLOGENEIC AND XENOGENEIC TRANSPLANTS OF DEMINERALIZED TOOTH AND BONE*

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(Received for publication 20 July 1970)

In postfetal life after embryonic differentiation has ceased, some cells of the connective tissue still remain in an undifferentiated state which persists lifelong. These primitive dormant cells have a remarkable attribute—they can be readily induced to differentiate by experimental means.

Under a certain set of conditions, grafts of demineralized matrix of dentin or bone in adult animals invariably and rapidly changed the phenotype of fibroblasts adjacent to the transplant. The visible and biochemical characters of the altered cells were changed so profoundly under these artificial conditions that we shall refer to the phenomenon as transformation. Under other circumstances cells of the graft survived but were not transformed.

The change from normal into cancer cell can be brought about by many different experimental procedures. In animals the change of normal cell into a normal cell of different sort has been accomplished only in a single cell type, the fibroblast (mesenchyma, stem cell of connective tissue). After transformation, the responding fibroblasts emerge as chondroblasts or osteoblasts and their fate is altered permanently.

In the present experiments useful and simple techniques to study transformation in vivo were developed. The results of allogeneic and xenogeneic transplantation are presented in this paper.

There are two distinctive experimental methods to alter the phenotype of competent fibroblasts; these consist of bringing them in contact with, respectively, (*a*) osteogenic epithelium or (*b*) demineralized matrix of tooth and bone.

The remarkable and unique mutability of fibroblasts which permits this radical change of their phenotype was found out in the dog (1). The surgical approximation of bladder epithelium with fascias of the trunk or limb evoked large amounts of bone which was evident in 10–12 days; it is noteworthy that

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Analysis of the Inorganic Component of Autogenous Tooth Bone Graft Material

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This study was performed to identify the calcium phosphate minerals, chemical element and Ca/P ratio and to examine the surface structure of autogenous tooth bone grafting material (AutoBT) which recently developed and applied clinically as a bone graft materials. The analytical results showed that AutoBT is composed of low-crystalline hydroxyapatite (HA) and possibly other calcium phosphate minerals, which is similar to the minerals of human bone tissues. And the dental crown portion was composed of high-crystalline calcium phosphate minerals (mainly HA) with higher Ca/P ratio while the root portion was mainly composed of low-crystalline calcium phosphates with relatively low Ca/P ratio.

Keywords: Bone Graft Material, Calcium Phosphate, Tooth.

RESEARCH ARTICLE

1. INTRODUCTION

Since 1993, we have conducted experiments to develop bone graft materials using human teeth, and we have obtained a Korean patent. Later, the development of bone graft materials using animal teeth was obtained a U.S. patent. The bone graft materials developed using the animal or human teeth were termed tooth-ash. The tooth-ash mainly consisted of a hydroxyapatite (HA) mineral.[1–7]

Based on the results of the previous studies, autogenous tooth bone graft materials (AutoBT) were commercialized in 2008, and the positive clinical results have been reported.[8] Therefore, this study was conducted to provide more detail information on AutoBT materials to clinicians in terms of their mineral composition as well as their surface structure.

2. EXPERIMENTAL DETAILS

2.1. Materials

Teeth extracted from patients that had been stored in ethyl alcohol and consigned to the Korea tooth bank. In order to analyze the surface structure and mineral components of the teeth, each tooth was divided into the two parts: the crown and the root. The crown consisted of enamel and dentin and the root consisted of dentin and cementum.

The powder samples of the two parts were prepared as bone graft materials: fresh sample, and AutoBT powder. Fresh samples (sample 1) were prepared by removing the soft tissues attached to the extracted teeth. The soft tissue removed samples were freeze-dried. The AutoBT powder (sample 2) was prepared by removing soft tissues, washing, defattening, partial decalcification, and freeze-drying. The two samples were divided into the crown and root portions and kept in a drying oven at 100 °C.

2.2. Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray Spectroscopy (EDS) Analysis

The surface structure of enamel, dentin, and cementum of a human tooth was examined using SEM (S-4800, Hitachi, Japan). For SEM study, the surface of the fresh sample was coated with 7 nm thick platinum (Pt) coating.

The chemical element and Ca/P ratio of each part of the tooth were quantitatively examined using EDS (X'Pert PRO, PANalytica, Netherlands) attached to SEM. The samples (fresh sample and AutoBT) used for the analysis of the composition ratio were prepared without Pt coating.

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Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology

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Development of a novel bone grafting material using autogenous teeth

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We developed a novel bone grafting material that incorporates autogenous teeth (AutoBT), and provided the basis for its clinical application. AutoBT contains organic and inorganic mineral components and is prepared from autogenous grafting material, thus eliminating the risk of an immune reaction that may lead to rejection. AutoBT was used at the time of implant placement, simultaneously with osteoinduction surgery, and excellent bony healing by osteoinduction and osteoconduction was confirmed. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109:496-503)**

Diverse biomaterials have been used in dental surgery and, with continuous research and development as well as academic advancements, a variety of new biomaterials have been commercialized. In oromaxillofacial surgery, periodontal surgery, implant surgery, and diverse other fields, grafting biomaterials are used to repair hard and soft tissue defects, in conjunction with guided tissue regeneration and guided bone regeneration, and in esthetic and reconstructive plastic surgery.

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Autogenous bone is an ideal material for the reconstruction of hard tissue defects, because it promotes osteogenesis, osteoinduction, osteoconduction, and rapid healing, but it does induce immune rejection. However, the disadvantages of autogenous bone as a grafting material are that the harvest volume is limited, resorption is unavoidable, and a second defect is induced in the donor area. To overcome these limitations, allogeneic bone, xenogeneic bone, and synthetic bone have been used in clinical practice; nevertheless, efforts have continued to develop more ideal bone grafting materials.[1] However, owing to concerns regarding the spread of infection and the high cost associated with allogeneic or xenogeneic bone, clinicians and patients may opt against these sources of grafting material. Synthetic bone, in contrast, is relatively inexpensive and involves no risk of disease, but it lacks the ability to promote osteogenesis and osteoinduction, and thus its utility is limited for the formation of viable bone.

