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RESUMEN

Hoy en día la diabetes es un problema mundial. La diabetes y la enfermedad periodontal son patologías crónicas, complementarias.

Las enfermedades periodontales se clasifican en dos grupos: la gingivitis y la periodontitis. La relación entre estas dos enfermedades es compleja, intima, una desregulación de una tiene consecuencias en la otra.

Los objetivos del trabajo son: identificar la influencia del control de la diabetes sobre la enfermedad periodontal, identificar la relación del control de la enfermedad periodontal sobre la diabetes y explicar cómo prevenir y tratar la periodontitis en pacientes diabéticos. Se ha hecho un análisis bibliográfico en las bases de datos PUBMED, MEDLINE, GOOGLE SCHOLAR. Con las palabras claves: Diabetes, enfermedad periodontal, prevención, tratamiento periodontal.

La diabetes genera múltiples problemas tanto al nivel vascular como inmune que potencian la aparición de enfermedad periodontal. El paciente diabético necesita un especial cuidado en la consulta dental. El control de la diabetes es fundamental para establecer, un plan de tratamiento. La prevención, la sensibilización a tratamientos adecuados, revisiones regulares permiten un mantenimiento de la enfermedad periodontal.

Este trabajo pone en evidencia la relación bidireccional de la diabetes y de la enfermedad periodontal. El paciente tiene que entender la importancia del control de su diabetes para la curación de su enfermedad periodontal. Al mismo tiempo tiene que estar sensibilizado a los tratamientos periodontales para una buena gestión de su diabetes.

ABSTRACT

Today diabetes is a global problem. Diabetes and periodontal disease are chronic, complementary pathologies. Periodontal disease are classified in two categories: gingivitis and periodontitis. The relationship between these two diseases is complex and intimate, a dysregulation of one has consequences on the other. Aims of this work are: identify the influence of the control of diabetes on periodontal disease, identify the relationship of the control of periodontal disease on diabetes and explain how to prevent and treat periodontitis in diabetic patients.

This work is based on a bibliographic analysis, has been done with PUBMED, MEDLINE, GOOGLE SCHOLAR databases. With the keywords: Diabetes, periodontal disease, prevention, periodontal treatment.

Diabetes generates a lot of complications, both at the vascular and immune levels that generate the appearance of periodontal disease. The diabetic patient needs special care in the dental office. The control of diabetes is essential to establish a treatment plan. Prevention, explications of appropriate treatments and regular check ups allow a cure of periodontal disease.

This work hightlights the bidirectional relationship between diabetes and periodontal disease. The patient has to understand the importance of diabetes's control for the cure of his periodontal disease. At the same time, you have to be aware of the introduction of periodontal treatments in the management of your diabetes.

INDICE

INTRODUCCION

Desde hace muchos años, varios análisis y artículos han mostrado la relación íntima entre la diabetes y las enfermedades periodontales. La diabetes es una enfermedad metabólica, sistémica y crónica que está afectando cada vez a más personas. Hoy en día es un nuevo problema de salud pública. En el mundo la prevalencia es de 4.7% en 1980 y ha subido a 8.5 % en 2014.

La prevalencia de la diabetes tipo 2 en España varia entre 4.8 y 18.7 %, la diabetes tipo 1 entre 0.08% y 0.2 %.[1] . En el estudio de Rojo-Martinez[2] se relaciona esta enfermedad con varias causas: la genética, la edad, la obesidad y el sexo. Esta enfermedad causa daños irreversibles y graves en el corazón, los vasos, los riñones, los ojos (retinopatías) y disminuye la esperanza de vida.[3]

La enfermedad periodontal es una enfermedad infecciosa que esta provocada por múltiples bacterias anaeróbicas GRAM negativas que van a producir una reacción inflamatoria en los tejidos periodontales de los dientes. Todo el mundo no reacciona de la misma forma a esta enfermedad, hay muchos factores que influyen, hay personas que son más susceptibles a tenerla que otras. Hoy en día los estudios confirman que algunas enfermedades sistémicas como la diabetes pueden modificar la expresión de la enfermedad periodontal.[4]

Diabetes enfermedad sistémica

La diabetes se puede clasificar de 3 formas: la diabetes tipo 1, el tipo 2 y la diabetes gestacional. Según la recomendación de la OMS, la mejor forma para diagnosticar la diabetes es la analítica de sangre. Se toman tomamos las medidas de la

glucemia en ayunas en un caso de un paciente diabético los valores son: >1.26 g/L o 7 mmol/L, los resultados se tienen que confirmar una segunda vez. La asociación americana de diabetes recomienda el examen de hemoglobina glicada (HbA1C) que permite mostrar los niveles de glucosa en los últimos 3 meses. En un paciente diabético el resultado será > 6.5 %.

Figura1: Criterios de diagnostico de la diabetes según la Organización mundial de la salud[5]

Diabetes	
Glucosa plasmática en ayunas	≥7,0 mmol/l (126 mg/dl)
	o bien
Glucosa plasmática a las 2 horas *	≥11,1 mmol/l (200 mg/dl)
	o bien
HbA1c	≥6,5 %
Alteraciones de la tolerancia a la glucosa (TTG)	
Glucosa plasmática en ayunas	<7,0 mmol/l (126 mg/dl)
	y además
Glucosa plasmática a las 2 horas*	≥7,8 y <11,1 mmol/l (140 mg/dl y 200 mg/dl)
Trastorno de la tolerancia a la glucosa (TTG)	
Glucosa plasmática en ayunas	de 6,1 a 6,9 mmol/l (de 110 mg/dl a 125 mg/dl)
	y (si se la mide)
Glucosa plasmática a las 2 horas*	<7,8 mmol/l (140 mg/dl)
Diabetes gestacional	
Uno o varios de los siguientes:	
Glucosa plasmática en ayunas	de 5,1 a 6,9 mmol/l (92-125 mgl/dl)
Glucosa plasmática 1 hora después**	≥10,0 mmol/l (180 mg/dl)
Glucosa plasmática a las 2 horas	8,5-11,0 mmol/l (153-199 mg/dl)

* Glucosa en plasma venoso 2 horas después de ingerir una carga oral de 75 g de glucosa.
** Glucosa en plasma venoso 1 hora después de ingerir una carga oral de 75 g de glucosa.

Si las personas no tienen síntomas, la prueba positiva a la diabetes se debe repetir otro día.[1]
La glucometría es relativamente sencilla y barata, de manera que debería poderse efectuar en el nivel de atención primaria.

Diabetes tipo I o insulinodependiente

La diabetes tipo I es una enfermedad autoinmune crónica se llama también “la diabetes juvenil”. Es una diabetes que aparece muy pronto, normalmente antes de los 30 años y más comúnmente durante la infancia. La enfermedad se explica por una desregulación en el nivel de la producción de insulina, es un defecto de las células beta del páncreas, hay una infiltración por linfocitos T CD4 y citotóxicos CD8 en los islotes de Langerhans.[6] Los pacientes que sufren de diabetes tipo I tiene como signos y síntomas : cansancio, poliuria (volumen de orina superior a lo normal), polifagia (aumento de hambre), polidipsia (aumento anormal de la sed), perdida de peso y retinopatía.[7]

Los pacientes que sufren de esta diabetes tienen múltiples opciones de tratamiento. Una de las opciones es la insulinoterapia que se hace a través de inyecciones de insulina. Existen tres tipos, la insulina de rápida acción 35 a 60 minutos para reducir la hiperglucemia postprandial, (los análogos de insulina rápida que tienen efectos de 15 a 25 minutos), las insulinas de acción intermediario 2 a 4 horas y la de acción lenta para mantener un nivel basal. El endocrino ajusta las pautas de manera individual, estos pacientes tienen que medir sus glucemias al menos 4 veces al día es lo que se llama el autocontrol.[8] Son los pacientes que se ponen las inyecciones subcutáneas. Tienen que seguir protocolos que son en ocasiones, complicados para ellos.

Desde los últimos años, los tratamientos han evolucionado, el paciente diabético debe tener un control estricto de su vida, la toma de las medidas de la glucemia varias veces al día es complicado para pacientes en particular para los niños. Por eso, se ha desarrollado la terapia con bombas de infusión continua de insulina subcutánea que

mejora la calidad de vida de los pacientes. Es un sistema que se autorregula sin la intervención del paciente, pero tienen que estar motivados; tienen que aprender a manejar la bomba y tener todos los conocimientos de su enfermedad. La bomba permite administrar bolos de insulina antes del consumo de comida y de modo basal. Tiene un sistema que va a liberar insulina de manera continua en los tejidos. Los objetivos de este sistema son: una regulación de la insulinemia, un mejor control de la HbA1c, menos episodios de hipoglucemia, la dosificación es mas fácil y es mucho más cómodo para pacientes.[8]

Los tratamientos farmacológicos en esta enfermedad sistémica son fundamentales. Pero a eso se tiene que añadir tratamientos no farmacológicos, por ejemplo, un control estricto de la alimentación. Los hábitos de los pacientes tienen que cambiar, hay un tiempo de adaptación, no es siempre fácil sobre todo en el caso de los niños. Tienen que llevar, además una dieta equilibrada. Lo que influye mucho en la variación de la glucemia es el azúcar, y todo los alimentos que contienen hidratos de carbono, es preferible no consumir azúcar o encontrar alternativas que incrementan la glucemia de forma lenta por ejemplo : las frutas, las verduras, alimentos con fibras.[8] Lo ideal es controlar su glucemia regularmente y pesar los alimentos. Conocer las cifras de azúcar que contienen. Los productos azucarados hoy en día son un problema ya que están presentes en muchos alimentos. Además, el ejercicio físico es muy importante en la enfermedad de la diabetes, pero para los pacientes que tienen el tipo I hay que tener cuidado por el riesgo de hipoglucemia, antes de nada, hay que hacer una interconsulta para variar las dosis de insulina en función del deporte, para evitar los problemas metabólicos. Los estudios, de momento no han encontrado beneficios altos de la

práctica de deporte en la enfermedad de diabetes de tipo I lo que no es el caso para el tipo II. [8]

Diabetes tipo II

La diabetes tipo II es la más frecuente, aparece normalmente en las personas con más de 40 años de edad. Cada vez más afecta a personas más precozmente. La insulina no se regula bien, se crea una insulino-resistencia, lo que se traduce por una glucemia mal controlada. Desde un punto metabólico, la resistencia es el resultado de un exceso de grasa al nivel de los músculos y del tejido adiposo alrededor de los órganos. Podemos explicar este tipo de diabetes por la combinación de múltiples factores: genéticos y ambientales.[9] Un sobrepeso, la obesidad, la hipertensión, la falta de ejercicio, la edad, la HTA son factores de riesgo. La aparición de la diabetes tipo II se relaciona con una pérdida o aumento de peso, orina nocturna, problema de visión, hipotensión ortostática.[9] A partir de 45 años la American Diabetes Asociación recomienda un análisis de sangre preventiva cada año.

El tratamiento de esta diabetes se hace con tomada de medicamentos orales anti-glucemientes, el más conocido es la metformina, que aumenta la sensibilidad del cuerpo a la insulina.[10] Lo importante es la pérdida de peso y entonces seguir una alimentación saludable. La necesidad de ejercicio físico es parte de las soluciones. Es un tipo de diabetes que se puede evitar, con la prevención de los factores de riesgo.[11]

La diabetes tipo II genera complicaciones importantes. La más conocida es la enfermedad cardiovascular, la prevalencia de ésta sube con el mal control de la diabetes. Se ve en el estudio de McGurnaghan que la prevalencia de enfermedades cardiovasculares es de 32% en los pacientes diabéticos, es una cifra que se puede

modificar con controles estrictos de la diabetes, toma de medicamentos, análisis regulares, estilo de vida saludable.[11]

Diabetes gestacional

La diabetes gestacional es la diabetes propia del embarazo. Se puede controlar con una alimentación equilibrada y un poco de ejercicio. Hay una deficiencia relativa a la insulina por las hormonas de la placenta.[12] Puede tener consecuencias importantes: problema de peso para el futuro bebe, cesárea complicación en el parto, riesgo de aumento de presión que puede generar preeclampsia.[13] En algunas situaciones la madre tiene que seguir tratamiento con insulina. Si no se trata o no está bien seguida, esta diabetes puede tener consecuencias futuras como la aparición de una diabetes tipo 2.[14]

Complicaciones de la diabetes

De forma general los pacientes diabéticos tienen una esperanza de vida más corte. Cuando los pacientes están diagnosticados de diabetes, el médico le explica todas las complicaciones que se puedan prevenir en lo posible. Hay que prevenir el riesgo de infecciones, estos pacientes no cicatrizan bien. Existen más probabilidades de generar una enfermedad cardiovascular, problemas micro vasculares como neuropatía o retinopatía.[15] Al nivel oral, hay riesgos de desarrollar enfermedades periodontales, es la sexta complicación de la diabetes.[16]

Enfermedad periodontal

El conjunto de los tejidos que están alrededor del diente se llama el periodonto. Un periodonto sano se caracteriza por un color rosa, de consistencia firmes. Se sitúan en los espacios interdentales para formar las papilas. El tejido gingival forma el periodonto superficial; el hueso alveolar, el ligamento periodontal y el cemento forman

el periodonto profundo. La enfermedad periodontal es una enfermedad infecciosa que se explica por la consecuencia de una inflamación crónica. Es la destrucción de los tejidos periodontales que conduce a la perdida de unión, a la destrucción ósea y la formación de bolsas.[17] Existen diferentes formas de enfermedad que resultan de un desequilibrio entre bacterias que conducen al proceso inflamatorio: la gingivitis y la periodontitis. Esta respuesta inflamatoria aparece en función de diferentes factores. La flora bacteriana cambia, las bacterias van a producir toxinas que activan los linfocitos T. Las citoquinas se activan lo que genera el proceso inflamatorio y destruye el tejido periodontal. Las bacterias aeróbicas más conocidas que originan estos procesos son: *Actinomycemetemcomitans*, *Campylobacter rectus* (CR), *Eikenella corrodens* (EC). En este tipo de enfermedad existe también la presencia de mayoría de bacterias anaeróbicas: *Porphyromonas gingivalis* (PG), *treponema denticola* (TD), *prevotella intermedia* (PI), *fusobacterium nucleatum* (FN), *eubacterium* y *spirochetes*.[18]

Factores de riesgo

La gravedad de la enfermedad periodontal varía en función de varios factores de riesgos. Una variable importante es la higiene bucal (1964 SILNESS LOE), la acumulación de placa es la principal causa. En los factores de riesgos asociados distinguimos: el tabaco, modifica de manera cualitativa pero también cuantitativa la flora bacteriana de la boca, disminuye el PH y produce vasoconstricción por la nicotina. Los pacientes que tienen enfermedades como: diabetes, gingivitis existentes, problema de tiroides, SIDA, leucemia son más susceptibles. La toma de medicamentos como anti-epilépticos, anti-inflamatorios pueden favorecer la aparición. La edad es un factor, la prevalencia de la enfermedad periodontal aumenta con la edad, de manera fisiológica hay una perdida, un despegamiento del periodonto y por eso la severidad en personas mayores sube.[19]

Gingivitis

La gingivitis es una inflamación superficial del periodonto que es reversible. No hay despegamiento del tejido conjuntivo. La reacción inflamatoria producida es debido en la mayoría de los casos a una acumulación de placa pero existe también gingivitis no producida por placa. La gingivitis se traduce por una encía roja, blanda y eritematosa, papilas inflamadas, sangre, presencia de pseudobolsas, ulceraciones, hay una vasodilatación al nivel capilar. Los cambios hormonales tienen una relación con la aparición de gingivitis (anti contraceptivos, pubertad, embarazo..)[20]. Hay otros factores de riesgo como factores nutricionales (déficit de vitamina C), la toma de medicamentos (antagonistas de calcio, vitamina A, anticoagulantes...), el sexo (más hombres son afectados, las mujeres tienen mejor higiene). La gingivitis en la mayoría de los casos es debido a una acumulación de biofilm dental que genera placa bacteriana.[20] Hay una acumulación de bacterias que cambia la flora bacteriana, las bacterias GRAM negativas anaeróbicas están más presentes. Hay revisión que relaciona las razas y la presencia de algunas bacterias, por ejemplo en la raza asiática y americana hay *Tannerella forsythia*, *Treponema denticola*, *Porphyromonas gingivalis*, los pacientes afroamericanos tienen más *PG*, y el origen étnico *el Actinobacillus actinomycetocomitans*.[17] La enfermedad periodontal puede ser la consecuencia de virus como: el herpesvirus, el cytomegalovirus, el virus Epstein Barr, el virus de la gingivoestomatitis herpética primaria y del herpes oral recidivante.[21-18] Los factores de riesgo no siempre son controlables, existen factores de origen genético, problemas de desregulación de hormonas como los estrógenos, problemas cardiovasculares e hipertensión que se relacionan también con la enfermedad periodontal.[18] La gingivitis además es la consecuencia de lesión química, de reacciones a cuerpos extraños.