We have been conducting research on the development of biomaterials using human teeth since 1993, and we recently reported the results of several of our advanced studies.[2-23] We obtained a Korean patent based on this research, and obtained an American patent for developing bone grafting materials using animal teeth.[24,25] Furthermore, the feasibility of repairing hard tissue defects using bone grafting material

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Induction of cartilage and bone by dentin demineralized in citric acid

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The capacity of a roll of dentin demineralized by either 0.6N HCl, pH 1 for 3 minutes or 3 hours, or by 3M (9N) citric acid, pH 1, for 3 minutes, to induce cartilage and bone when implanted in muscle, was investigated. Serial sections of specimens were examined 7, 10, 14, 17, and 21 days after implantation, and randomly selected sections analyzed histomorphometrically. Cartilage was induced on the internal aspect of the citric acid-demineralized dentin roll, but significantly less than that induced after demineralization with HCl. The quantity of bone deposited subsequently did not significantly exceed the amount of cartilage that preceded it in relation to any of the preparations used. The results suggest that citric acid-demineralized dentin induces chondrogenesis and osteogenesis when implanted in muscle, but does so less effectively than does HCl-demineralized dentin, and only within the confines of a microenvironment. It is therefore unlikely that citric acid demineralization of root surface results in induction of cementum by this mechanism.

(Accepted for publication November 1, 1985)

Introduction

Bone and dentin matrix that has been demineralized with 0.6 N HCl induces endochondral ossification when implanted subcutaneously or into muscle (Urist 1965, Yeomans & Urist 1967, Bang & Urist 1967, Dubuc & Urist 1967, Urist et al. 1968, Huggins & Urist 1970, Urist 1971, Reddi & Huggins 1972, Bang 1973, Reddi & Huggins 1973, Reddi 1974, Reddi & Huggins 1975, Reddi & Anderson 1976, Weiss & Reddi 1980, Reddi 1981, Sampath, De Simone & Reddi 1982, Urist et al. 1982, Urist, De Lange & Finerman 1983, Somerman et al. 1983, Sampath & Reddi 1984). A constituent of the organic matrix of bone, bone morphogenetic protein (BMP) (Urist et al. 1982, Urist et al. 1983), and the nature of the charge on the surface of the particles (Reddi 1981, Sampath & Reddi 1984), have both been implicated in the process of induction.

A number of investigators (Register 1973, Register & Burdick 1975, 1976, Crigger et al. 1978, Nilveus & Egelberg 1980, Bogle et al. 1981, Nalbandian & Cote 1982) have reported increased formation of cementum during healing of experimental wounds in the periodontium following demineralization of exposed root surface by citric acid, pH 1, for 3 min as compared with undemineralized controls. It is therefore possible that demineralization of the root surface with citric acid could induce cementogenesis during healing.

The purpose of the present study was to compare the capacity of dentin that had

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Bone induction of human tooth and bone crushed by newly developed automatic mill

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A novel automatic mill of teeth and bone has been developed for bone engineering. A human frozen-tooth and/or a human frozen-bone block were put into the Zirconium oxide (ZrO_2) ceramics vessel of the machine, and crushed for 1 min with 20 saline-ice blocks (1 × 1 × 1 cm^3/block) at 12000 rpm of ZrO_2 blade. The crushed granules were demineralized completely in 2% HNO_3 solution for 20 min, and rinsed in cold saline. We named each biomaterial after the acid treatment and washing, demineralized dentin matrices (DDM), demineralized bone matrices (DBM). Five wisdom teeth (total wet volume: 10.0 g) were crushed, decalcified, and lyophilized. The distribution of freeze-dried DDM granules was fine granules (0.5–1.0 mm: 0.27 g), moderate (1.0–2.0 mm: 0.46 g), and large (2.0–5.0 mm: 0.64 g). The fine granules of human DDM or DBM were implanted into the subcutaneous tissue of 4 week-old nude mice, and their tissue-inductive properties were estimated at 4 weeks after implantation histologically. The explanted samples were demineralized, embedded in paraffin, and sectioned. The specimens were stained with hematoxylin and eosin. We confirmed that DDM induced bone and cartilage independently, and DBM induced cartilage, bone and marrow at 4 weeks in the back skin of nude mice. These results indicated that our material preparation system by the novel mill with a vessel and a blade of ZrO_2 under ice-cooling maintained the bone-inducing activity of human dentin and bone.

Key-words : Human, Dentin, Bone, Demineralization, Bone induction, Crush

[Received February 9, 2010; Accepted April 15, 2010]

1. Introduction

Bone-inducing property in rabbit dentin was confirmed in the intramuscular pockets in 1967,[1),2)] after the discovery of bone induction by rabbit demineralized bone matrices (DBM).[3)] The rabbit studies reported that demineralized dentin matrics (DDM) induced bone at 4 weeks, while non-demineralized dentin (so-called, calcified dentin) induced bone at 8–12 weeks after implantation.[2)] We confirmed histologically that human completely demineralized dentin granules by hand-made method using hammer induced bone and cartilage independently at 4 weeks,[4),5)] and have obtained successful results in clinical studies of the autograft of DDM for bone regeneration.[6)] The preparation of DDM granules by the conventionally hand-made method needs a very complicated process and take one day. Until now, there is no mill that is clinically available for teeth. For standardization of DDM autograft, the automatic mill will be needed in the clinical fields.

The purposes of this study are to develop an automatic mill for teeth and bone, and to estimate the bone-inducing capability of human tooth-derived dentin and human bone-derived granules after automatic crushing with our newly developed mill, histologically.