La reacción que resulta de este cúmulo de bacterias, de biofilm es la inflamación. El mecanismo es simple, el numero de neutrófilos sube, hay fibrina que se va a acumular en las fibras de colágeno que se destruyen poco a poco.

La histopatología de la gingivitis se describe por diferentes estadios[20]

- Fase inicial: respuesta de leucocitos frente a la placa bacteriana su numero aumenta, la respuesta en los vasos sanguíneos es una vasodilatación producida por citoquinas. Existe una aumentación de la producción del fluido gingival.
- Fase temprana: el número de neutrófilos aumenta, cambio de color de la encía. Las proteínas se activan.
- Lesión establecida: respuesta inmune, aumento de macrófagos, células plasmáticas, linfocitos T y B. Aparición del sangrado gingival. A este estadio la destrucción tisular es aumentado pero el hueso alveolar es intacto.
- Lesión avanzada: transición entre gingivitis y periodontitis, despegamiento del periodonto, afectación de los tejidos de sostén.

Los signos y síntomas son variables: dolor, sangrado, halitosis. La gingivitis, se soluciona, quitando el factor causal, teniendo mejor higiene, enjuagues, en casos graves se puede hacer gingivectomia. La gingivitis es reversible.[22] Hay que prevenir la gingivitis, no tratada puede empeorar y generar periodontitis.[20]

Periodontitis

La periodontitis es una enfermedad infecciosa de origen bacteriana, irreversible que se describe por la destrucción del periodonto profundo. Los signos clínicos son: una perdida ósea, una inflamación gingival, un sangrado espontaneo, bolsas periodontales

profundas y movilidad. La periodontitis puede ser la consecuencia de una gingivitis no tratada.

Hoy en día se puede clasificar la periodontitis en cuatro estadios según la gravedad (Tonetti y cols 2018)[23]

- Estadio I: se caracteriza por bolsas de menos de 4 mm, sin pérdida dentaria, pérdida ósea horizontal, pérdida ósea del tercio coronal de 15 %.
- Estadio II: bolsas de menos de 5 mm, perdida ósea horizontal, perdida ósea coronal entre 15 y 33 %.
- Estadio III: perdida ósea hasta el tercio medio, bolsas de 6-7 mm, pérdida ósea vertical.
- Estadio IV: pérdida ósea hacia tercio apical, profundidad de bolsa superior a 8 mm.

El mecanismo de acción del desarrollo de la periodontitis es complejo. La presencia de biofilm bacteriano que adhiere al esmalte, es lo que empieza a producir reacción inflamatoria lo que genera la producción de enzimas (peptidasa, proteasas..), de productos citotóxicos (ácidos grasos) que desencadena la patogenia de la enfermedad periodontal.[24] Las bacterias implicadas más activas en la destrucción tisular son: PG, *Prevotella intermedia, Forsythensis, Actinomycetemcomitan*.[17]

La respuesta inflamatoria se divide en dos tipos: la respuesta adquirida e innata (aguda). Las bacterias presentes en la boca van a estimular una respuesta inflamatoria que genera problemas colaterales por la producción de enzimas líticas, que destruyen las células tisulares. Los mediadores son las citoquinas que regulan la amplitud de la reacción, las interleukinas-1 están producidas por los macrófagos. Su actividad va a

amplificar la respuesta inflamatoria.[24]La interleukina 1 se relaciona con la pérdida de hueso. El tumor necrosis factor (TNF) es la base de la pérdida osea. El TNF se explica por ser dos proteínas la alpha y la beta. El TNF-alpha es el resultado de los macrófagos, destruyen los fibroblastos, asociados a la interleukina-1 generan la destrucción tisular. Van a favorecer la actividad osteoclasticas, la apoptosis de células generadoras de periodonto.[25]

La enfermedad periodontal es multifactorial, muchos indicadores influyen en su agresividad. En estos factores de riesgos, la diabetes es de primera importancia.

OBJETIVOS

El objetivo principal que se analizará en este trabajo consiste en:

Relacionar la diabetes con la enfermedad periodontal

Objetivos secundarios:

- Identificar la influencia del control de la diabetes sobre la enfermedad periodontal y viceversa.
- Prevenir y tratar la periodontitis en pacientes diabéticos

MATERIALES Y METODOS

Diseño del trabajo: Este trabajo se ha realizado a través de un análisis bibliográfico con 44 artículos del año 2002 al 2020 encontrados en las bases de datos: Pubmed, Medline, Google Scholar y la Biblioteca Dulce Chacon. Para encontrar artículos se han introducido las palabras claves siguientes: "*diabetes", "periodontal disease" "inflammation", "periodontal treatment" "Chronic periodontitis" "resveratrol*".

Al principio de la búsqueda, ha salido 50 artículos interesantes que hemos organizados, resumidos y quitados en función de diferentes criterios.

Criterios de inclusión de la selección de los artículos:

- informaciones recientes: meta-análisis, protocolos, guías revistas médicas de periodoncia de los últimos años.

- artículos con contenido íntegro y completo

- informaciones de la organización colegial de dentistas en España

- idiomas de los artículos: ingles, castellano y francés.

Criterios de exclusión:

- Artículos con fecha anterior a 2002
- Artículos que están en blogs
- Artículos no completos, únicamente resumidos.

Tabla de recogida de datos para la realización del trabajo. (ANEXOS)

DISCUSÍON

Influencia de la diabetes en la enfermedad periodontal

La diabetes factor de riesgo de la enfermedad periodontal

La enfermedad periodontal tiene una asociación directa con la diabetes, muchos estudios muestran que la prevalencia de la enfermedad periodontal está aumentada en los pacientes diabéticos comparado a los no diabéticos. La evidencia de una correlación entre la periodontitis y la diabetes es más frecuente en el caso de la diabetes tipo 2[26], la periodontitis es la sexta complicación de la diabetes según Loe 1993. Según el estudio de Loe de 1993:

- la pérdida de inserción de tejidos dentales es más precoz en los diabéticos,

- la pérdida dental aumenta con la duración de la diabetes,

- la periodontitis es dos veces más frecuente en el paciente diabético no controlado que en pacientes controlados.

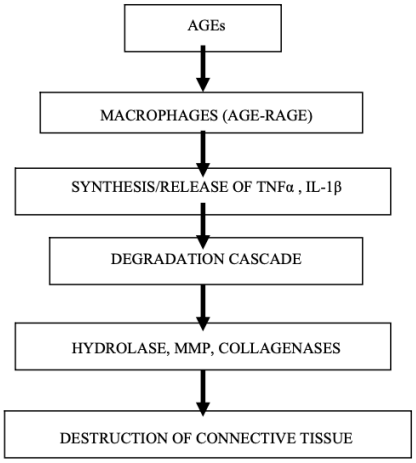
La diabetes tiene consecuencias múltiples en la cavidad bucal. La desregulación de las glándulas salivares es provocada por la alteración metabólica debido a las complicaciones neurológicas. Hay presencia posible de xerostomía, hipertrofia de glándulas salivares, afectaciones de las mucosas, mucositis y retraso de la cicatrización.[27]La disminución de la saliva en boca tiene consecuencias como acumulación de placa bacteriana en los dientes, aparición de caries, aumento de la sed, más probabilidad de infecciones fúngicas (inmunosupresión sistémica), sangrado de encías.[22] Las revisiones al dentista de forma regular son recomendadas, el control de la

enfermedad de la diabetes es primordial. Estudios muestran que la hiperglucemia genera estrés oxidante con consecuencias inflamatorias, el control de la diabetes mejora este estrés y reduce la circulación de las citoquinas, lo que permite mejorar la salud periodontal.[4]

Consecuencias de la hiperglucemia

La hiperglucemia es responsable del aumento de la inflamación, del estrés oxidativo y de la apoptosis celular. De la diabetes resulta una hiperglucemia crónica, que va a alterar la adherencia, el poder de fagocitosis de los leucocitos y genera una respuesta exagerada de los monocitos y macrófagos. La diabetes no controlada genera niveles altos de mediadores de la inflamación: prostaglandinas (PGE2) interleukinas-1 (IL-1), factor de necrosis tumoral (TNF-alpha) lo que aumenta la presencia de enfermedad periodontal.[4] La hiperglucemia se expresa en el fluido gingival de los pacientes, favorece el crecimiento bacteriano, la placa bacteriana y entonces el cambio de flora bacteriana. La diabetes tiene relación con la severidad de la enfermedad periodontal. Durante la hiperglucemia, las proteínas son expuestas durante mucho tiempo a glucosa, lo que va a cambiar de manera irreversible su estructura es el fenómeno de glicación, estas proteínas circulan después en las paredes vasculares y se encuentran en las superficies de los glóbulos rojos.[28] La formación de los productos de glicación AGE (advanced glycation endproducts) es el resultado de los radicales libres. Los AGE son el origen del estrés oxidativo y de la modificación del colágeno, favoreciendo la destrucción tisular.[29]

Figura 2: Modelo de como la diabetes contribuye al desarrollo de la enfermedad periodontal. AGE= advanced glycation end product, RAGE = receptor for AGE, TNF = factor tumoral necrosis, IL-1B= interleukina-1 beta.[29]



La diabetes está implicada en la severidad de la periodontitis y acelera la reabsorción ósea, el grado de la perdida ósea es relacionado con una falta de control metabólico.[28]

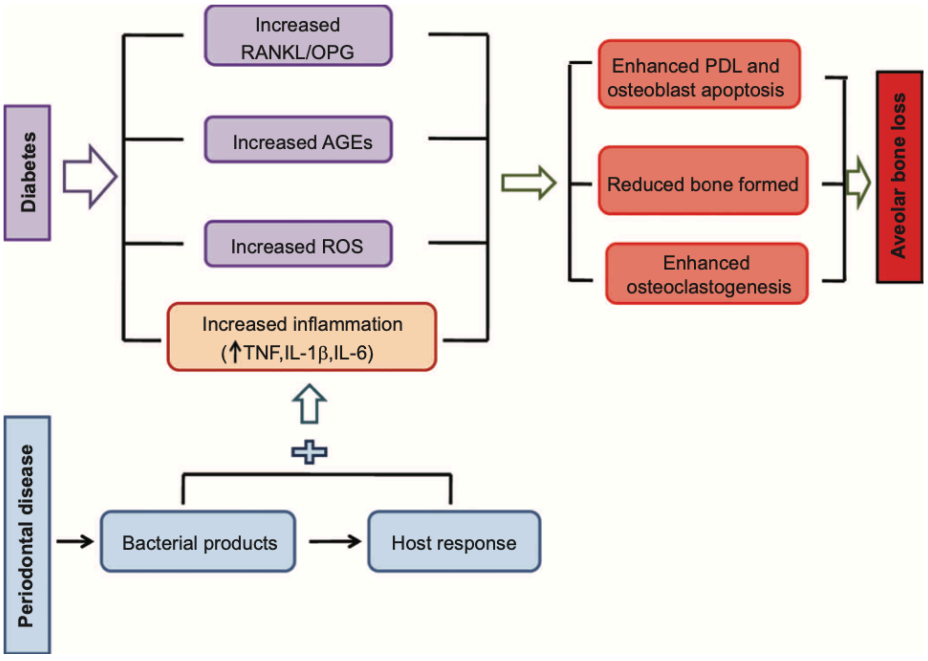
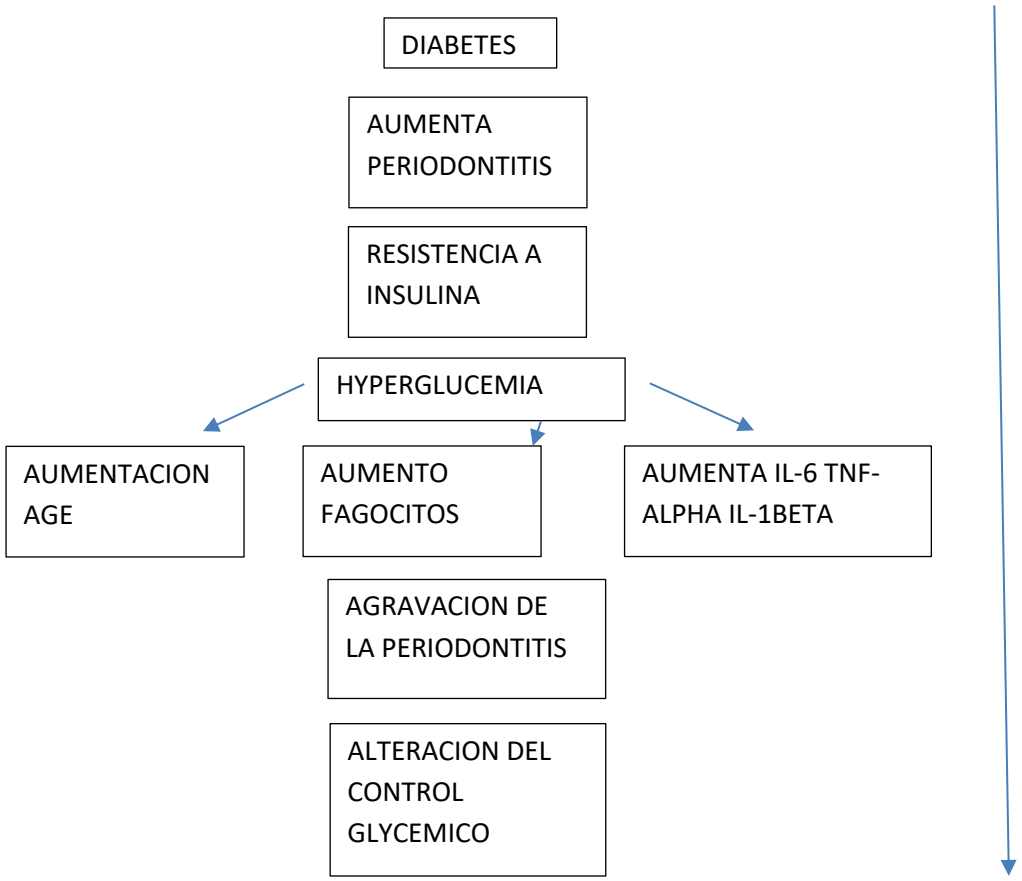


Figura 3: Relación entre diabetes y perdida ósea en la enfermedad periodontal[28]

El control de la glucemia es fundamental para evitar las complicaciones al nivel periodontal. Un mal control de la enfermedad demuestra la aparición de enfermedad periodontal de forma generalizada, inflamación de encías y lesión hemorrágicas.[30] El control de la diabetes es fundamental al nivel de la cicatrización de los tejidos y al desarrollo de una flora bacteriana adecuada.[31]

Resumen de las consecuencias de la diabetes (elaboración propia):



Mecanismo vascular

La diabetes contribuye a cambios microvasculares al nivel de las encías y de los alveolos. Hay cambios de estructura, composición y permeabilidad de la membrana basal. Se observa una membrana basal de los capilares más espesa que resulta de una estimulación de lípidos que se acumulan en el endotelio, lo que disminuye los cambios de nutrición de las células y la luz de los vasos.[28] La glucosa presente en la sangre provoca

aumento de las AGE en las paredes de los vasos lo que se traduce por paredes menos permeables que reducen el camino del oxigeno y de los factores inmunes en los tejidos gingivales. Estos cambios al nivel de la membrana basal generan una disminución de la migración leucocitaria y hormonales necesarias para la salud periodontal.[32] Hay también cambios al nivel macro vascular, que pueden generar patologías graves. La más conocida es la aterosclerosis que es la consecuencia de una inflamación crónica de la arteria, se desarrolla por la estimulación de lípidos.[28]

Desregulación del sistema de síntesis del colágeno

El colágeno es lo que constituye el tejido periodontal en su gran mayoría. Son los fibroblastos de la encía y del ligamento periodontal que lo sintetizan. En los pacientes diabéticos hay una disminución de la síntesis de colágeno comparado a una persona sana.[32] La hiperglucemia es responsable de la disminución del crecimiento de los fibroblastos.

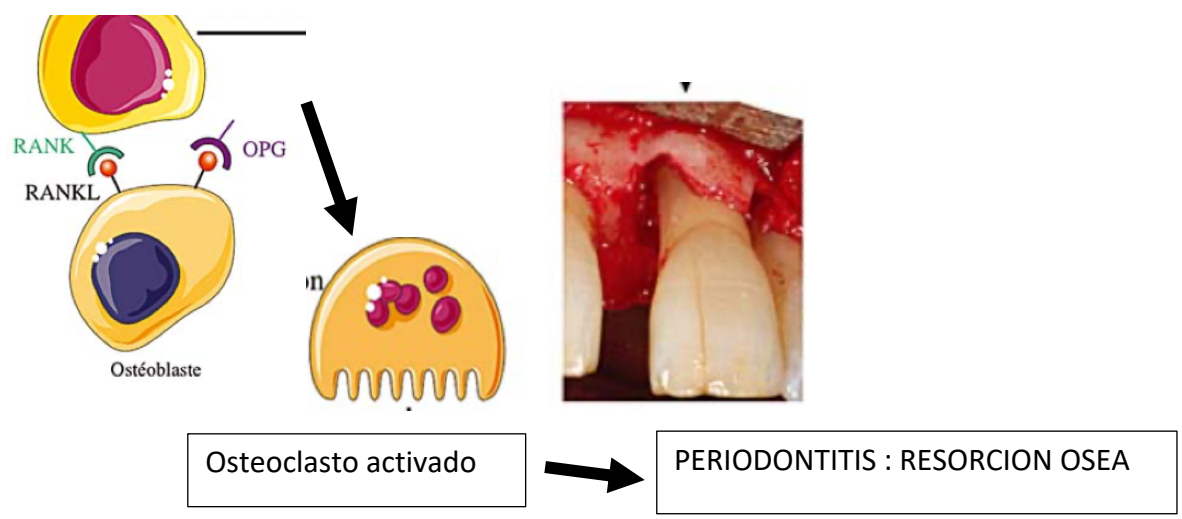
Mecanismo inmunológico

Estudios muestran que el disfuncionamiento de los polinucleares neutrófilos está relacionado con la gravedad de la enfermedad periodontal en el paciente diabético. La adherencia, la chimiotaxis y la fagocitosis son fases alteradas con la diabetes.[28] Se relaciona con la resistencia del cuerpo a la insulina, los factores pre inflamatorios como: el factor de tumor necrótico (TNF-ALPHA), la interleukina-1B, 6 y 18 son más elevados en pacientes enfermos que sanos. [28]

La patogénesis de la enfermedad periodontal está relacionada con mediadores de la inflamación: TNF-ALPHA, las citoquinas. Algunos estudios recientes muestran que la

periodontitis está relacionada por una competición que hay entre el complejo del receptor activador del factor nuclear kappa B (RANKL) y la osteoprotegerina (OPG) producto de los osteoblastos para adherirse al receptor activador del factor nuclear kappa B (RANK) que están en los precursores de osteoclastos. Un ratio RANKL/OPG elevado favorece la resorción ósea, es el caso en los pacientes diabéticos.[33]

Figura 4: resumen de la patogénesis de la resorción ósea[33]



Influencia de la enfermedad periodontal en la diabetes

Un dentista puede diagnosticar una diabetes precoz no diagnosticado, previamente a través de la enfermedad periodontal. Un paciente que acude a la consulta por una enfermedad periodontal severa no explicada, con la presencia de una flora periodontal asociada con síntomas (polidipsia, poliuria) puede ser relacionado con la diabetes. La anamnesis es una etapa de la consulta dental primordial, estas dos enfermedades: la diabetes y la enfermedad periodontal tienen aspectos hereditarios.

Según Mariano Sanz and cols.[4], un paciente que tiene enfermedad periodontal es mas susceptible de desarrollar en un futuro un pre-diabetes o diabetes. No se ha demostrado que la periodontitis afecta a las complicaciones de la diabetes según estos autores.

Analizan que los tratamientos de la enfermedad periodontal permiten reducir el TNF-alpha en diabéticos.

La enfermedad periodontal se caracteriza por un cambio de flora bacteriana en la boca, estudios muestran que la bacteria más encontrada es *el Porphyromonas gingivalis*, esta bacteria tiene influencia en el control de la glucemia del diabético.[30] Los radicales libres producidos por los monocitos en casos de periodontitis favorecen situación de pre-diabetes. Un estado inflamatorio crónico como en pacientes que tienen periodontitis es considerado como un factor de riesgo de diabetes tipo II. Los TNF-ALPHA y los IL-6 favorecen la aparición de la diabetes. Hay una relación intima entre la destrucción tisular y la hiperglucemia. La gravedad de la enfermedad periodontal afecta a la diabetes y su control metabólico.[29]

La periodontitis se exprima de diferentes formas. Hoy es posible de clasificarla en cuatro estadios:

- Estadio I: perdida ósea del tercio coronal (<15%), sin perdida dentaria, profundidad de sondaje menor a 4 mm, la perdida ósea es principalmente horizontal.
- Estadio II: perdida ósea del tercio coronal (15-33%), sin perdida dentaria, profundidad de sondaje menor a 5 mm.
- Estadio III: perdida ósea hasta el tercio medio o apical de la raíz, con un máximo de cuatro dientes por razones periodontales. Profundidad de sondaje de mas de 6 mm. Se observa afectación de furca grado II o III.

- Estadio IV: pérdida ósea que se extiende al tercio medio o apical de la raíz, con una pérdida de mas de 5 piezas dentales por razones periodontales. La profundidad del sondaje es mayor a 6 mm. El defecto alveolar es avanzado.[23]

Figura 5: Nueva clasificación de periodontitis por grados basado en factores modificadores, evidencia directa e indirecta. Según Tonetti y cols (2018)

		Grado A	Grado B	Grado C
Evidencia directa	Radiografías o evaluación periodontal en los 5 años anteriores	No evidencia de pérdida de hueso/inserción	Pérdida < 2 mm	Pérdida ≥ 2 mm
Evidencia indirecta	Pérdida ósea vs. edad	< 0,25	0,25-1,0	> 1,0
	Fenotipo	Grandes depósitos de *biofilm* con niveles bajos de destrucción	Destrucción proporcional a los depósitos de *biofilm*	El grado de destrucción supera las expectativas teniendo en cuenta los depósitos de *biofilm*; patrones clínicos específicos que sugieren periodos de progresión rápida y/o patología de aparición temprana... Por ejemplo, patrón molar-incisivo; falta de respuesta prevista a tratamientos de control bacteriano habituales
Factores modificadores	Tabaquismo	No fumador	< 10 cig./día	≥ 10 cig./día
	Diabetes	Normal con/sin diabetes	HbA1c < 7 con diabetes	HbA1c > 7 con diabetes

Control y prevención de la enfermedad periodontal

Diabetes y tratamiento periodontal

El tratamiento periodontal es complejo y necesita un diagnóstico preciso y la cooperación del paciente. Existen dos categorías de tratamientos: los no quirúrgicos y los quirúrgicos. Los tratamientos no quirúrgicos que se llaman también tratamientos periodontales básicos (raspajes, profilaxis) tienen como objetivo eliminar el biofilm sub y supra gingival, son útiles para restablecer la hemostasia de los tejidos y parar la progresión de la enfermedad periodontal: en los pacientes diabéticos son también útiles, pero no combinados no son satisfactorios. Los tratamientos más complejos con presencia de furcas, bolsas importantes tienen que ser combinados con tratamientos

antimicrobianos.[34] El tratamiento no quirúrgico asociado a la toma de doxycyclina durante 15 días muestra una evidencia de reducción del sangrado de encías y de bolsas profundas de más de 6mm. Los tratamientos no quirúrgicos de periodontitis son beneficiosos en la reducción de glucosa en pacientes diabéticos.[35]La colaboración del paciente es fundamental, un estudio pone en evidencia que una pobre higiene bucal, ausencia del uso de hilo dental, de cepillados interdentales son asociados a un mal control glucémico que generan un aumento de placa dental. Es importante que el paciente se crea una rutina, tenemos que enseñar las técnicas de higiene adecuadas por ejemplo la técnica de Bass. La técnica de Bass es una técnica muy útil en pacientes sanos como periodontales, el cepillado se pone con una angulación de 45 grados, haciendo movimientos de oscilaciones sin presión. La prevención permite evitar la progresión del proceso patológico. [36] Un estudio ha analizado los efectos del tratamiento periodontal en el paciente diabético. Se basa en el seguimiento de los pacientes durante 3 meses. La conclusión del estudio muestra que un control de la enfermedad periodontal genera una disminución de los niveles de HbA1c en los pacientes diabéticos tipo 2.[37]

Varios estudios muestran que la utilización de antibióticos sistémicos mejoran el pronostico de la enfermedad periodontal y el control de la diabetes, por ejemplo en el estudio se prescribe 100 mg de doxycyclina y se observa una reducción de 0.6% de HbA1c en pacientes.[29]

De otra parte, existe el tratamiento quirúrgico, que es de segunda elección, se hace después de una re-evaluación del tratamiento no quirúrgico, el objetivo será quitar las bolsas profundas. El tratamiento quirúrgico se hace con la condición que los pacientes

tienen un HbA1c < 7 %, nunca se hará tratamientos quirúrgicos en pacientes diabéticos no controlados.[38]

El mantenimiento periodontal, es la llave del tratamiento, con el fin de mantener los beneficios de los tratamientos periodontales, revisiones frecuentes cada 3 meses son obligatorias. Las medidas de higiene tienen que ser seguidas, y el dentista tiene que efectuar controles para intervenir en cualquier nueva infeción.[36]

Gestión de la diabetes durante el tratamiento periodontal

Se sabe que en diabéticos el tiempo de cicatrización es alterado, el control sérico de HbA1c (control de la glucemia sobre 3 meses) es fundamental. La diabetes tiene que ser controlada antes de cualquiera intervención. Los resultados terapéuticos positivos en pacientes no controlado son bajos. Se necesita interconsultas con el médico para hacer cirugías. Pacientes con pobre control glucémico genera más sangrado, pérdida de hueso y destrucción periodontal más severa. Un nivel HbA1c elevado afecta el tiempo de cicatrización.[36] Los pacientes diabéticos necesitan una atención particular, las citas tienen que estar programadas por la mañana, los pacientes tienen que comer antes, las citas tienen que ser cortas para reducir el estrés, la evaluación del nivel de glucosa es primordial, las revisiones tienen que ser recurrentes. Podemos utilizar anestésicos sin vasoconstrictor.

En la consulta, hay que tener el material en caso de coma: dextrosa al 50%, glucagón intramuscular, insulina de acción rápida, suero salino. Estos pacientes necesitan un control preciso de la infección, un diabético mal controlado tiene una mala cicatrización, la profilaxis bacteriana es fundamental, la suturas post extracción son recomendadas.[39]

Resveratrol : una nueva esperanza terapéutica

Resveratrol como hipoglucemiante

Es un medicamento que forma parte de los fenoles, es un estilbenoide que encontramos en diferentes plantas, respuesta a condiciones estresantes. Su nombre es el 3,5,4'- trihydroxystilbene. Esta molécula se encuentra en la alimentación en algunas frutas por ejemplo en uvas y arándanos. Ya se ha estudiado el efecto del resveratrol en el cáncer, tiene propiedad de inhibición de apoptosis.[40] En 2015 según estudios de Hausenblas and al se confirma que el resveratrol influye en la reducción de la resistencia a insulina, del glucosa, de la hemoglobina A1c y que tiene sensibilidad a la insulina.[40]

El resveratrol permite activar una proteina que se llama l'AMP-K: Adenosina mono fosfata kinasa para ejercer su poder hypoglucemiente. A través de la reacción bioquímica de glycolisis l'AMP-K activa la formación de la adenosine triphosphate (ADN). Esta activación disminuye la hiperlipidemia que hay en la diabetes. La proteína SIRT1 (NAD-dependent deacetylasa sirtuin-1) es también relacionado con la longevidad de la vida y el retraso de enfermedades ligadas con la edad. Estudios de Bordone and coll. ponen en evidencia que permite reducir el colesterol y la insulina.[41]

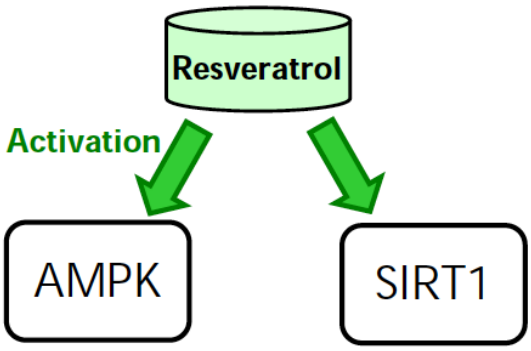


Figura 6: Efecto hipoglucemiante del resveratrol a través de la activación de la AMPK y la SIRT1.[41]

Un estudio clínico muestra que la prisa de 5 mg de resveratrol 2 veces por días durante 4 semanas disminuye la resistencia a la insulina y mejora el estrés oxidativo.[41] Pero no hay suficientes estudios para afirmarlo.

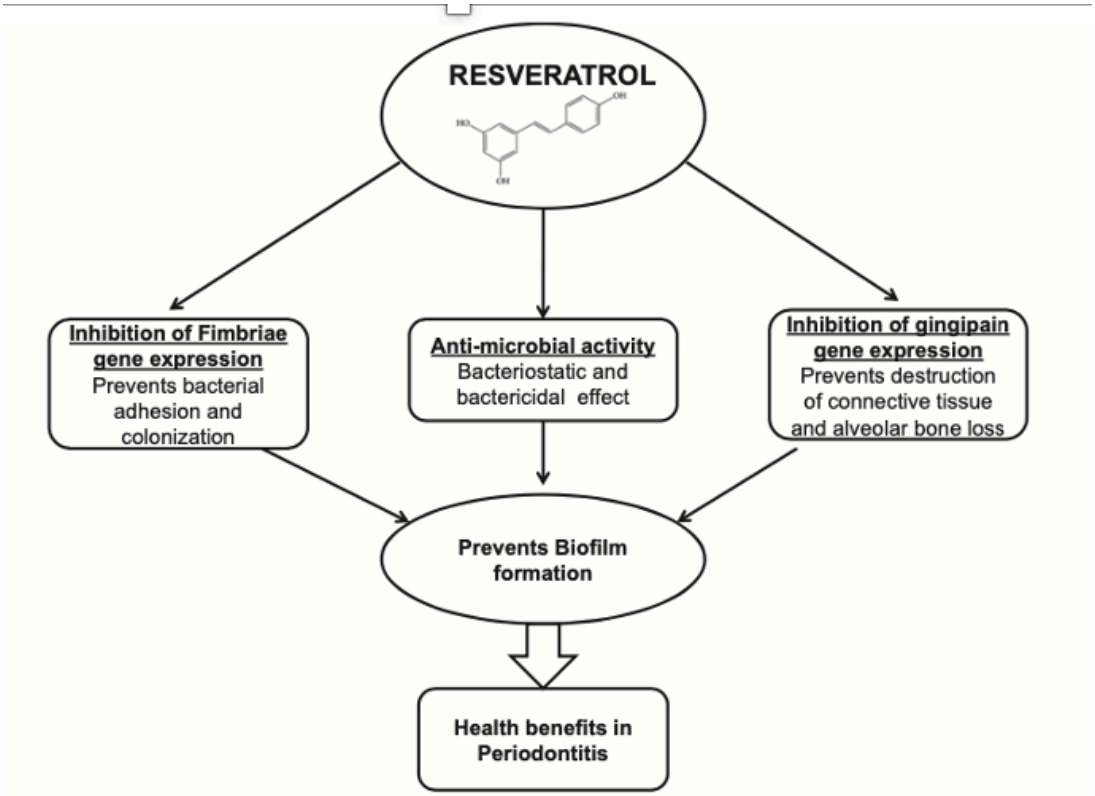
Resveratrol como anti-inflamatorio nuevo tratamiento de la enfermedad periodontal

Los últimos estudios, muestran que el resveratrol inhibe algunos mediadores de la reacción inflamatoria. El resveratol inhibe la COX-2 (ciclooxigenasa-2) y el NFkB.[41] Este nuevo tratamiento tiene resistencia a los antibióticos y tiene propiedades anti-inflamatorias, lo que es interesante para establecer un tratamiento periodontal.[40] La patología periodontal desencadena una reacción inflamatoria es por eso que se puede esperar resultados frente a la enfermedad periodontal.