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2. Experimental procedures

2.1 Conventional hand-operated method using order-made stainless steel apparatus

We designed a hand-operated apparatus for crushing tooth and especially ordered to make a stainless steal vessel and a bar.[4)] Frozen tooth was crushed by hammer in liquid nitrogen (**Fig. 1**).

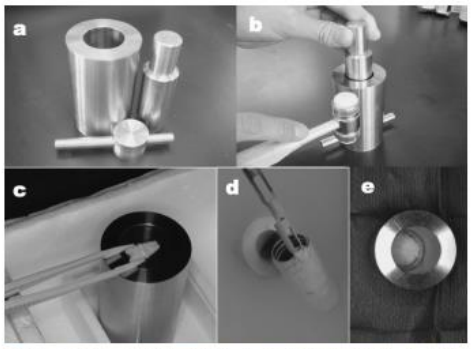

Fig. 1. Stainless steel apparatus. a. parts of apparatus, b. aspect, c. frozen tooth, d. adding of liquid N_2, e. tooth-derived granules.

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Clinical Report

Radiological Evaluation of Human Dentin Autografts in Bangladesh

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(Accepted for publication May 21, 2014)

Abstract: In Dhaka 2013, autografts of demineralized dentin matrix (DDM) were first used as bone regenerative therapy with two patients in Bangladesh. In Case 1, a 29 year-old male presented with an infected periapical lesion involving #11 and #12. Root canal treatment followed by periapical surgery were done to remove the lesion. Tooth-derived granules were prepared from a vital non-functional tooth (#38) by hand-operated crush method, demineralized in 2 % HNO_3 for 30 min and washed vigorously. DDM was grafted in the bone defect after the extirpation of the lesion. At 1 year after DDM graft, post-operative radiography indicated excellent bone healing by remodeling with dentin matrix. The pathological diagnosis was radicular granuloma. In Case 2, a 20 year-old female presented with a mesially inclined impacted 3rd molar (#48). Extraction of the impacted tooth and the autograft of the DDM were done simultaneously. Post-operative radiographs showed the extracted socket healed fully with new bone. The patient-own DDM granules from non-functional teeth could be recycled as osteoinductive materials for local bone regeneration. This works suggest that dentin might become a realistic alternative biomaterial to bone.

Key words: Human, Demineralized dentin matrix, Bone regeneration, Autograft

Introduction

In spite of advancements in field of dentistry, bone regenerative therapy for the repair of bone defect either due to surgical or pathological cause by using osteoinductive biomaterials still remains a daunting task for oral surgeons. Recently, many studies have been performed attempting to accelerate bone repair using different osteoinductive materials. Autogenous bone as a gold standard grafting material has been generally carried out for the regeneration of lost bone. To avoid secondary surgery for harvesting of grafts and morbidity resulting from it, the study for bone substitutes as an alternative of autogenous bone have begun[1,2]. Therefore, diverse biomaterials have been used in different dental surgery and with continuous research and development as well as clinical advancements, a variety of new biomaterials have been introduced in bone regenerative field. To repair hard and soft tissue defects in conjunction with guided tissue regeneration by grafting materials seems to play a key role not only providing the support to the teeth but also to maintain width and height of alveolar ridge for future prosthesis placement thus improving the quality of patient's life[3].

In advanced biomaterials sciences, bone inducing materials have a dominant impact on regenerative medicine. Both in medical and dental field there is always a need for biomaterial that allow new bone formation as well as gradual absorption as to be replaced by bone. That's why we have been conducting research on the development of biomaterials using human dentin in co-operation with bone remodeling[1]. While a first clinical report of human bone autograft was done in 1820, human dentin autograft was reported first in IADR 2003 which was a case of sinus lifting using a patient-own DDM granules for bone augmentation[4]. In 2009, Korea Tooth Bank (KTB) was established in Seoul for the processing of tooth-derived biomaterials which acted as an innovative medical service system making a realistic alternative to bone grafting[1,2].

Human tooth is a composite of both organic and inorganic components. Although the structure between dentin and bone are different, both are almost similar in biochemical composition. Dentin and cortical bone consist of body fluid (10 %), collagen (18 %), non-collagenous proteins (NCPs: 2 %) and hydroxyapatite (HAp: 70 %) in weight volume. After demineralization, both demineralized dentin matrix (DDM) and demineralized bone

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Clinical Report

Tooth Bank System for Bone Regeneration
- Safety Report -

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Abstract: The use of auto-tooth bone grafts fabricated from patients' own extracted teeth has become possible due to the development of tooth banking procedures. The Korea Tooth Bank (KTB), established in Seoul in 2009, is one such tooth-banking facility that can procure and store teeth, and then process them into bone graft substitutes. Another is the Hospital Tooth Bank (HTB) at Seoul National University Bundang Hospital (SNUBH), established in 2010 for performing storage and grafting of auto-tooth bone grafts based on experimental and clinical research. Extracted teeth are sent to the above-mentioned facility units and then delivered back to the patients for clinical use, and thus the safety of the auto-tooth bone graft materials as well as the clinical effectiveness must be guaranteed through proper quality assurance (QA) procedures. For the purpose of this investigation, we analyzed written documents for QA at KTB, and we performed histopathologic and microbiologic examinations against the banked tooth materials at the HTB. The results suggest that the tooth banking systems at both KTB and HTB sufficiently ensure patient safety.