Resveratrol como antibacteriano

Los antibióticos son cada vez más utilizados, la resistencia bacteriana hoy en día es un problema de alta importancia. Por eso, se buscan alternativas. Se ha estudiado que el resveratrol tiene poder anti-adhesivo, el biofilm dental es inhibido por este tratamiento.[42]

Figura 7: Efectos del resveratrol en el biofilm dental.[42]



La virulencia de algunos genes de la bacteria PG está disminuida, es por eso que se puede afirmar que el resveratrol tiene poder anti-bacteriano, se pone en evidencia que inhibe la degradación del colágeno tipo I por eso, se encuentra en las alternativas de tratamiento de las enfermedades periodontales.[4243] En el estudio de Lagha and co., se analiza la capacidad del resveratrol a actuar en el crecimiento de la P. gingivalis, por eso se evalúa el crecimiento de la bacteria en función de la concentración que se pone de resveratrol (figura 8). Se concluye del estudio que el crecimiento bacteriano es reducido de 77.35% cuando se pone 125 µg/ml.[43]

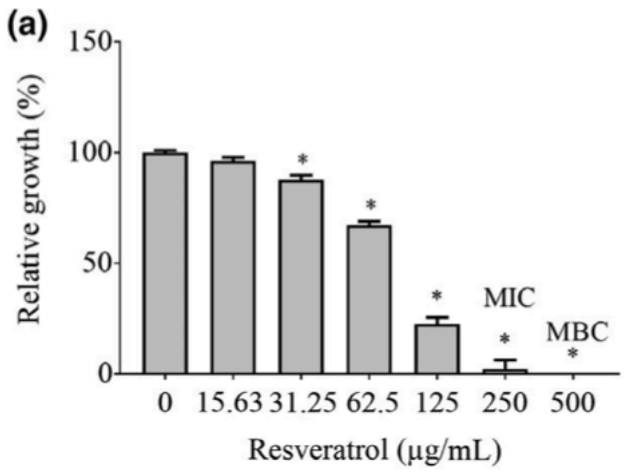


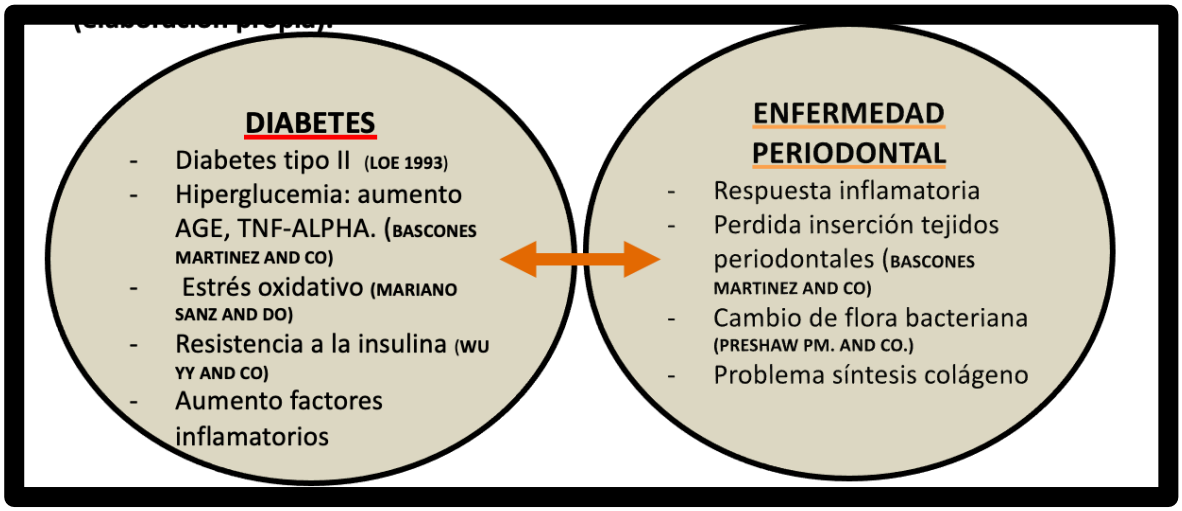
Figura 8: Efecto del resveratrol en el crecimiento de la porphyromonas gingivalis[43]

Resveratrol como antioxidante

El estrés oxidativo se ha visto en las consecuencias en la diabetes, que genera la formación de AGEs, que desencadena cambios en las proteínas de colágeno, lo que disminuye la oxigenación tisular de los tejidos periodontales. En los pacientes diabéticos la toma de resveratrol previene la formación de los AGE y entonces la destrucción tisular.[44]

El resveratrol, como tiene muchas propiedades se toma para varias causas: para cáncer, para mejorar el envejecimiento, disminuir el estrés oxidativo y enfermedades inflamatorias. Sobre algunos pacientes es posible tomar este medicamento diariamente, para los diabéticos se ha mostrado capacidad anti-inflamatoria como antibacteriana.

Figura 9 : Resumen de la relación intima entre diabetes y enfermedad periodontal (elaboración propia).



CONCLUSIÓNES

1- La diabetes genera problemas tanto micro vasculares como macro vasculares, la enfermedad periodontal forma parte de las complicaciones de la diabetes. Es un factor de riesgo en el desarrollo de patologías periodontales.

2- Estudios afirman que la gravedad de la enfermedad periodontal y su prevalencia está en relación con la diabetes. Un mal control de la enfermedad tiene repercusiones en la glucemia del paciente. Al contrario una hiperglucemia mal controlada genera problemas en la enfermedad inflamatoria.

3- La relación íntima entre la diabetes y la enfermedad periodontal hace que sea imprescindible una comunicación entre el dentista y el especialista que siguen al paciente para establecer planes de tratamientos. Los tratamientos cada vez evolucionan y los autores se multiplican para descubrir soluciones sobre esta enfermedad mundial.

RESPONSABILIDAD

La diabetes hoy en día es un problema de salud publica mundial. Es un problema social que afecta a toda la sociedad. Crea desigualdades sociales, la población más afectada por esta enfermedad es de categoría social desfavorecida La prevención es primordial, la diabetes de tipo II se produce después de una higiene de vida no saludable: obesidad, sobrepeso, sedentarismo. La promoción de un modo de vida saludable permite reducir el desarrollo de esta enfermedad.

De un punto económico, la diabetes afecta a gente cada vez más joven, las consecuencias cardiovasculares hacen que esta población no trabaja. El desempleo es una consecuencia de esta enfermedad. Para los países desarrollados es un real problema económico, mucho dinero es dedicado a los tratamientos para los diabéticos que pueden ni trabajar ni contribuir a la vida en sociedad.

Las enfermedades periodontales es un problema económico para los pacientes, no tratadas producen la perdida temprana de dientes, que necesitan gastos importantes para una rehabilitación protética. Un buen control de la enfermedad periodontal permite estabilizar la diabetes y no generar daños mas importantes.

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ANEXOS

AUTORES	Diabetes	Enfermedad periodontal
MARIANO SANZ AND CO. 2019.	- Pobre control de la glucemia - Hba1c mal controlado - No hay evidencia que la flora bacteriana en boca cambia - Mejor control mejora estrés oxidativo, reduce las citoquinas.	- Mayor riesgo de desarrollar una prediabetes o diabetes. - Reducción de la función de las células beta, eleva el estrés oxidativo - No se ha demostrado que la periodontitis afecta a las complicaciones de la diabetes - Tratamientos de la enfermedad periodontal reducen TNF-alpha en personas con diabetes.
WU YY AND CO. 2015.	Diabetes -> hiperglucemia crónica. Altera adherencia -> respuesta exagerada de los monocitos y macrófagos. Diabetes relación con la severidad de la enfermedad periodontal. Presencia con mas probabilidad en pacientes enfermos del factor TNF ALPHA.	
PRESHAW PM AND CO. 2011.		Cambio de flora bacteriana presencia en mayoría de porphyromonas gingivalis -> influye la glucemia.
BASCONES- MARTINEZ A. AND CO. 2012	La formación de los productos de glycacion (AGE= advanced glycacion endoproducts)	Relación destrucción tisular y hiperglucemia.

	es el resultado de los radicales productos. Los AGE son el origen del estrés oxidativo, de la modificación del colágeno favoreciendo la destrucción tisular.	
OMS	Consecuencias -> corazón riñones, ojos, disminuye la esperanza de vida.	
RATHEE PRACHI, 2021.		Histopatología de la gingivitis 4 estadios.
TONETTI Y COLS. 2018		4 estadios de la periodontitis
BLANCO, VILLAR, MARTINEZ AND CO. 2003.	Disminucion en estos pacientes de la síntesis de colágeno	
JAVID, HORMOZNEJAD AND CO. 2016.	Resveratrol nueva terapéutica -> efecto hipoglucemiante, sensibilidad a la insulina.	
VALLIANOU, EVANGELOPOULOS AND CO. 2013.	Resveratrol activa la AMP-K, la activación va a disminuir la hiperlipidemia. Disminuye el colesterol y insulina. 5 mg de resveratrol -> disminuye la resistencia a la insulina.	
LAGHA, ANDRIAN, 2018.	Resveratrol efecto antibacteriano	
CHIN, CHENG, SHIH, 2017.	Resveratrol previene la formación de los AGE que desancadena el estrés oxidativo.	Resveratrol previene las enferdades inflamatorias.

Articulo 1

La diabetes mellitus en España: mortalidad, prevalencia, incidencia, costes económicos y desigualdades

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(Mellitus diabetes in Spain: death rates, prevalence, impact, costs and inequalities)

Resumen

Objetivo: Describir la situación de la diabetes mellitus (DM) en España desde una perspectiva de salud pública.

Material y método: Se ha realizado una búsqueda manual de libros y otros documentos sobre DM en España, además una búsqueda específica de artículo usando los términos *MeSH diabetes mortality, morbidity, cost, inequalities and Spain,* realizada en Medline a través de PubMed. También se han utilizado los últimos datos disponibles de mortalidad y del Conjunto Mínimo Básico de Datos Hospitalarios por Comunidad Autónoma.

Resultados: La DM es una de las primeras causas de mortalidad, en las mujeres ocupa el tercer lugar. Por Comunidades Autónomas, Canarias junto con Andalucía y las ciudades autónomas de Ceuta y Melilla presentan la mayor mortalidad, con una tendencia descendente. Los diabéticos tienen una mayor mortalidad que los no diabéticos, sus complicaciones son las principales causas de la mayor mortalidad, sobre todo la enfermedad isquémica del corazón. Las estimaciones de prevalencia de DM tipo 2 (DM2) en España varían entre el 4,8 y el 18,7%, las de DM tipo 1 (DM1) entre el 0,08 y el 0,2%. Para la DM en el embarazo se han descrito prevalencias entre el 4,5 y el 16,1%. En cuanto a incidencia anual, se estima entre 146 y 820 por 100.000 personas para la DM2 y entre 10 y 17 nuevos casos anuales por 100.000 personas para la DM1. Los costes económicos de la DM1 van de 1.262 a 3.311 €/persona/año. Los costes de la DM2 oscilan entre 381 y 2.560 €/paciente/año. Los estudios que estiman costes totales los sitúan entre 758 y 4.348 €/persona/año. Se ha demostrado que a menor nivel socioeconómico peor es el control de la enfermedad y mayores su frecuencia y los otros factores de riesgo de DM2.

Conclusiones: Se puede afirmar que la DM es un importante problema de salud pública que irá incrementándose en los próximos años (fundamentalmente la DM2) si no se toman las medidas de prevención y control oportunas.

Palabras clave: Diabetes mellitus. Mortalidad. Prevalencia. Incidencia. Costes económicos. Desigualdades.

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Abstract

Objective: Describing the situation of diabetes mellitus (DM) in Spain from a public health perspective.

Matherial and method: A manual review of books and other documents on diabetes mellitus in Spain was conduced. In addition, a specific research of articles published using MeSH terms diabetes mortality, prevalence, incidence, cost, inequalities and Spain was conduced in Medline through Internet (PubMed). Minimun Basic Data Set was utilized as source for complication description by Communities Autonomus.

Results: DM is one of the leading cause of mortality and the third one in women. With regard to Autonomous Communities, Canary Islands, Ceuta y Melilla and Andalusia show the greatest mortality with a downward trend. Diabetics present grater mortality than non diabetic patients, being complications the main cause of the over-mortality, especially ischemic heart disease. Estimations of prevalence for DM2 range from 4.8% to 18.7% and for DM1, from .08% to .2%. In pregnancy, it has been noted a prevalence ranging from 4.5% to 16.1%. With respect to incidence per year, it is estimated a range from 146 to 820 per 100 000 inhabitants for DM2 and a range from 10 to 17 mew cases annually per 100 000 inhabitants for DM1. Costs for DM1 show very different results, averaging between 1,262 and 3,311 € per people and year. There are differences for DM2 costs as well, averaging between 381 and 2,560 € per patient and year. Total costs estimated range from 758 to 4,348 € per person and year. Relationship between a low socioeconomic level (LSL) and DM2 risk has been proved. Moreover, it has been noted that the less LSL the worse is the disease control, coupled with a greater frequency and more frequent factors of DM2 risk.

Conclusions: The knowledge about the situation of the DM as a Public Health problem in Spain is limited. Mortality data available does not gather its real magnitude, and prevalence, incidence, costs and inequalities research are very poor and hardly comparable. In spite of this degree of incertitude, we can state that DM is an important public health problem with a continuous increase, especially DM2, if the appropriate prevention and control measures are not taken.

Key words: Diabetes mellitus. Mortality. Prevalence. Incidence. Costs. Inequalities.

Articulo 2

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OPEN

Incidence of diabetes mellitus in Spain as results of the nation-wide cohort di@bet.es study

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Our aim was to determine the incidence of type 2 diabetes mellitus in a nation-wide population based cohort from Spain (di@bet.es study). The target was the Spanish population. In total 5072 people older than 18 years,were randomly selected from all over Spain). Socio-demographic and clinical data, survey on habits (physical activity and food consumption) and weight, height, waist, hip and blood pressure were recorder. A fasting blood draw and an oral glucose tolerance test were performed. Determinations of serum glucose were made. In the follow-up the same variables were collected and HbA1c was determined. A total of 2408 subjects participated in the follow-up. In total, 154 people developed diabetes (6.4% cumulative incidence in 7.5 years of follow-up). The incidence of diabetes adjusted for the structure of age and sex of the Spanish population was 11.6 cases/1000 person-years (IC95% = 11.1–12.1). The incidence of known diabetes was 3.7 cases/1000 person-years (IC95% = 2.8–4.6). The main risk factors for developing diabetes were the presence of prediabetes in cross-sectional study, age, male sex, obesity, central obesity, increase in weight, and family history of diabetes. This work provides data about population-based incidence rates of diabetes and associated risk factors in a nation-wide cohort of Spanish population.