Key words: Tooth bank, Auto-tooth, Bone graft, Tooth, Bone

Introduction

Autologous bone has been considered a gold standard for the regeneration of bone defect, however, it has disadvantages of not only the limited amount, but also donor site morbidity and etc. To overcome these limitations, much effort has continued to develop more ideal bone grafting materials[1]. Based on many dentin reports, we have been interested in both the osteoinduction capacities of dentin and the possibilities of bio-recycling of teeth which considered as medical waste for a long dental history[1-11]. The use of autotooth bone graft materials, which are made from patient's own extracted teeth, is nowadays a standard dental procedure in Korea[2]. While a first clinical report of human bone autograft was done in 1820, dentin autograft for sinus lifting was achieved in 2002, using a patient's own DDM granules, and reported in 81st IADR, 2003[4]. It is widely used for repair of alveolar bone defects in cases of simple bone graft, guided bone regeneration (GBR) as well as sinus bone graft[1,12-18]. We began to use the tooth which were transformed into either the powder type or the block type to be processed as demineralized dentin matrix under the patent "on method for processing a bone graft material using teeth and a bone graft material manufactured thereby" on October 31, 2012 (No: 10-1198115) and "on block membrane implants using autologous tooth and a machining method of the same capable of improving stability of implant surgical operation" August 30, 2011 (No: 10-1062381)[19,20] (Fig. 1). So that in 2009, Korea Tooth Bank (KTB) which is performing transformatin of tooth into bone graft materials and Hospital Tooth Bank (HTB) in Seoul National University Bundang Hospital performing storage and grafting of bone graft materials from patient-own teeth are established in accordance with the definition of Tooth Bank which is deemed to exist that human teeth from a dentist are collected, stored, processed into graft material for alveolar bone repair[21]. Even though Korea FDA defined this item as medical services only in case of using for the patient's own as well as we had clinical evidences of effectiveness for this novel biomaterials, the safety of processing procedures is of paramount important and quality assurance is inevitable for human clinical trials because this is human tissues not categorized at this moment.

The aim of this report is to investigate the quality assurance of

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Original

Bone Regeneration by Demineralized Dentin Matrix in Skull Defects of Rats

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Abstract: Alveolar bone defects may result in functional and morphological abnormalities. In such cases, bone can be regenerated by grafting fresh autogenous bone into the defect. Subsequently, we focused on the dentin of third molars, which are usually discarded after extraction, or teeth removed faor orthodontic therapy. As in bone, type I collagen is the main component of the organic matrix in dentin. Also, it has been proven that the organic matrix of dentin contains osteoinductive bone morphogenetic protein (BMP). It would be safe to perform grafting with the dentin of extracted teeth used as an autogenous bone substitute. Therefore, the objective of the present study was to reuse extracted teeth as a bone substitute material. Demineralized dentin matrix (DDM), an organic material derived from the dentine of bovine teeth, was grafted in rat skull defects to determine its bone regeneration ability and the possibility of its use as a bone substitute. In the present study, new bone formed from the defect margin in the control group, but in the graft group, new bone formation occurred from individual DDM granules within the defect, and not just from the margin. At Week 8, defect repair was limited in the control group. In contrast, most of the defect was covered by osseous tissue in the graft group. In conclusion, DDM may be a useful bone substitute that serves as a scaffold for bone regeneration by inducing a high level of new bone formation soon after surgery.

Key words: Bone regeneration, Demineralized dentin matrix, BMPs, Bone substitute, Micro CT

Introduction

Alveolar bone defects may result in functional and morphological abnormalities. In such cases, bone can be regenerated by grafting fresh autogenous bone into the bone defect. Fresh autogenous bone grafting is widely performed because it has no risk of infection or rejection, and favorable results have been obtained [1]. However, harvesting autogenous bone has disadvantages such as surgical invasiveness, wound infection, chronic pain, nerve paralysis and scarring [2]. Also, the volume of bone that can be harvested is limited. Therefore, methods that use a bone substitute material instead of autogenous bone are being investigated.

At present, bone substitute materials consisting of natural bone tissue, such as allogeneic and xenogenic bone, are used for bone grafting. Hydroxyapatite, an artificial biomaterial, is also widely used because of its high tissue affinity and osteoconductive properties [3]. However, hydroxyapatite is nonresorbable and remains in the body for a long period of time [4]. Hydroxyapatite acts as a scaffold for bone formation, but does not induce new bone tissue. Therefore, bone formation may be delayed [5].

Subsequently, we focused on the dentin of third molars that are usually discarded after extraction or teeth removed for orthodontic therapy. As in bone, type I collagen is the main component—accounting for about 20% by weight—of the organic matrix in dentin. Also, it has been proven that the organic matrix in dentin contains osteoinductive bone morphogenetic protein (BMP) [6]. We have demonstrated that demineralized dentin matrix (DDM) acts as a scaffold for repair of articular cartilage defects [7]. Moreover, recent studies examine a multi-component technique consisting of a novel side population of multi-purpose stem cells cultured on demineralized bone and dentin matrix, for tissue engineering applications [8-13]. The dentin of extracted teeth used as an autogenous bone substitute would be safe for grafting. Therefore, the objective of the present study was to reuse extracted teeth as a bone substitute material.

DDM, an organic material derived from the dentine of bovine teeth, was grafted in rat skull defects to determine its bone regeneration ability and the possibility of its use as a bone

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A Bovine Low Molecular Weight Bone Morphogenetic Protein (BMP) Fraction

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Bone, the hallmark of vertebrate species, is the only tissue in the body that is continuously renewed throughout postfetal life. Bone regeneration, particularly in young individuals, is complete and flawless. In contrast, other tissues regenerate only partially and heal wounds with scar. Bone marrow, skin, mucosa, kidney, and liver are renewed to a limited degree in response to wear, aging, and functional demand. Central nervous system tissues are not appreciably renewed and do not regenerate in mammalian species.