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Articulo 3

España

Población total: 46 122 000
Grupo de ingresos: Altos

Mortalidad

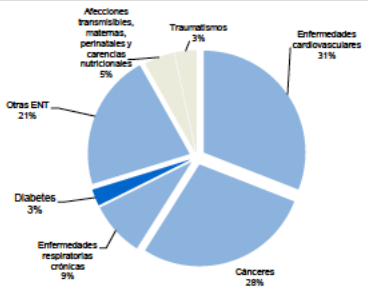
Número de muertes por diabetes

	hombres	mujeres
30-69 años	730	350
70 años o más	3 730	5 610

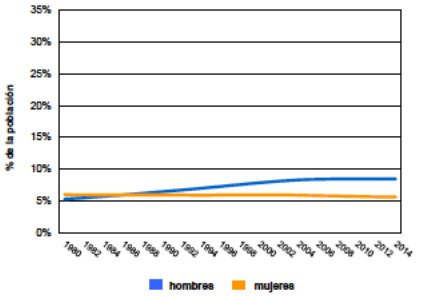
Número de muertes atribuibles a la hiperglucemia

	hombres	mujeres
30-69 años	2 090	630
70 años o más	8 590	11 100

Mortalidad proporcional (% del total de muertes, todas las edades)



Tendencias en la diabetes estandarizadas por edades



Prevalencia de la diabetes y de los factores de riesgo conexos

	hombres	mujeres	total
Diabetes	10.6%	8.2%	9.4%
Sobrepeso	70.3%	60.9%	65.6%
Obesidad	24.9%	28.0%	26.5%
Inactividad física	29.2%	37.4%	33.4%

Respuesta nacional contra la diabetes

Políticas, directrices y vigilancia

Política/estrategia/plan de acción contra la diabetes	*Sí*
Política/estrategia/plan de acción para reducir el sobrepeso y la obesidad	*Sí*
Política/estrategia/plan de acción para reducir la inactividad física	*Sí*
Directrices/protocolos/normas nacionales basados en datos probatorios contra la diabetes	*Existen y se aplican plenamente*
Criterios normalizados para la derivación de pacientes desde la atención primaria a un nivel superior	*Existen y se aplican plenamente*
Registro de casos de diabetes	*No*
Última encuesta nacional sobre factores de riesgo en la que se midió la glucemia	*No*

Disponibilidad de medicamentos, técnicas básicas y procedimientos en el sector de salud pública

Medicamentos disponibles en los establecimientos de atención primaria

Insulina	●
Metformina	●
Sulfonilurea	●

Procedimientos

Fotocoagulación retiniana	●
Diálisis	●
Trasplante renal	●

Técnicas básicas disponibles en los establecimientos de atención primaria

Medición de la glucemia	●
Prueba oral de tolerancia a la glucosa	●
Prueba de la HbA1c	●
Oftalmoscopia con dilatación	●
Percepción de la vibración del pie con diapasón	●
Prueba Doppler para determinar el estado vascular del pie	●
Tiras para medir la glucosa y las cetonas en la orina	●

○ = En general no disponible ● = En general disponible

Organización Mundial de la Salud – Perfiles de los países para la diabetes, 2016.

Articulo 4

Scientific evidence on the links between periodontal diseases and diabetes:

Sanz, Mariano; Ceriello, Antonio; Buysschaert, Martin; Chapple, Iain; Demmer, Ryan T; Graziani, Filippo; Herrera, David; Jepsen, Søren; Lione, Luca; Madianos, Phoebus; Mathur, Manu; Montanya, Eduard; Shapira, Lior; Tonetti, Maurizio; Vegh, Daniel

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https://doi.org/10.1111/jcpe.12808

Articulo 6

JRHS
Journal of Research in Health Sciences
journal homepage: www.umsha.ac.ir/jrhs

Original Article

Dental Health Status and Hygiene in Children and Adolescents with Type 1 Diabetes Mellitus

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Periodontal Disease
Type 1 Diabetes Mellitus

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ABSTRACT

Background: There is disagreement on the effect of diabetes on oral hygiene. The purpose of this study was to assess the oral health and hygiene status of type 1 diabetic patients.

Methods: In this case control study, periodontal health and hygiene of 80 children and adolescents (5–18 yr of age) with type 1 diabetes mellitus referred to Pediatric Endocrine Clinic of Besat Hospital Hamadan Iran 2013 – 2014 and 80 non diabetic control subjects were clinically assessed. The required data such as sex, age, duration of the diabetes, type and number of insulin injections per day were obtained from self-administered questionnaire and the patient's medical records. Participants in both groups were examined for Decay-missing- filled teeth (DMFT); dmft (for primary teeth), oral hygiene using O'Leary plaque index (PI) and gingivitis index (GI). $P<0.05$ was considered significant.

Results: The mean age of the study and the control group was 12.5±4.05 and 12.08±3.47 yr, respectively. There were no significant difference between two groups in terms of DMFT ($P=0.158$) and PI indices ($P=0.373$). The GI index difference was statistically significant in diabetic group ($P=0.001$). Interestingly, a higher dmft index was observed in the control group ($P=0.008$). In diabetic groups, GI and DMFT index increased significantly with duration of diabetes .

Conclusions: Apart from higher scores of GI index, frequency of oral and periodontal disease was not different in diabetic patients compared with healthy subjects. Findings of present study are insufficient to support a significant effect of diabetes on increasing the risk of oral and periodontal diseases. However, diabetic children and adolescents should receive oral hygiene instructions.

Citation: Rafatjou R, Razavi Z, Tayebi S, Khalili M, Farhadian M. Dental Health Status and Hygiene in Children and Adolescents with Type 1 Diabetes Mellitus. J Res Health Sci. 2016; 16(3):122-126.

Introduction

Type 1 diabetes mellitus (T1DM) is a common metabolic disease of childhood. About 1 in every 400-600 children and adolescents has T1DM. In adults, T1DM constitutes approximately 5% of all diagnosed cases of diabetes chronic illness[1,2]. A 2011 report from the US Centers for Disease Control and Prevention (CDC) estimated that approximately one million Americans have T1DM[1]. Onset most often occurs in childhood, but the disease can also develop in adults in their late 30s and early[1].

In this type of diabetes, an autoimmune destruction of the beta cells of the pancreatic islets leading to defects in insulin secretion. This results in persistent hyperglycemia and the clinical manifestation of the disease with dependence on exogenous insulin to prevent ketosis. The disease manifests itself in genetically predisposed individuals (polygenic genetic predisposition). Oral disease include xerostomia, periodontal disease (gingivitis and periodontitis), dental abscesses, tooth loss, soft tissue lesions, dry mouth and dental caries have been proposed as the 6th most prevalent complication of diabetes mellitus following the other diabetic complications[3-5]. The co-morbid presence of various inflammatory diseases and soft tissue pathologies in oral cavities in turn, adversely affect glycemic control and the treatment of oral complications can lead to improved metabolic control in diabetes patients[6-8]. Although patients with diabetes face a significantly higher risk for oral complications than healthy subjects[9-11], there is controversy on the impact of diabetes on oral and periodontal diseases and the mechanisms through which this occurs[12,13].

Considering the fact that some studies have reported a high prevalence of diabetes in Iran[14] and controversies about the impact of diabetes on oral health's status of T1DM and lack of public awareness in this regard further studies in this area is reasonable. Accordingly, we aimed to evaluate the oral health status of young patients with T1DM compared to healthy subjects in Hamadan west province of Iran.

Articulo 7

Mini Review

HORMONE RESEARCH IN PÆDIATRICS

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Diabetes Insipidus – Diagnosis and Management

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Key Words
Central diabetes insipidus · Langerhans cell histiocytosis · Pituitary stalk · Vasopressin

Abstract
Central diabetes insipidus (CDI) is the end result of a number of conditions that affect the hypothalamic-neurohypophyseal system. The known causes include germinoma/craniopharyngioma, Langerhans cell histiocytosis (LCH), local inflammatory, autoimmune or vascular diseases, trauma resulting from surgery or an accident, sarcoidosis, metastases and midline cerebral and cranial malformations. In rare cases, the underlying cause can be genetic defects in vasopressin synthesis that are inherited as autosomal dominant, autosomal recessive or X-linked recessive traits. The diagnosis of the underlying condition is challenging and raises several concerns for patients and parents as it requires long-term follow-up. Proper etiological diagnosis can be achieved via a series of steps that start with clinical observations and then progress to more sophisticated tools. Specifically, MRI identification of pituitary hyperintensity in the posterior part of the sella, now considered a clear marker of neurohypophyseal functional integrity, together with the careful analysis of pituitary stalk shape and size, have provided the most striking findings contributing to the diagnosis and understanding of some forms of 'idiopathic' CDI. MRI STIR (short-inversion-time inversion recovery sequencing) is a promising technology for the early identification of LCH-dependent CDI.

Definition/Classification

Diabetes insipidus is a disease in which large volumes of dilute urine (polyuria) are excreted due to vasopressin (AVP) deficiency [central diabetes insipidus (CDI)], AVP resistance [nephrogenic diabetes insipidus (NDI)], or excessive water intake (primary polydipsia). Polyuria is characterized by a urine volume in excess of 2 l/m^2/24 h or approximately 150 ml/kg/24 h at birth, 100–110 ml/kg/24 h until the age of 2 years and 40–50 ml/kg/24 h in the older child and adult.

Etiology

In many patients, CDI is caused by the destruction or degeneration of neurons originating in the supraoptic and paraventricular nuclei. The known causes of these lesions include local inflammatory or autoimmune dis-

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Parte del libro (8)

CAPÍTULO 23

DIABETES MELLITUS TIPO 1
TRATAMIENTO
SEGUIMIENTO
COMPLICACIONES AGUDAS

SOCIEDAD ESPAÑOLA DE ENDOCRINOLOGÍA PEDIÁTRICA

1

Articulo 9

ETIOPATHOGÉNIE ET PHYSIOPATHOLOGIE DU DIABÈTE DE TYPE 2

F. FÉRY (1), N. PAQUOT (2)

RÉSUMÉ : L'étiopathogénie du diabète de type 2 est complexe et reste imparfaitement connue. Son étiologie est déterminée par l'interaction de facteurs génétiques et environnementaux. La contribution génétique est importante, de nature polygénique. L'obésité, surtout celle à répartition abdominale, est le plus puissant facteur prédisposant au diabète de type 2 et près de 80 % des sujets diabétiques présentent un excès pondéral. L'effet diabétogène de l'obésité est lié à sa capacité d'induire ou d'aggraver l'insulinorésistance de ces sujets. La sédentarité croissante des populations industrialisées représente également un facteur favorisant le diabète; car elle majore la résistance à l'insuline. Sur le plan physiopathologique, le développement du diabète de type 2 résulte de la coexistence d'anomalies de la sécrétion et de l'action de l'insuline. Le dysfonctionnement sécrétoire, dont la cause demeure mal comprise, se traduit toujours par une carence relative plus ou moins sévère en insuline. La résistance à l'action de l'insuline s'exerce au niveau du foie (augmentation de la production hépatique de glucose), du muscle squelettique (réduction de l'utilisation musculaire du glucose) et du tissu adipeux (lipolyse exagérée avec élévation des acides gras libres plasmatiques). Les mesures hygiéno-diététiques (réduction pondérale, activité physique régulière) permettent de prévenir ou de retarder l'apparition du diabète de type 2.

MOTS-CLÉS : *Diabète de type 2 – Etiopathogénie – Génétique - Insulinorésistance – Insulinosécrétion - Physiopathologie*

ETIOPATHOGENESIS AND PATHOPHYSIOLOGY OF TYPE 2 DIABETES

SUMMARY : Etiopathogenesis of type 2 diabetes is complex and still partially unknown. Its etiology is determined by the interaction of genetic and environmental factors. The genetic contribution is important, but has a polygenic origin. Obesity, especially when fat mass is preferably located in the abdomen, is the main predisposing factor for type 2 diabetes, and almost 80 % of diabetic patients are overweight or obese. The diabetogenic effect of obesity is due to the capacity of excessive fat mass to induce or aggravate insulin resistance. Increasing lack of physical activity is also a contributing factor as it increases insulin resistance. As far as pathophysiology is concerned, the development of type 2 diabetes results from the coexistence of abnormalities of insulin secretion and insulin action. Insulin secretory dysfunction, whose underlying mechanism remains poorly understood, is characterized by a relative defect in circulating insulin levels of variable severity. Resistance to insulin action is located in the liver (increased hepatic glucose production), in the skeletal muscle (decreased muscular glucose uptake) and in the adipose tissue (exaggerated lipolysis with elevated plasma free fatty acids). Changes in life-style habits (weight reduction, regular physical activity) are able to prevent or delay the development of type 2 diabetes.

KEYWORDS : *Type 2 diabetes – Etiopathogenesis – Genetics – Insulin resistance – Insulin secretion - Pathophysiology*

INTRODUCTION

Le diabète de type 2 est l'affection métabolique la plus répandue dans le monde. Sa prévalence s'accroît de manière exponentielle et, selon les prévisions de l'OMS, plus de 300 millions d'individus seront diabétiques en 2025. Contrairement au diabète de type 1, le diabète de type 2 est une maladie complexe s'inscrivant généralement dans le cadre plus large du syndrome métabolique. Son étiologie est déterminée par l'interaction de facteurs génétiques et environnementaux. Au plan physiopathologique, elle résulte de la combinaison, à des degrés variables, d'anomalies de la sécrétion et de l'action de l'insuline, ce qui rend compte de son phénotype hétérogène.

ETIOLOGIE

FACTEURS GÉNÉTIQUES

La contribution génétique à l'étiologie du diabète de type 2 est très importante comme en témoigne le taux élevé (60-90%) de concordance chez les jumeaux homozygotes et l'agrégation familiale de cette maladie (1). On estime que le risque de développer un diabète est d'environ 30 % si l'on a un parent diabétique et approche les 70 % si les 2 parents sont diabétiques. Une histoire familiale de diabète constitue donc un facteur de risque majeur de développer la maladie. Néanmoins, étant donné la prévalence élevée du diabète de type 2 dans la population générale, il est fort probable que les gènes de susceptibilité soient très nombreux, très répandus et de faible pénétrance, ce qui les rend difficiles à identifier. La majorité des experts s'accordent, en effet, pour penser qu'il s'agit très vraisemblablement d'une affection polygénique (nécessitant la présence conjointe de plusieurs gènes anormaux pour s'exprimer) et multigénique (pouvant résulter de différentes combinaisons d'anomalies génétiques), ce qui cadre bien avec l'hétérogénéité phénotypique de la maladie. L'étude de la génétique du diabète de type 2 (qualifiée de cauchemar par les généticiens) est particulièrement délicate en raison des caractéristiques propres à cette affection. Celle-ci apparaît à un âge tardif, elle est souvent méconnue, son phénotype est mal défini et, enfin, elle est fortement influencée par des facteurs environnementaux (2).

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Articulo 10

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REVIEW
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Drug Delivery System in the Treatment of Diabetes Mellitus

Ruichen Zhao[1,2], Zhiguo Lu[1,2], Jun Yang[1], Liqun Zhang[3], Yan Li[1]* and Xin Zhang[1]**

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Diabetes mellitus has been described as a chronic endocrine and metabolic disease, which is characterized by hyperglycemia and the coexistence of multiple complications. At present, the drugs widely applied in clinical treatment of diabetes mellitus mainly include insulin, insulin analogs, non-insulin oral hypoglycemic drugs and genetic drugs. Nevertheless, there is still no complete therapy strategy for diabetes mellitus management by far due to the intrinsic deficiencies of drugs and limits in administration routes such as the adverse reactions caused by long-term subcutaneous injection and various challenges in oral administration, such as enzymatic degradation, chemical instability and poor gastrointestinal absorption. Therefore, it is remarkably necessary to develop appropriate delivery systems and explore complete therapy strategies according to the characters of drugs and diabetes mellitus. Delivery systems have been found to be potentially beneficial in many aspects for effective diabetes treatment, such as improving the stability of drugs, overcoming different biological barriers *in vivo* to increase bioavailability, and acting as an intelligent automatized system to mimic endogenous insulin delivery and reduce the risk of hypoglycemia. This review aims to provide an overview related with the research advances, development trend of drug therapy and the application of delivery systems in the treatment diabetes mellitus, which could offer reference for the application of various drugs in the field of diabetes mellitus treatment.

Keywords: diabetes mellitus, drug delivery, insulin, gene therapy, nanoparticle

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INTRODUCTION

In recent decades, the prevalence of diabetes mellitus has increased globally. According to the 9th edition of Diabetes Atlas by the International Diabetes Federation (IDF), the number of global diabetes patients in 2019 is estimated to be 463 million, which will increase to 578 million by 2030 and 700 million by 2045 (Saeedi et al., 2019). At present, diabetes mellitus has become a kind of serious non-communicable disease that causes high mortality and morbidity rate just next to cardiovascular disease and malignant tumor. As one of the most common chronic diseases, diabetes mellitus is an endocrine and metabolic disease characterized by hyperglycemia and multiple complications. Diabetes mellitus is mainly caused by genetic, environmental influence, microbial infection, immune system dysfunction, and mental factors that result in insufficient insulin secretion and insulin resistance. Patients with diabetes mellitus have long suffered from the devastating complications that could lower their quality of life and threaten their lives.

Articulo 11

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Research: Complications

Cardiovascular disease prevalence and risk factor prevalence in Type 2 diabetes: a contemporary analysis

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Accepted 20 September 2018

Abstract

Aims To describe the prevalence of major cardiovascular disease (CVD) and risk factor control in a contemporary population with Type 2 diabetes.

Methods We used data from the national registry in Scotland, Scottish Care Information-Diabetes, linked to hospital admissions. Using descriptive statistics and logistic regression we described associations of risk factors with CVD. CVD was defined based on diagnostic codes in primary or secondary care data for ischaemic heart disease, cerebrovascular disease peripheral arterial disease, heart failure, cardiac arrhythmia, hypertensive heart disease and revascularization procedures.

Results Among 248 400 people with Type 2 diabetes with a median age of 67.5 years (IQR 58.2, 76.1) and median diabetes duration of 7.8 years (3.8, 13.0), 32% had prior CVD (35% of men, 29% of women). Median HbA_{1c} overall was 55 mmol/mol (7.2%), median SBP was 132 mmHg, median total cholesterol was 4.1 mmol/l and mean BMI was 32 kg/m^2. Overall two-thirds (65% of men, 68% of women) have two or more of the following CVD risk factor thresholds: $HbA_{1c} \geq 53$ mmol/mol (7%), SBP > 130 mmHg or DBP > 80 mmHg, total cholesterol ≥ 5 mmol/l or BMI ≥ 30 kg/m^2, or were currently smoking. Overall 84% were taking anti-hypertensives and 75% a statin. Use of metformin was common at 58%, but other diabetes drugs that reduce CVD were rarely used.

Conclusions There continues to be a high prevalence of CVD among people with Type 2 diabetes and a high level of unmet need for risk factor control. This implies substantial scope for reducing the excess risk of CVD in diabetes through improved management of known risk factors.

Diabet. Med. 36: 718–725 (2019)

Introduction

Total mortality rates are currently 40% higher in men and 50% higher in women with Type 2 diabetes mellitus compared with the background population [1]. Cardiovascular disease (CVD) remains the leading cause of loss of life expectancy in Type 2 diabetes and rates remain elevated compared with those without diabetes. Ongoing elevations in risk have been reported in recent data from Scotland [2], Sweden and the USA [3,4].

Key aspects of the prevention of primary and secondary CVD in diabetes include smoking prevention, weight control, blood pressure reduction, cholesterol lowering and glycaemic control. With regards to glycaemic control, evidence of vascular benefit has been demonstrated for metformin with respect to myocardial infarction and pioglitazone with respect to CVD; by contrast heart failure is increased [5–7]. For newer drugs, major cardiovascular outcome trials have been conducted in recent years [8]. In four drugs from two anti-diabetes drug classes, sodium glucose co-transporter 2 inhibitors (SGLT2i) and glucagon-like peptide 1 receptor agonists (GLP-1RA), evidence of reduced risk of major CVD events has been demonstrated. These four drugs are canagliflozin (SGLT2i), empagliflozin (SGLT2i), liraglutide

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Trying to understand gestational diabetes

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Abstract

Women with normal glucose tolerance pre-gravid and developing gestational diabetes in late gestation have subclinical metabolic dysfunction prior to conception compared with women with normal glucose tolerance. Because of the 60 % decrease in insulin sensitivity with normal pregnancy, these women develop clinical hyperglycaemia/gestational diabetes in late gestation. The metabolic dysfunction includes impaired insulin response, decreased hepatic suppression of glucose production during insulin infusion and decreased insulin-stimulated glucose uptake in skeletal muscle, i.e. peripheral insulin resistance. The insulin resistance in normal glucose tolerance pregnancy is related to a decrease in the post-receptor insulin signalling cascade, specifically decreased insulin receptor substrate 1 tyrosine phosphorylation. In women with normal glucose tolerance this is reversed post-partum. In contrast, in gestational diabetes, in addition to the decrease in insulin receptor substrate 1 tyrosine phosphorylation, there is an additional decrease in tyrosine phosphorylation of the intracellular portion of the insulin receptor that is not related to the insulin receptor protein content. Post-partum women with gestational diabetes, who had retention of gestational weight gain, had no significant improvement in insulin sensitivity and increased inflammation expressed as increased plasma and skeletal muscle tumour necrosis factor alpha. The increased inflammation or meta-inflammation is a hallmark of obesity and during pregnancy develops in both white adipose tissue and placenta. Last gene array studies of placenta were associated with alterations in gene expression relating primarily to lipid in contrast to glucose metabolic pathways in gestational diabetes compared with Type 1 diabetes. Future studies are directed at decreasing inflammation prior to and during pregnancy using various lifestyle and nutritional interventions.

Introduction

The purpose of this review is to describe the development of the pathophysiology of gestational diabetes and potential treatment options resulting from my collaboration with a number of investigators. I had the great fortune of training in an academic environment during my residency in Obstetrics and Gynecology and fellowship in Maternal Fetal Medicine at the University of Vermont. Although initial attempts at research were directed

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This manuscript is a review based on my presentation of the Jorgen Pedersen Lecture at the 43rd Diabetes in Pregnancy Group (DPSG) of the European Association for the Study of Diabetes (EASD) held on 22–25 September 2011 at Queens' College, Cambridge University.

Competing interests None declared.

Articulo 13

Inflamatory response in pregnant women with high risk of preterm delivery and its relationship with periodontal disease. A pilot study

Francina Escobar-Arregoces[1], Catalina Latorre-Uriza[1], Juliana Velosa-Porras[1], Nelly Roa-Molina[1], Alvaro J Ruiz[2], Jaime Silva[3], Estefania Arias[4], Juliana Echeverri[4]

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ABSTRACT

Periodontal disease and its inflammatory response have been related to adverse outcomes in pregnancy such as preterm birth, preeclampsia and low birth weight. This study analyzed systemic inflammatory response in patients with high risk of preterm delivery and its relationship to periodontal disease. A pilot study was conducted for a case and control study, on 23 patients at risk of preterm delivery and 23 patients without risk of preterm delivery as controls. Exclusion criteria were patients who had received periodontal treatment, antibiotic or antimicrobial agents within the past three months, or with infections or baseline diseases such as diabetes or hypercholesterolemia. All patients underwent periodontal assessment, laboratory tests (complete blood count, lipid profile, baseline glycemia) and quantification of cytokines (IL-2, IL-4, IL-6, IL-10, TNF-α and INF-γ). Higher levels of pro-inflammatory cytokines (IL-2, IL-4, IL-6, IL-10, TNF-α and INF-γ) were found in patients with chronic periodontitis than in patients with gingivitis or periodontal health. These cytokines, in particular IL-2, IL-10 and TNF- α, were higher in patients at high risk of preterm delivery. Patients with high risk of preterm delivery had higher severity of periodontal disease as well as higher levels of the pro-inflammatory markers IL-2, IL-4, IL-6, IL-10, TNF- α and INF-γ.

Key words: *Chronic periodontitis, Pregnancy, Preterm birth, Preterm labor, cytokines.*

Respuesta inflamatoria en pacientes embarazadas con alto riesgo de parto pretérmino y su relación con la enfermedad periodontal. Estudio piloto

RESUMEN

La enfermedad periodontal y su repuesta inflamatoria ha sido relacionada con desenlaces adversos del embarazo como el parto pretérmino, preeclampsia y bajo peso al nacer. La presente investigación analizó la respuesta inflamatoria sistémica en pacientes embarazadas con alto riesgo de parto pretérmino y su relación con la enfermedad periodontal. Se realizó un estudio piloto de casos y controles, en el cual se contó con 23 pacientes que presentaban riesgo de parto pretérmino como casos y 23 pacientes sin riesgo de parto pretérmino como controles. Fueron excluidas las pacientes que hubieran recibido tratamiento periodontal, antibióticos o antimicrobianos en los últimos tres meses, que tuvieran infecciones, o enfermedades de base como diabetes o hipercolesterolemia. A todas las pacientes se les hicieron valoración periodontal, exámenes de laboratorio (cuadro hemático, perfil lipídico, glucemia basal) y cuantificación de citocinas (IL-2, IL-4, IL-6, IL-10, TNF- α e INF-γ). En las pacientes con periodontitis crónica se encontraron niveles más elevados en las citocinas proinflamatorias (IL-2, IL-4, IL-6, IL-10, TNF- α e INF-γ) en comparación con las pacientes con gingivitis o sanas periodontales. Estas citocinas se encontraron más elevadas en las pacientes con alto riesgo de parto pretérmino, en especial la IL-2, IL-10 y TNF- α. Las pacientes con alto riesgo de parto pretérmino presentaron mayor severidad de la enfermedad periodontal y adicionalmente niveles aumentados de los marcadores pro inflamatorios IL-2, IL-4, IL-6, IL-10, TNF- α e INF-γ.

Palabras clave: *periodontitis crónica, embarazo, nacimiento prematuro, parto prematuro, citocinas.*

Articulo 14

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Prevalence of Gestational Diabetes and Risk of Progression to Type 2 Diabetes: a Global Perspective

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Abstract

Despite the increasing epidemic of diabetes mellitus affecting populations at different life stages, the global burden of gestational diabetes mellitus (GDM) is not well assessed. Systematically synthesized data on global prevalence estimates of GDM are lacking, particularly among developing countries. The hyperglycemic intrauterine environment as exemplified in pregnancies complicated by GDM might not only reflect but also fuel the epidemic of type 2 diabetes mellitus (T2DM). We comprehensively reviewed available data in the past decade in an attempt to estimate the contemporary global prevalence of GDM by country and region. We reviewed the risk of progression from GDM to T2DM as well. Synthesized data demonstrate wide variations in both prevalence estimates of GDM and the risk of progression from GDM to T2DM. Direct comparisons of GDM burden across countries or regions are challenging given the great heterogeneity in screening approaches, diagnostic criteria, and underlying population characteristics. In this regard, collaborative efforts to estimate global GDM prevalence would be a large but important leap forward. Such efforts may have substantial public health implications in terms of informing health policy makers and healthcare providers for disease burden and for developing more targeted and effective diabetes prevention and management strategies globally.

Keywords

Gestational diabetes; Prevalence; Screening; Diagnosis; Type 2 diabetes; Pregnancy

Introduction

Due to the epidemiologic transition of the population towards aging and more sedentary lifestyle related to urbanization during the past few decades, the prevalence of type 2 diabetes mellitus (T2DM) has been rapidly increasing and the age of onset becomes younger globally [1]. Many developing countries are currently suffering from the increasing burden

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Conflict of Interest Yeyi Zhu and Cuilin Zhang declare that they have no conflict of interest.

Compliance with Ethical Standards

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Articulo 15

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Drug Delivery System in the Treatment of Diabetes Mellitus

Ruichen Zhao[1,2], Zhiguo Lu[1,2], Jun Yang[1], Liqun Zhang[3], Yan Li[1]* and Xin Zhang[1]**

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Diabetes mellitus has been described as a chronic endocrine and metabolic disease, which is characterized by hyperglycemia and the coexistence of multiple complications. At present, the drugs widely applied in clinical treatment of diabetes mellitus mainly include insulin, insulin analogs, non-insulin oral hypoglycemic drugs and genetic drugs. Nevertheless, there is still no complete therapy strategy for diabetes mellitus management by far due to the intrinsic deficiencies of drugs and limits in administration routes such as the adverse reactions caused by long-term subcutaneous injection and various challenges in oral administration, [redacted] instability and poor gastrointestinal absor[redacted] to develop appropriate delivery systems [redacted] according to the characters of drugs an[redacted] been found to be potentially beneficial in many aspects for effective diabetes treatment, such as improving the stability of drugs, overcoming different biological barriers *in vivo* to increase bioavailability, and acting as an intelligent automatized system to mimic endogenous insulin delivery and reduce the risk of hypoglycemia. This review aims to provide an overview related with the research advances, development trend of drug therapy and the application of delivery systems in the treatment diabetes mellitus, which could offer reference for the application of various drugs in the field of diabetes mellitus treatment.

Keywords: diabetes mellitus, drug delivery, insulin, gene therapy, nanoparticle

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In recent decades, the prevalence of diabetes mellitus has increased globally. According to the 9th edition of Diabetes Atlas by the International Diabetes Federation (IDF), the number of global diabetes patients in 2019 is estimated to be 463 million, which will increase to 578 million by 2030 and 700 million by 2045 (Saeedi et al., 2019). At present, diabetes mellitus has become a kind of serious non-communicable disease that causes high mortality and morbidity rate just next to cardiovascular disease and malignant tumor. As one of the most common chronic diseases, diabetes mellitus is an endocrine and metabolic disease characterized by hyperglycemia and multiple complications. Diabetes mellitus is mainly caused by genetic, environmental influence, microbial infection, immune system dysfunction, and mental factors that result in insufficient insulin secretion and insulin resistance. Patients with diabetes mellitus have long suffered from the devastating complications that could lower their quality of life and threaten their lives.

Articulo 17

REVISIÓN

oral 2016; 17(54): 1374-1378.

Bacterias asociadas a enfermedades periodontales

Bacterial related to periodontal diseases

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Resumen

Las enfermedades periodontales como la gingivitis y la periodontitis, son comunes en todo el mundo. La periodontitis crónica es una enfermedad inflamatoria de los tejidos del periodonto, es de origen multifactorial y es la segunda causa de pérdida parcial o total de la dentadura en adultos mayores a nivel mundial. Recientemente, se ha determinado que alrededor de 50 especies de bacterias son causantes de la enfermedad periodontal. Encontrándose con mayor frecuencia y proporción algunas especies de bacterias anaerobias estrictas, por lo cual, se les considera los principales agentes etiológicos de este padecimiento. No obstante, en los últimos años se han aislado especies de bacterias no comunes de la familia Enterobcateriaceae, Pseudomonaceae, Acinetobacter y Staphylococcus; así como Streptococcus beta hemolítico de bolsas periodontales. A pesar de que la cavidad bucal se considera un ambiente hostil, estos microorganismos encuentran en ella un micro hábitat idóneo para su desarrollo. Si bien, el periodonto patógeno está presente, el huésped debe manifestar ciertos factores de riesgo, ya sean inherentes a él mismo o de conducta para que la enfermedad periodontal ocurra. Con el fin de brindar un tratamiento adecuado a los pacientes con enfermedad periodontal es relevante conocer los microorganismos causales de la misma.

Palabras clave: periodontitis, periodonto patógenos, factores asociados.

Abstract

Periodontal diseases such as gingivitis and periodontitis are worldwide common. The chronic periodontitis is an inflamatory disease of the periodontal tissues, it has a multifactorial origen, and is the second cause of parcial or total tooth loss in adulthood in all over the world. Recently, around 50 bacterial species are related to periodontal diseases. Although, some species of strict anaerobic bacteria are most frecuent and a major proportion, there why are designated the prime etilogical agents of periodontal disease. However, in recent year's non common bacteria species of the families Enterobcateriaceae, Pseudomonaceae, Acinetobacter y Staphylococcus; as well as beta-hemolotic Streptococcus have been isolated of the periodontal pockets. Although, oral cavity is considered a hostile environment these microorganisms found there in a suitable microhabitat for development. While the periodontal microorganism is present, the host must manifest certain risk factors whether inherent to him or behavioral to develop the periodontal disease. In order to providing a suitable treatment to the patients with periodontal disease is important to know the microorganisms related to it.