The regeneration factor that sets bone apart from other vertebrate tissues has been an object of inquiry since antiquity and has been investigated in experimental animals, including man, for over a century. The literature of the nineteenth and early twentieth centuries has been summarized by Sir Arthur Keith.[10] In the late 19th century, Senn[22] used demineralized bovine bone as a vehicle for installation of antiseptics (iodoform) in ten patients with osteomyelitis and in 14 dogs with skull defects, and reported only equivocal evidence of enhanced bone repair. The twentieth century literature on induced bone formation includes reports by Leriche and Policard,[13] LaCroix,[11,12] Levander,[14] Huggins *et al.*[9] and Urist and associates.[26-35] As nearly as can be determined from much literature in many languages, the first unequivocal demonstration of matrix-induced bone formation was not until 1965 in a report on a specified preparation of allogeneic bone matrix implanted in muscle.[26]

In recent years, research work on induced osteogenesis has progressed along two separate but related lines: one consists of clinical investigations of bone matrix induced-repair of craniofacial,[5,6,17,18] periodontal,[15,20] and orthopedic[27,29] defects; the other consists of biochemical investigations of bone growth,[3] coupling,[8] and osteogenetic factors[7,23] and a bone morphogenetic protein (BMP) fraction.[28,32-34] The BMP fraction is found in rabbit bone matrix,[28] dentin matrix,[4] and in mouse[7,23] and human[2] osteosarcoma tissues.

The histophysiology and products of cell differentiation,[25,26,31,32] initiated by the BMP of bone matrix, have been previously described in detail both *in vivo*[31] and *in vitro*.[35] Recent observations suggest that BMP is a hydrophobic glycoprotein.[33] In this report, we demonstrate that large quantities of bone are required to obtain BMP fractions in amounts suitable for standard methods of purification and characterization of glycoproteins. To prepare sufficient BMP for simultaneous analytical and bioassay experiments, we have scaled up and modified

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RESEARCH ARTICLE

Bone Regeneration Using Dentin Matrix Depends on the Degree of Demineralization and Particle Size

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Abstract

Objectives

This study aimed to examine the influence of particle size and extent of demineralization of dentin matrix on bone regeneration.

Materials and Methods

Extracted human teeth were pulverized and divided into 3 groups according to particle size; 200, 500, and 1000 μm. Each group was divided into 3 groups depending on the extent of demineralization; undemineralized dentin (UDD), partially demineralized dentin matrix (PDDM), and completely demineralized dentin matrix (CDDM). The dentin sample was implanted into rat calvarial bone defects. After 4 and 8 weeks, the bone regeneration was evaluated with micro-CT images, histomorphometric and immunohistochemical analyses. Osteoblasts were cultured on UDD and DDM to evaluate the cell attachment using electron microscope.

Results

Micro-CT images and histological observation revealed that CDDM had largely resorbed but UDD had not, and both of them induced little bone formation, whereas all particle sizes of PDDM induced more new bone, especially the 1000 μm. Electron microscopic observation showed osteoblasts attached to DDM but not to UDD.

Conclusions

PDDM with larger particle size induced prominent bone regeneration, probably because PDDM possessed a suitable surface for cell attachment. There might be an exquisite balance between its resorption and bone formation on it. PDDM could be considered as a potential bone substitute.

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NON-COLLAGENOUS COMPONENTS OF THE ORGANIC MATRIX OF RABBIT INCISOR DENTINE

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Summary—EDTA extracts of rabbit incisor dentine fractionated by DEAE-cellulose chromatography, gave five fractions, two of which were separated by gel filtration into three more fractions. Eight of the total nine fractions were analysed. Four were less-acidic glycoproteins similar to some of the corresponding fractions of human dentine. A further three fractions were anionic glycoproteins with some similarities to those of human dentine, but containing little phosphorus. The final fraction from DEAE-cellulose appeared to be a proteoglycan consisting mainly of chondroitin-4-sulphate together with a protein less acidic than the corresponding fractions of human dentine and bovine bone.

INTRODUCTION

Considerable progress has been made in the isolation and characterization of the non-collagenous components of the human dentine matrix. These include plasma proteins (Thomas and Leaver, 1975), anionic glycoproteins (Jones and Leaver, 1974a; Leaver, Thomas and Holbrook, 1977), less-acidic glycoproteins (Thomas and Leaver, 1977) and a glycosaminoglycan fraction (Jones and Leaver, 1974b). These fractions were obtained from non-collagenous matrix (NCM) preparations obtained by EDTA demineralization of dentine followed by digestion of the insoluble residues with collagenase, both procedures being carried out successively in dialysis sacs. EDTA demineralization, however, releases into solution 70 per cent of the NCM including most of the fractions isolated from so-called total NCM preparations. Collagenase digestion of the insoluble residues obtained after EDTA demineralization of human dentine gave rise to soluble collagenase-released proteins (Leaver *et al.*, 1975; Thomas, 1975) and an insoluble fraction (Leaver, Price and Smith, 1978). The anionic glycoproteins contained organic phosphate and exhibited combined aspartic acid and serine levels of 440 residues per thousand. They resembled the soluble phosphoproteins of bovine dentine (Veis, Spector and Zamoscianyk, 1972) and rat incisors (Butler, Finch and Desteno, 1972), although these contained levels of aspartic acid and serine of 750–800 residues per 1000 and exhibited rather higher phosphorus content.

Studies on the NCM of the dentines of species other than man have, in the main, been confined to these phosphoproteins, although Butler, Mikulski and Urist (1977) reported the presence of collagenase-released proteins in rat dentine; earlier investigations of bovine dentine revealed the presence of EDTA-soluble proteins other than the phosphoproteins. Richardson *et al.* (1977) isolated soluble phosphoproteins, closely resembling those of bovine and rat dentine, from rabbit dentine.

The rabbit, suitable for investigations using labelled compounds, has been used in studies of the tissue distribution and of the metabolism of certain bone glycoproteins (Owen and Shetlar, 1968; Triffitt and Owen, 1973). As we intend to carry out similar investigations in relation to dentine it was essential to obtain information concerning the composition of the non-collagenous components of rabbit dentine.