Key words: *periodontitis, periodontal microorganism and risk factors.*

INTRODUCCIÓN

Actualmente las enfermedades periodontales son consideradas un problema de salud pública debido a que afectan a la mayoría de la población adulta en el mundo, siendo los países en vías de desarrollo los que presentan mayor incidencia y de acuerdo a la Organización Mundial de la salud (OMS)[1] estos padecimientos son la segunda causa de enfermedades en la cavidad bucal después de la caries.[2]

El origen de las enfermedades periodontales es la acumulación de bacterias que forman parte de la placa bacte-

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Articulo 18

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Periodontal disease and diabetes mellitus

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ABSTRACT

Periodontal disease (PD) is one of the most commonly known human chronic disorders. The relationship between PD and several systemic diseases such as diabetes mellitus (DM) has been increasingly recognized over the past decades. Objective: The purpose of this review is to provide the reader with knowledge concerning the relationship between PD and DM. Many articles have been published in the English and Portuguese literature over the last 50 years examining the relationship between these two chronic diseases. Data interpretation is often confounded by varying definitions of DM, PD and different clinical criteria were applied to determine the prevalence, extent and severity of PD, levels of glycemic control and diabetes-related complications. Methods: This paper provides a broad overview of the predominant findings from research conducted using the BBO (Bibliografia Brasileira de Odontologia), MEDLINE, LILACS and PubMed for Controlled Trials databases, in English and Portuguese languages published from 1960 to October 2012. Primary research reports on investigations of relationships between DM/DM control, PD/periodontal treatment and PD/DM/diabetes-related complications identified relevant papers and meta-analyses published in this period. Results: This paper describes the relationship between PD and DM and answers the following questions: 1- The effect of DM on PD, 2- The effects of glycemic control on PD and 3- The effects of PD on glycemic control and on diabetes-related complications. Conclusions: The scientific evidence reviewed supports diabetes having an adverse effect on periodontal health and PD having an adverse effect on glycemic control and on diabetes-related complications. Further research is needed to clarify these relationships and larger, prospective, controlled trials with ethnically diverse populations are warranted to establish that treating PD can positively influence glycemic control and possibly reduce the burden of diabetes-related complications.

Key words: Periodontal diseases. Diabetes mellitus. Diabetes mellitus, Type 1. Diabetes mellitus, Type 2. Gestational diabetes. Glycemic control. Diabetes complications.

INTRODUCTION

In the last decades health professionals have been often organized into many specialties and subspecialties directed to several body organs and systems. The human organism is a unity that is composed by an infinite number of biologic processes so strongly linked that abnormalities in any part of the body and/or its processes may have deep effects in many other body areas, exemplified in this review by two highly prevalent diseases: PD and DM[25].

PD is a chronic infectious disease, caused by Gram-negative microorganisms. An imbalance between a localized infection and an exaggerated host inflammatory response plays a pivotal role in determining gingival tissue damage. Recent evidence suggests that the effect of PD might not be limited just to the oral cavity but it might have systemic consequences. Indeed, PD has also been associated with a moderate systemic inflammatory response. Although, the mechanisms behind this association remain unclear, PD might represent one distant source of low-grade systemic inflammation. This association could explain the increased risk of impaired metabolic control in diabetes-related

Articulo 19

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Global risk factors and risk indicators for periodontal diseases

JASIM M. ALBANDAR

A commendable appreciation of risk factors for destructive forms of periodontal diseases requires a good understanding of the etiological factors and pathogenesis of these diseases. Periodontal diseases are chronic infectious disorders caused primarily by bacteria. Gingivitis is a nondestructive form of periodontal diseases (158, 179). Experimental gingivitis studies (146, 211) provided the first empiric evidence that accumulation of dental plaque biofilms on clean tooth surfaces results in the development of an inflammatory process encompassing local gingival and periodontal tissues around teeth. Research has also shown that the local inflammation will persist as long as the bacterial biofilm is present adjacent to the gingival tissues, and that the inflammation may resolve subsequent to meticulous removal of the microbial biofilm (211). Hence, chronic gingivitis is a predictable consequence of growth of dental plaque biofilms on tooth surfaces adjacent to periodontal tissues.

Other nondestructive forms of periodontal diseases include infections of nonbacterial origin and noninfectious periodontal diseases (114). The first group includes acute gingival inflammation caused by viruses, such as herpetic gingivostomatitis and HIV infections (42, 49, 112). Non-infectious periodontal diseases include gingival inflammation caused by mechanical, thermal, and chemical factors (90, 123). Little is known about the pathogenesis of gingival inflammation caused by viral infections, and the predictability of the tissue response following these infections is difficult to assess. On the other hand, exposure of the gingival tissues to a traumatic agent will invariably result in a local inflammation.

Evidence of the existence of risk factors for periodontitis

Epidemiological studies show that gingivitis is ubiquitous both in children and adults. Albandar *et al.* (13) assessed the prevalence of overt gingival inflammation in a large group of adolescents without periodontitis, who were a subgroup among a larger group examined in the national survey of the oral health of United States children, and found that 82.1% of the subjects had gingival bleeding. Other studies reported similar findings of a very high prevalence of gingivitis in children and adolescents in other parts of the world (23, 88). A high prevalence of gingivitis has also been reported for adults. For instance, it has been estimated that about half of the U. S. adult population have gingival bleeding, suggesting that overt gingival inflammation is common (18, 21).

Studies in animals and humans show that periodontitis is preceded by gingivitis (131, 144, 177, 198) and although the accumulation and maturation of a microbial dental plaque biofilm will predictably lead to the development of inflammation in the nearby gingival tissues, the duration of onset (146, 179, 211) and the intensity (18, 175) of the inflammatory process vary considerably from person to person, as well as between teeth and tooth sites within the same person. Furthermore, there is evidence that only a subset of individuals and a limited percentage of sites in these individuals will experience severe loss of periodontal tissue (16, 17, 175).

There are data suggesting that only a proportion of individuals and tooth sites with gingival inflammation may develop periodontal tissue loss. Albandar

Articulo 20

Gingivitis

Manu Rathee; Prachi Jain.

Author Information

Last Update: February 13, 2021.

Continuing Education Activity

Go to:

Gingivitis is an inflammatory condition of the gingival tissue or the gums most commonly due to a bacterial infection. It is inflammation of the gingiva with the attachment of the connective tissue to the tooth remaining at the original level, i.e., without attachment loss. This activity describes the evaluation and management of gingivitis and highlights the role of the interprofessional team in managing patients with this condition.

Objectives:

- Describe the etiology of gingivitis.
- Identify the presentation of a patient with gingivitis.
- Review the management considerations for patients with gingivitis.
- Outline the importance of improving care coordination among the interprofessional team to enhance the delivery of care for patients affected by gingivitis.

Earn continuing education credits (CME/CE) on this topic.

Articulo 21

Abstract

Periodontal Disease includes a wide variety of infectious entities with various clinical manifestations in the oral cavity and responses to treatment. The determinants of clinical manifestations of periodontal disease include the type of infectious agent, the host immune response and environmental factors. Aggressive periodontitis (AP) is defined as a type of inflammation with specific clinical and laboratory features, which distinguish it from other types of periodontitis, with high incidence rates in a sub-group of individuals. Bacteria have been frequently mentioned as the agent inciting gingival inflammation and tissue destruction that underlies the pathogenesis of periodontitis. However, recent studies, with some controversial results, have suggested that the herpes family of viruses, including CMV and EBV-1 as well as papillomaviruses, HIV, Human T-lymphotropic virus type 1, Torquetenovirus and hepatitis B and C occur with high frequency in active periodontal lesions. There is a lack of information about this disease and the role of herpesviruses in its pathophysiology. This review provides a critical analysis of the scientific evidence linking bacteria and viruses with AP and their potential impact on clinical characteristics, prognosis and therapy.

Keywords: Aggressive periodontitis, herpes viruses, periodontal microorganisms

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Articulo 22

Periodontal Disease – The Overlooked Diabetes Complication

CNE Continuing Nursing Education

Trisha Dunning

"He had one peculiar weakness, he had faced death in many forms but he had never faced a dentist."
– H.G. Wells (p. 75)

Periodontal diseases are infectious processes that occur in the presence of bacteria, which trigger an inflammatory response. Periodontal disease is associated with many medical conditions, including diabetes mellitus and its complications (such as kidney disease). It has been described as the "sixth diabetes complication" but is often overlooked in routine diabetes management and complication screening processes. Proactive, preventative dental and diabetes self care, as well as regular dental and diabetes assessment, are important management strategies because periodontal disease contributes to the progression of impaired glucose tolerance to diabetes mellitus and to hyperglycemia in individuals with established diabetes.

Dunning, T. (2009). Periodontal disease – The overlooked diabetes complication. *Nephrology Nursing Journal, 36(5),* 489-496.

Goal
To provide an overview of periodontal disease and its relationship to diabetes.

Objectives
1. Identify various explanations for the association between diabetes and periodontal disease.
2. Discuss prevention strategies and management of periodontal disease.

Diabetes mellitus is a chronic, incurable modern epidemic that affects more than 171 million individuals globally (Wild, Roglic, Green, Sicree, & King, 2004). There are two main types of diabetes: type 1, which usually occurs in young people, but can occur at any age; and type 2, which usually occurs in people over age 40. However, there is increasing prevalence of impaired glucose tolerance (IGT) or pre-diabetes and type 2 diabetes in children and adolescents (Zimmet et al., 2007). Both type 1 and type 2 are associated with significant, long-term complications, such as microvascular and macrovascular disease, neuropathy, and depression, causing significant morbidity and mortality. In addition, many individuals also have other comorbidities, such as arthritis.

The underlying pathophysiology of diabetes-related long-term complications largely arises from the effects of chronic hyperglycemia, tissue glycosylation, changes in collagen metabolism, and oxidative stress (Brownlee 1995; Hammes et al., 1999; Nishimura, Soga, Iwamoto, Kudo, & Murayama, 2005). Diabetes is recognized as a significant risk factor for serious, progressive periodontal disease (Southerland, Taylor, & Offenbacher, 2005). Likewise, periodontal disease may contribute to the progression of IGT to diabetes (Andersen, Flyvbjerg, & Holmstrup, 2007). Löe (1993) described periodontal disease as the "sixth diabetes complication" (p. 330). However, it could also be described as the "overlooked complication" because it is not included in most diabetes management strategies, education programs, or complication screening processes. This article focuses on the relationship between diabetes and periodontal disease, possible underlying causal factors, and suggested management strategies.

Overview of Periodontal Disease

The condition of the oral cavity reflects and affects the overall health status of the individual. Between 60% to 65% of the U.S. population has periodontal disease; the prevalence increas-

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Articulo 23

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DIAGNÓSTICO Y TRATAMIENTO PERIODONTAL

Directores invitados:
José Javier Echeverría y Niklaus P. Lang

diagnóstico y tratamiento periodontal

Articulo 24

DOI: 10.1111/prd.12269

REVIEW ARTICLE

Periodontology 2000 WILEY

Role of inflammasomes in the pathogenesis of periodontal disease and therapeutics

Julie T. Marchesan[1] | Mustafa Saadat Girnary[1] | Kevin Moss[2] | Eugenia Timofeev Monaghan[1] | Grant Joseph Egnatz[1] | Yizu Jiao[1] | Shaoping Zhang[3] | Jim Beck[4] | Karen V. Swanson[5]

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1 | INTRODUCTION

The innate immune response is the body's first line of defense against pathogens. The innate immune system recognizes pathogens, including bacteria and viruses, by engagement of the germline encoded pattern recognition receptors (PRR). There are five families of PRRs that are able to sense a vast array of microbial components, referred to as pathogen-associated molecular patterns (PAMP) and damage-associated molecular patterns (DAMP), that are host cell components produced during inflammation or environmentally derived, such as exposure to silica. Although PRRs are predominately expressed by innate immune cells, many of the PRRs are also found on other cells, including epithelial, endothelial and cells of the adaptive immune system. PRR engagement by its ligand induces downstream signaling cascades that induce multiple effects, including activation of innate immune cells and cytokine/chemokine production for the recruitment of immune cells to the site of infection or tissue damage.

A key function of the innate immune system is inflammasome activation. In response to PAMPs or DAMPS, some PRRs assemble inflammasomes (Figure 1) for the activation of cellular caspases that, in turn, induce the maturation of the proinflammatory cytokines interleukin-1β and interleukin-18 together with the induction of inflammation-induced programmed cell death (pyroptotic). Although it had been known since the early 1990s that caspase-1 was able to cleave pro-interleukin-1β and trigger cell death (later termed pyroptosis in contrast to apoptosis), it was not until a decade later, with a seminal paper by Martinon et al[1] that the details of how caspase-1 is activated were unraveled with the discovery of the inflammasome.

Inflammasomes are multimeric protein structures composed of a sensor molecule (the PRR), typically the adapter molecule apoptosis-associated speck-like protein containing a caspase-recruitment domain (CARD), and the protease caspase-1. There are multiple inflammasomes that can be formed, which are named for their sensor PRR that induces its activation. Inflammasome sensor molecules

Articulo 25

CRITICAL REVIEWS IN ORAL BIOLOGY & MEDICINE

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Inflammation and Uncoupling as Mechanisms of Periodontal Bone Loss

ABSTRACT

Periodontal disease is characterized by both inflammation and bone loss. Advances in research in both these areas have led to a new appreciation of not only each field but also the intimate relationship between inflammation and bone loss. This relationship has resulted in a new field of science called osteoimmunology and provides a context for better understanding the pathogenesis of periodontal disease. In this review, we discuss several aspects of the immuno-inflammatory host response that ultimately results in loss of alveolar bone. A proposal is made that periodontal inflammation not only stimulates osteoclastogenesis but also interferes with the uncoupling of bone formation and bone resorption, consistent with a pathologic process. Furthermore, arguments based on experimental animal models suggest a critical role of the spatial and temporal aspects of inflammation in the periodontium. A review of these findings leads to a new paradigm to help explain more fully the impact of inflammation on alveolar bone in periodontal disease so that it includes the effects of inflammation on uncoupling of bone formation from resorption.

KEY WORDS: adaptive immunity, bone matrix, cytokine, innate immunity, IL-1, osteoblast, osteoclast, RANK ligand, TNF.

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INTRODUCTION

It is widely recognized that bacteria initiate periodontal disease. Early studies by Löe and others (Löe *et al*., 1965; Theilade *et al*., 1966) demonstrated a direct relationship between bacterial plaque accumulation and gingival disease. In these studies, tissues without bacterial plaque had little inflammation, while those with plaque exhibited a strong inflammatory reaction. This process was reversible, indicating a direct correlation with bacterial plaque. Other studies in animals demonstrated a relationship among microbial plaque, inflammation, and periodontal bone loss (Keyes and Jordan, 1964; Saxe *et al*., 1967; Lindhe *et al*., 1975). These early studies established the bacterial etiology of gingivitis and periodontal diseases involving bone loss.

More recent studies have not only reinforced the bacterial etiology of periodontal disease but have also emphasized the role of inflammation in the pathologic process. These studies were performed in animal models to establish a cause-and-effect relationship between bacteria and the initiation of periodontal disease. In one animal model, a ligature is tied around the teeth, causing plaque accumulation and facilitating bacterial penetration into the gingival, which leads to inflammation and alveolar bone resorption (Graves *et al*., 2008). In contrast, the placement of ligatures in gnotobiotic rats does not cause significant increases in gingival inflammation or periodontal bone loss (Rovin *et al*., 1966), again demonstrating the essential role of bacteria as an initiating trigger. Further studies with other animal models also reinforce the relationship between bacteria and periodontal disease. For example, treatment of animals with antibiotics or topical application of chlorhexidine reduces the bacterial load and significantly reduces bone resorption (Weiner *et al*., 1979; Kenworthy and Baverel, 1981). In contrast to reducing bacteria, an increase in bacterial load enhances periodontal disease (Nagahata *et al*., 1982). In other animal models, the inoculation of periodontal pathogens into the oral cavities of rodents induced bone loss. In several studies, the introduction of *Porphyromonas gingivalis* into the oral cavity by oral gavage induced alveolar bone resorption in the mouse (Baker *et al*., 1994, 1999, 2000; Lalla *et al*., 1998). Similarly, oral gavage with *Actinobacillus actinomycetemcomitans* (Garlet *et al*., 2006) or *Tannerella forsythia* (Sharma *et al*., 2005) has been reported to stimulate periodontal bone loss. Introduction of *A. actinomycetemcomitans* in rats leads to colonization and the loss of alveolar bone (Schreiner *et al*., 2003; Fine *et al*., 2005). Thus, experimental studies in animal models support the human clinical trials implicating bacteria in the initiation of inflammation and periodontal disease (Reddy *et al*., 2003; Kirkwood *et al*., 2007).