The rabbit is diphyodont and its whole dentition is of continuous growth, thereby differing from the rat where only the incisors exhibit continuous growth. We have serious reservations concerning the use of rabbit molar teeth in metabolic studies and intend to use only incisors. Therefore, although we carried out some analyses of molar dentine, only those relating to incisors are reported here. We describe the fractionation of the EDTA-soluble materials only; certain fractions obtained by subsequent collagenase digestion of the insoluble residues have been described in a preliminary report (Price and Leaver, 1978).

MATERIALS AND METHODS

Incisor teeth were extracted from the jaws of 16 albino rabbits, shortly after death and stored in saturated sodium chloride solution prior to water-washing and air-drying. After standing in absolute ethanol for 20 h, the teeth were again air-dried, the pulps removed and the surfaces cleaned with a scalpel. They were then powdered by the successive use of percussion mill and ball mill, under liquid nitrogen conditions, as described by Jones and Leaver (1974a).

Powder of particle size <60 mesh was subjected to flotation in bromoform/acetone (sp. gr. 2.70) to remove enamel. Dentine powder, free of cementum, was obtained by subsequent flotations first at sp. gr. 2.42, and finally at 2.07. It was then washed with acetone and air-dried.

Demineralization of dentine

The powdered dentine was demineralized in 10 per cent (w/v) EDTA at pH 7.5 at 4°C, several changes of EDTA being made until the u.v. absorption of the extracts was minimal and the phosphorus content of the insoluble residue, as determined by the method of Chen, Toribara and Warner (1956), reached a constant low level of 0.05 per cent. The insoluble residues were removed by filtration and the EDTA extracts

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Dissolution of bio-active dentine matrix components by mineral trioxide aggregate

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ABSTRACT

Objectives: To analyze the soluble components of setting and set mineral trioxide aggregate (MTA), assess the abilities of two varieties of MTA and $Ca(OH)_2$ solutions to solubilise dentine matrix proteins (DMPs) and determine if these extracts contain signalling molecules important to pulpal repair and regeneration.

Methods: The metallic ion composition of solutions of white and grey MTA (pH 11.7), 0.02 M $Ca(OH)_2$ (pH 11.9) and 10% EDTA (pH 7.2) was determined using atomic absorption spectroscopy. Extracellular dentine matrix components from powdered human dentine were extracted using all solutions over 14 days. Extracts were analysed for concentrations of non-collagenous proteins (NCPs) and glycosaminoglycans (GAGs), and protein profiles were examined using 1D-polyacrylamide gel electrophoresis (1D-PAGE). ELISAs for TGF-β1 and adrenomedullin (ADM) were also performed.

Results: Aluminium, calcium, potassium, and sodium ions were detected in both white and grey MTA solutions. MTA and $Ca(OH)_2$ solutions liberated similar amounts of GAGs and NCPs although yields were considerably lower than those obtained using the EDTA solution. 1D-PAGE analysis demonstrated differences in protein profiles solubilised from dentine for all solutions. All extracts contained TGF-β1 and ADM, EDTA solution liberated significantly greater amounts of TGF-β1, and $Ca(OH)_2$ and grey MTA solutions released more ADM.

Conclusions: These data imply that when placed clinically soluble components of set and setting MTA may release dentine matrix components that potentially influence cellular events for dentine repair and regeneration.

1. Introduction

Mineral trioxide aggregate (MTA) was developed in the 1990s initially for use as a root-end filling material due to its ability to set in the presence of moisture.[1] Whilst its chemistry was based on that of ordinary Portland cement, significant differences preclude use of the latter as a clinical substitute.[2] MTA has been shown capable of inducing mineralised tissue formation at a variety of oral and dental tissue sites and subsequently its potential applications within dentistry have expanded.[3] The chemical composition of MTA is a mixture of oxides with approximately 65% being calcium

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Processed bovine dentine as a bone substitute

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Abstract

Objectives: Different forms of allogenic dentine have been studied for their potential use as bone substitutes. We report a new method for processing bovine dentine that results in a sterile bioactive material for repair and regeneration of bone.
Methods: Extracted bovine dentine was processed mechanically and chemically with inorganic and organic solvents, and sterilised. The *in vitro* biocompatibility on human gingival fibroblasts was assessed by the Alamar Blue assay and the *in vivo* biocompatibility evaluated by implantation of the processed dentine into rats' femurs.
Results: The dentine showed excellent biocompatibility *in vitro*, stimulated formation of new bone and was completely incorporated into the new bone *in vivo*.
Significance: Processed bovine dentine has the potential to be used as a suitable substitute in bone repair and regeneration.

Keywords: Dentine; Bone regeneration; Biocompatibility; Alamar Blue assay

Introduction

Substitutes for bone provide osteoconductive scaffolding similar to those of autogenous bone. They eliminate morbidity of the donor site; reduce operating time, complexity, and treatment costs; and improve satisfaction for patients.[1]

Replantation of avulsed teeth after elimination of the periodontal ligament results in dentoalveolar ankylosis, followed by long-term resorption of roots and replacement of bone.[2] This phenomenon indicates that dentine has the potential to be used as a suitable osteoconductive material in repair and regeneration of bone. Different forms of allogenic dentine have been studied for their potential use as bony substitutes. These include freeze-dried dentine, demineralised dentine, and particulate dentine (tooth ash). Freeze-dried allogenic dentine is non-irritant and compatible with periapical tissue as an apical barrier material;[3] it has also been used clinically in the repair of periodontal osseous defects.[4] It has been reported that demineralised dentine stimulates new bone formation and completely incorporates into the new bone. It is then resorbed during repair of bone and results in fast healing of bony defects.[5,6] Particulate dentine has been studied in its pure form or combined with Plaster of Paris as a bony substitute. However, these materials are less effective than processed bone-derived products.[7]

To obtain a pure dentine matrix and eliminate all other components that might cause inflammatory reactions, we have developed a new method for processing bovine dentine that results in a sterile bioactive material for bony repair and regeneration in periodontal, maxillofacial, or other bone defects.

The aim of this study was to assess *in vitro* and *in vivo* biocompatibility of the processed dentine and to evaluate its effectiveness in repair and regeneration of bone.

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Bone and Tissue Regeneration Insights

SHORT REPORT

Properties of Hydroxyapatite from Bovine Teeth

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Abstract: The objective of this work was to study the production of hydroxyapatite (HA) from bovine teeth. Hydroxyapatite (HA) was produced from bovine teeth powder after calcination at 1150 °C. It was discovered that the sample preparation process influences its properties, so, crystal structure and thermal stability of HA were investigated. The X-Ray diffraction analysis (XRD) results confirmed that HA has been successfully produced. Fourier transform infrared spectroscopic (FT-IR) study confirmed the presence of hydroxyl (OH^-) and phosphate (PO_4^{-3}) functional groups. The scanning electronic microscope (SEM) was employed to identify the surface morphology of HA, and showed the nanoporous structure throughout the matrix. The sample constituents such as Ca, P, K ... etc., and their values were determined by Energy dispersive X-Ray (EDX).

Keywords: bovine teeth, bovine hydroxyapatite (BHA), hydroxyapatite properties, XRD, SEM, calcium and phosphate, FT-IR, EDX

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Quantitation of Growth Factors IGF-I, SGF/IGF-II, and TGF-β in Human Dentin

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ABSTRACT

Human bone matrix is known to contain a battery of polypeptide growth factors. Since dentin is a mineralized tissue similar to bone in composition and perhaps in formation, human dentin was assayed for the presence of similar growth factors.

Root dentin proteins were extracted by demineralization in 4 M guanidine hydrochloride (Gu) and 30 mM Tris (pH 7.4) containing 20% EDTA and proteinase inhibitors. Gu-EDTA extracts were desalted and used for the following assays: (1) bone cell proliferation in chick calvarial cell mitogenic assay using the incorporation of [^{3}H]thymidine into TCA-insoluble material; (2) osteocalcin by radioimmunoassay (RIA); (3) insulinlike growth factor I (IGF-I) by RIA; (4) skeletal growth factor/insulinlike growth factor II (SGF/IGF-II) by radioreceptor assay; and (5) transforming growth factor beta (TGF-β) by bioassay.

Gu-EDTA extracts stimulated bone cell proliferation. At 10 μg/ml, dentin proteins increased the incorporation of [^{3}H]thymidine by calvarial cells to 320% of that by BSA-treated control cells. Consistent with the presence of mitogenic activity, growth factors were found in dentin in the following concentrations (ng/μg Gu-EDTA protein): (1) IGF-I, 0.06; (2) SGF/IGF-II, 0.52; and (3) TGF-β, 0.017. All three growth factors were present in concentrations lower than that found in human bone. Osteocalcin was detected at a concentration of 3.0 mg/g Gu-EDTA protein, also much lower than that in bone.

INTRODUCTION

Evidence has accumulated in support of the hypothesis that the regulation of bone volume may be due to local as well as systemic agents. Research from this laboratory and others suggests that proteins derived from bone may act locally to regulate bone formation or resorption.[1,2] Growth factors from bone matrix may have a variety of effects on bone cells, including stimulation of the proliferation of preosteoblasts[3-5] and of collagen production by mature osteoblasts.[4] These factors may act locally on bone or other cells in vivo or may be sequestered into bone matrix to be released later during bone resorption; thus, these factors have been suggested to act as autocrine, paracrine, or delayed paracrine agents to mediate the local coupling of bone formation to resorption.[1,6,7]

Skeletal tissue is a reservoir of polypeptide growth factors.[8] Growth factors identified in human bone matrix to date include insulinlike growth factor I (IGF-I), skeletal growth factor/insulinlike growth factor II (SGF/IGF-II), transforming growth factor beta (TGF-β), platelet-derived growth factor (PDGF), and acidic and basic fibroblast growth factor (aFGF and bFGF).[9] SGF/IGF-II was originally discovered and partially purified as an 83 kDa bone cell mitogen termed skeletal growth factor (SGF).[10] More recently, however, a smaller human SGF (M_r = 11,000) that retained full biologic activity was purified to homogeneity.[11] Of the SGF molecule, 75% has since been un-

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The nature and functional significance of dentin extracellular matrix proteins

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ABSTRACT **Odontoblasts are responsible for formation of predentin, which is transformed to dentin when apatite crystals are formed and the fibrillar matrix becomes mineralized. Odontoblasts are specialized cells that synthesize and secrete a unique set of non-collagenous proteins (NCPs), as well as the collagenous matrix largely comprised of type I collagen. The NCPs consist of dentin specific and mineralized tissue specific proteins, as well as other proteins that are found in a variety of tissues. Three dentin specific proteins have been recognized to date: dentin phosphoprotein (DPP), also called phosphophoryn, AG1 (dentin matrix protein 1, Dmp1) and dentin sialoprotein (DSP). DPP appears to be made by odontoblasts and appears at the mineralization front within a short time. It may be secreted via odontoblastic processes. DPP binds to collagen and potentially initiates formation of apatite crystals. A second DPP function appears to be to bind to the 100 face of growing apatite crystals and to inhibit or slow their growth; thus, DPP may play a dual role by initiating mineralization and then affecting the crystal growth and perhaps the habit of the crystals. Although no function has been ascribed to AG1 or DSP, they should prove to be important markers for the odontoblast phenotype. A recent unique finding is that two separate genes appear to code for more than one DSP mRNA; other transcripts may result from differential splicing. Examples of mineralized tissue specific proteins expressed by osteoblasts as well as odontoblasts are bone sialoprotein (BSP) and osteocalcin. Some NCPs expressed by osteoblasts, odontoblasts and several other tissues include osteopontin (OPN) and the chondroitin sulfate containing proteoglycans, decorin and biglycan. We propose that characterization of odontoblasts in tissues and cultures should rely upon utilization of sets of markers for the above NCPs and their mRNAs. Similar approaches are commonly used in investigations on osteoblasts. Finally, dentin (like bone) contains other molecules such as growth factors, and serum derived proteins, found within the matrix; no functional significance has yet been placed upon this finding. Future experiments should focus upon the elucidation of the three dimensional structures of the collagenous fibrillar network and of the NCPs to determine the relationships to mineralization. The role played by odontoblasts in controlling extracellular events, such as by selective secretory routes, will require careful exploration.**

KEY WORDS: *dentin, predentin, collagen, phosphoproteins, sialoprotein, mineralization*

Odontoblasts

Odontoblasts are directly responsible for formation of the fibrillar ECM of dentin and for bringing about the deposition of carbonate apatite mineral within and around the collagenous fibers in a more indirect manner. These cells are aligned in a single layer at the margin of the dental pulp, and in their fully differentiated state, secrete ECM unidirectionally (Fig. 1). Mature odontoblasts originate from dental papilla mesenchyme, the differentiation process being characterized by specific morphological features and gene expression (Ruch, 1985; Thesleff, 1992). Whenever the odontoblastic precursor cells leave the cell cycle, they polarize such that the nucleus is removed from the apical, secretory portion. They develop characteristics of secretory cells as revealed by numerous rER, Golgi apparati and secretory granules (Weinstock and Leblond, 1974). The initial stages of secretion involve an uncalcified matrix, predentin, formed by young odontoblasts. As the odontoblasts continue to form additional ECM that calcifies to form dentin, they recede pulpally, leaving behind cell processes (odontoblastic processes) contained in numerous dentinal tubules, coursing through predentin and dentin (Fig. 1). Mature odontoblasts form several types of dentin (for a review see Linde and Goldberg, 1993). The initial thin layer, mantle dentin, located adjacent to

Abbreviations used in this paper: ALP, alkaline phosphatase; BAG-75, bone acidic glycoprotein 75; CNBr, cyanogen bromide; DPPs, dentin phosphoproteins; DSP, dentin sialoprotein; BSP, bone sialoprotein; ECM, extracellular matrix; HAP, hydroxyapatite; NCPs, non-collagenous proteins; PGs, proteoglycans; rER, rough endoplasmic reticulum.

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Reconstruction using an autograft containing tumour treated by liquid nitrogen

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We describe a method of reconstruction using tumour-bearing autograft treated by liquid nitrogen in 28 patients. The operative technique consisted of *en bloc* excision of the tumour, removal of soft tissue, curettage of the tumour, drilling and preparation for internal fixation or prosthetic replacement before incubation for 20 minutes in liquid nitrogen, thawing at room temperature for 15 minutes, thawing in distilled water for ten minutes, and internal fixation with an intramedullary nail, plate or composite use of prosthetic replacement. Bone graft or cement was used to augment bone strength when necessary.

The limb function was rated as excellent in 20 patients (71.4%), good in three (10.7%), fair in three (10.7%), and poor in two (7.1%). At the final follow-up six patients had died at a mean of 19.8 months after the operation, while 21 remained free from disease with a mean follow-up of 28.1 months (10 to 54). One patient is alive with disease. Bony union was seen at a mean of 6.7 months after the operation in 26 patients. Complications were encountered in seven patients, including three deep infections, two fractures, and two local recurrences. All were managed successfully. Our results suggest that this is a simple and effective method of biological reconstruction.

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Advances in diagnostic imaging, neoadjuvant chemotherapy, and operative technique have made it possible to treat malignant tumours of bone and soft tissue by limb salvage. With multidisciplinary treatment, such techniques produce a functional and durable limb without reducing the long-term results. All the established methods of reconstruction such as the use of massive prostheses, allografts, combinations of allografts and prostheses or with bone cement have made limb salvage possible. Endoprosthetic replacement after excision of the tumour can provide excellent results more quickly than with other methods. In a large series[1] the probability of a patient avoiding aseptic loosening for five years was 93.8% for a proximal femoral replacement, 67.4% for a distal femoral prosthesis and 58% for a proximal tibial implant. The survival rates for reconstructions around the knee now exceed 85% at five years.[2] Survival at ten years after massive prosthetic replacement of the distal femur is approximately 50%[3] while that of prostheses in the proximal humerus with mechanical failure as the end-point is 86.5% at 20 years.[4] Development of extendible prostheses now allows their use in growing children.[5-7]

Biological reconstruction may employ either living or dead bone. Recently, epiphyseal preservation and reconstruction with distraction osteogenesis have provided excellent function of the limb in selected cases.[8-10] Anatomical remodelling of the hip reconstructed with a massive allograft combined with a vascularised fibular transplant has been achieved in a child.[11] Allografts are an example of biological reconstruction utilising dead bone. Mankin[12] found that 77% of the allografts were still functional and competent. The best results were obtained with intercalary grafts while the poorest were with allograft arthrodesis. Fracture and nonunion reduce the rate of success. The addition of intramedullary cement to large-segment allografts improves their survival by decreasing the risk of fracture.[13] Allograft prosthetic composite arthroplasty has also been used to solve the problem of degenerative changes occurring in osteoarticular allografts.[14]

Allograft is difficult to obtain in some Asian countries, especially in Japan, for socio-religious reasons. Therefore, recycling of bone has been widely used. Several methods have been developed to re-use the resected bone for reconstruction, including irradiation,[15,16] autoclaving[17,18] and pasteurisation.[19,20] These methods require special equipment and strict thermal control. Heat treatment causes weak-