HOST RESPONSE AND PERIODONTAL BONE LOSS

It has been well established that manipulation of the host response can attenuate periodontal bone loss (Graves, 2008). When the host response is reduced

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Correlation between periodontal disease management and metabolic control of type 2 diabetes mellitus. A systematic literature review

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Abstract

Background: Diabetes and periodontal disease share common features in terms of inflammatory responses. Current scientific evidence suggests that treatment of periodontal disease might contribute to glycemic control. The objective of the study is a review of the last three years.

Material and Methods: A literature search was performed in the MEDLINE (PubMed), Cochrane, and Scopus databases, for articles published between 01-01-2013 and 30-06-2015, applying the key terms "periodontal disease" AND "diabetes mellitus". The review analyzed clinical trials of humans published in English and Spanish.

Results: Thirteen clinical trials were reviewed, representing a total of 1,912 patients. Three of them had samples of <40 patients, making a total of 108 patients and the remaining ten samples had >40 patients, representing a total of 1,804. Only one article achieved a Jadad score of five. Seven articles (998 patients, 52.3% total), presented a statistically significant decrease in HbA1c ($p<0.05$) as a result of periodontal treatment. In the six remaining articles (representing 914 patients, 47.8% of the total), the decrease in HbA1c was not significant. Patient follow-up varied between 3 to 12 months. In three articles, the follow-up was of 3, 4, and 9 months, in two 6 and 12 months.

Conclusions: The majority of clinical trials showed that radicular curettage and smoothing, whether associated with antibiotics or not, can improve periodontal conditions in patients with diabetes mellitus. However, few studies suggest that this periodontal treatment improves metabolic control. However, there is no clear evidence of a relation between periodontal treatment and improved glycemic control in patients with type 2 diabetes mellitus.

Key words: *Diabetes, periodontal disease, HbA1c, metabolic control.*

Articulo 27

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Review Article

Xerostomia, Hyposalivation, and Salivary Flow in Diabetes Patients

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The presence of xerostomia and hyposalivation is frequent among diabetes mellitus (DM) patients. It is not clear if the presence of xerostomia and hyposalivation is greater in DM than non-DM patients. The aims of this systematic review are (1) to compare the prevalence rates of xerostomia, (2) to evaluate the salivary flow rate, and (3) to compare the prevalence rates of hyposalivation in DM versus non-DM population. This systematic review was conducted according to the PRISMA group guidelines by performing systematic literature searches in biomedical databases from 1970 until January 18th, 2016. All studies showed higher prevalence of xerostomia in DM patients in relation to non-DM population, 12.5%–53.5% versus 0–30%. Studies that analyzed the quantity of saliva in DM population in relation to non-DM patients reported higher flow rates in non-DM than in DM patients. The variation flow rate among different studies in each group (DM/CG) is very large. Only one existing study showed higher hyposalivation prevalence in DM than non-DM patients (45% versus 2.5%). In addition, quality assessment showed the low quality of the existing studies. We recommend new studies that use more precise and current definitions concerning the determination and diagnosis of DM patients and salivary flow collection.

1. Introduction

Diabetes mellitus (DM) is an endocrine disease characterized by a deficit in the production of insulin with consequent alteration of the process of assimilation, metabolism, and balance of blood glucose concentration. DM has become a worldwide public health problem. In recent years, the global prevalence of DM has increased substantially, reaching 8.3% in 2014, which corresponds to 387 million patients [1]. Essentially, there are two types of DM: type 1 DM (T1DM) and type 2 DM (T2DM). T1DM accounts for approximately 5% of diagnosed diabetes cases [2].

Xerostomia is a subjective complaint of dry mouth, whereas hyposalivation is an objective decreased of salivary flow. The clinical method most often employed for the diagnosis of salivary dysfunction is a sialometry test. Hyposalivation is considered to appear when salivary flow rates are under 0.1 mL/min at rest (UWS) or 0.7 mL/min under stimulation (SWS). Xerostomia is often associated with hyposalivation, but not always. And many cases of xerostomia have been described in patients with a normal salivary flow rate [3–6].

Several factors are capable of inducing salivary disorders in DM patients such as ageing, head and neck radiotherapy, systemic disorders, and several drugs [5]. Systemic diseases associated with xerostomia include rheumatologic chronic inflammatory disorders (Sjögren syndrome, rheumatoid arthritis, and systemic lupus erythematosus), endocrine disorders (DM, hyperthyroidism, and hypothyroidism), neurologic disorders (depression and Parkinson's disease), genetic disorders, metabolic disorders (dehydration, bulimia, anaemia, and alcohol abuse), infectious disorders (HIV/AIDS, HCV infection), and others (fibromyalgia, graft-versus-host-disease, sarcoidosis, and chronic pancreatitis). Many cases of xerostomia are also related to psychological conditions like depression and anxiety [5, 6].

Both types of DM, T1DM and T2DM, have been associated previously with xerostomia [7–12]. There are also studies

Articulo 28

OPEN

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www.nature.com/ijos

REVIEW

Diabetes mellitus related bone metabolism and periodontal disease

Ying-Ying Wu[1,2], E Xiao[2,3] and Dana T Graves[2]

Diabetes mellitus and periodontal disease are chronic diseases affecting a large number of populations worldwide. Changed bone metabolism is one of the important long-term complications associated with diabetes mellitus. Alveolar bone loss is one of the main outcomes of periodontitis, and diabetes is among the primary risk factors for periodontal disease. In this review, we summarise the adverse effects of diabetes on the periodontium in periodontitis subjects, focusing on alveolar bone loss. Bone remodelling begins with osteoclasts resorbing bone, followed by new bone formation by osteoblasts in the resorption lacunae. Therefore, we discuss the potential mechanism of diabetes-enhanced bone loss in relation to osteoblasts and osteoclasts.
International Journal of Oral Science (2015) **7**, 63–72; doi:10.1038/ijos.2015.2; published 10 April 2015

Keywords: bone loss; diabetes mellitus; hyperglycemia; inflammation; osseous; osteoblast; osteoclast; periodontitis

DIABETES: INTRODUCTION

Diabetes mellitus is a heterogeneous group of disorders and is characterized by high blood glucose levels.[1] Type 1 diabetes mellitus (T1DM) results from an absolute deficiency of insulin, which is most commonly due to auto-immunological destruction of the insulin-producing pancreatic β cells but which can be caused by other etiologies. In type 2 diabetes mellitus (T2DM), muscle, fat and other cells become resistant to the actions of insulin. This results in the activation of a compensatory mechanism that induces β cells to secrete more insulin. T2DM occurs when the compensatory increase in insulin is insufficient to maintain blood glucose levels within a normal physiological range.[2–3] By 2025, 300 million people are projected to be afflicted with diabetes worldwide, with a prevalence of 6.4%.[4–5] The countries with the most people suffering from diabetes by the year 2025 are predicted to be India, China and the United States. T1DM represents 5%–10% of the total number of diabetes cases worldwide[6] and is the main type of diabetes in youth, representing 85% or more of all diabetes cases in individuals younger than 20 years of age worldwide.[7] On average, males and females are equally affected with T1DM in young populations.[8] T2DM accounts for 90% of diabetes cases globally.[4] This disorder has traditionally been considered a metabolic disorder of adults; however, it has recently become more common in young adults, adolescents and occasionally, in children.[9]

PATHOGENIC MECHANISMS OF DIABETES

T1DM is a polygenic autoimmune disease that is characterized by the destruction of insulin-secreting pancreatic beta cells.[10] T1DM typically occurs as a consequence of a breakdown in immune regulation, resulting in an expansion of auto-reactive $CD4^+$ and $CD8^+$ T cells and auto-antibody-producing B lymphocytes and activation of the innate immune system, which collaborates to destroy insulin-producing beta cells.[11] In an animal model, $CD11c^+$ dendritic cells and ER-$MP23^+$ macrophages are the first cells to infiltrate the pancreas of non-obese diabetic mice, at approximately 3 weeks of age. At the same time, potentially pathogenic T cells can be detected surrounding the islet, resulting in peri-insulitis.[12] Genetic susceptibility and environmental triggers are thought to contribute to the development of T1DM.[13]

T2DM is a metabolic disorder that is characterized by hyperglycemia and altered lipid metabolism, which is caused by the inability of islet β cells to secrete adequate insulin in response to varying degrees of insulin resistance caused by over-nutrition, inactivity or obesity. Metabolic defects that contribute to the development of T2DM include an inability of islet β cells to compensate for high glucose levels that are associated with excess food intake, increased glucagon secretion and reduced incretin response, impaired expansion of subcutaneous adipose tissue, hypoadiponectinaemia, inflammation of adipose tissue, increased endogenous glucose production and the development of peripheral insulin resistance.[14] Chronic caloric excess is the primary pathogenic event that drives the development of type 2 diabetes in genetically and epigenetically susceptible individuals.[15–16]

PATHOGENIC CHANGES IN BOTH T1DM AND T2DM

Hyperglycemia

Hyperglycemia is due to impaired insulin secretion in T1DM and insulin resistance in T2DM. Beta cell destruction in T1DM and inadequate expression of glucose transporter 2 in T2DM are thought to contribute to hyperglycemia.[17] Several pathways are thought to exhibit increased activity under hyperglycemic conditions and to contribute to oxidative stress via the polyol pathway,[18] the hexosamine

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Articulo 29

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REVIEW

Periodontitis and diabetes: a two-way relationship

P. M. Preshaw · A. L. Alba · D. Herrera · S. Jepsen · A. Konstantinidis · K. Makrilakis · R. Taylor

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Abstract Periodontitis is a common chronic inflammatory disease characterised by destruction of the supporting structures of the teeth (the periodontal ligament and alveolar bone). It is highly prevalent (severe periodontitis affects 10–15% of adults) and has multiple negative impacts on quality of life. Epidemiological data confirm that diabetes is a major risk factor for periodontitis; susceptibility to periodontitis is increased by approximately threefold in people with diabetes. There is a clear relationship between degree of hyperglycaemia and severity of periodontitis. The mechanisms that underpin the links between these two conditions are not completely understood, but involve aspects of immune functioning, neutrophil activity, and cytokine biology. There is emerging evidence to support the existence of a two-way relationship between diabetes and periodontitis, with diabetes increasing the risk for periodontitis, and periodontal inflammation negatively affecting glycaemic control. Incidences of macroalbuminuria and end-stage renal disease are increased twofold and threefold, respectively, in diabetic individuals who also have severe periodontitis compared to diabetic individuals without severe periodontitis. Furthermore, the risk of cardiorenal mortality (ischaemic heart disease and diabetic nephropathy combined) is three times higher in diabetic people with severe periodontitis than in diabetic people without severe periodontitis. Treatment of periodontitis is associated with HbA_{1c} reductions of approximately 0.4%. Oral and periodontal health should be promoted as integral components of diabetes management.

Keywords Diabetes · Diabetes complications · Periodontal diseases · Periodontitis · Type 1 diabetes mellitus · Type 2 diabetes mellitus

Abbreviations

CRP	C-reactive protein
ESRD	End-stage renal disease
GCF	Gingival crevicular fluid
INVEST	Oral Infections and Vascular Disease Epidemiology Study
MMP	Matrix metalloproteinase

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Articulo 30

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Periodontal disease and diabetes-Review of the literature

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Abstract

Aims: To provide updated knowledge on the relationship between periodontal disease and diabetes from an oral health perspective.

Methods: A review of the English-language literature was performed, gathering articles on the two diseases published over the past 10 years.

Results: Both diseases result from the confluence of various triggering and modifying factors, and there are inter-individual differences in the risk of their development. Recent research has shown that diabetes may increase the risk of periodontitis, and it has been proposed that chronic periodontal disease may influence the natural course of diabetes. There appears to be an association among oral infections, impaired sugar metabolism, and atherosclerosis, indicating a theoretical link between metabolic syndrome and periodontal disease.

Clinical implications: Control of periodontal disease may enhance glycemic control in patients with type 2 diabetes. In turn, improved glycemic control may contribute to a better control of periodontal disease.

Key words: *Diabetes mellitus, metabolic syndrome, periodontal disease, cardiovascular disease.*

Articulo 31

Critical Reviews in Oral Biology & Medicine

The Oral Microbiota Is Modified by Systemic Diseases

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Abstract

Periodontal diseases are initiated by bacteria that accumulate in a biofilm on the tooth surface and affect the adjacent periodontal tissue. Systemic diseases such as diabetes, rheumatoid arthritis (RA), and systemic lupus erythematosus (SLE) increase susceptibility to destructive periodontal diseases. In human studies and in animal models, these diseases have been shown to enhance inflammation in the periodontium and increase the risk or severity of periodontitis. All 3 systemic diseases are linked to a decrease in bacterial taxa associated with health and an increase in taxa associated with disease. Although there is controversy regarding the specific oral bacterial changes associated with each disease, it has been reported that diabetes increases the levels of *Capnocytophaga, Porphyromonas*, and *Pseudomonas*, while *Prevotella* and *Selenomonas* are increased in RA and *Selenomonas, Leptotrichia*, and *Prevotella* in SLE. In an animal model, diabetes increased the pathogenicity of the oral microbiome, as shown by increased inflammation, osteoclastogenesis, and periodontal bone loss when transferred to normal germ-free hosts. Moreover, in diabetic animals, the increased pathogenicity could be substantially reversed by inhibition of IL-17, indicating that host inflammation altered the microbial pathogenicity. Increased IL-17 has also been shown in SLE, RA, and leukocyte adhesion deficiency and may contribute to oral microbial changes in these diseases. Successful RA treatment with anti-inflammatory drugs partially reverses the oral microbial dysbiosis. Together, these data demonstrate that systemic diseases characterized by enhanced inflammation disturb the oral microbiota and point to IL-17 as key mediator in this process.

Keywords: bacteria, biofilm, dysbiosis, periodontitis, periodontium, inflammation

Oral Microbiome in Health

The microbiome has a significant impact on the host, as germ-free mice have increased immune diseases, such as asthma and inflammatory bowel disease, indicating a dynamic relationship between them (Olszak et al. 2012). The oral microbiome includes bacteria, fungi, archaea, viruses, and protozoa (Dewhirst et al. 2010). The bacterial component is the best understood and is the focus of this review. The formation of dental plaque is affected by the mode of delivery (vaginal or caesarean), breast or bottle-feeding, and proximity to siblings and pets (Dewhirst et al. 2010). Bacteria can be found on all oral tissues, and there is overlap in the bacteria found on each. The most abundant bacteria are *Streptococcus oralis, Streptococcus mitis*, and *Streptococcus peroris*. Bacteria associated with periodontal health include *Streptococcus, Granulicatella, Neisseria, Haemophilus, Corynebacterium, Rothia, Actinomyces, Prevotella*, and *Capnocytophaga* (Segata et al. 2012). A biofilm forms on the tooth surface, initiated by a pellicle that promotes bacterial adhesion, with *Streptococcus* and *Actinomyces* as early colonizers (Socransky and Haffajee 2005). The latter facilitate formation of a multispecies biofilm that is spatially organized and

Changes in the Oral Microbiota Caused by Periodontal Disease

In a National Health and Nutrition Examination Study, 47% of US adults had evidence of periodontitis, and 10% to 15% had advanced periodontitis (Kinane et al. 2017). Periodontal diseases are thought to result from opportunistic infections. The specific factors leading to changes in bacteria that cause periodontal diseases are unknown, although it is recognized that nonideal restorations, genetic conditions that alter the host response, and systemic diseases, such as diabetes and rheumatoid arthritis (RA), predispose to disease (Kinane et al. 2017). The relationships between the biofilm and the host immune response are dynamic, and the ecologic interactions between them determine local homeostasis or transition to a state of disease (Dewhirst 2010; Griffen 2012). Inflammation occurs when bacteria or their products encounter leukocytes in the

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Med Oral 2003;8:233-47. Diabetes mellitus / *Diabetes mellitus*

Problemas bucodentales en pacientes con diabetes mellitus (II): Indice gingival y enfermedad periodontal

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Arrieta-Blanco JJ, Bartolomé-Villar B, Jiménez-Martinez E, Saavedra-Vallejo P, Arrieta-Blanco FJ. Problemas bucodentales en pacientes con diabetes mellitus (II): Índice gingival y enfermedad periodontal. Med Oral 2003;8:233-47.

RESUMEN

Entre las complicaciones tardías asociadas a la diabetes mellitus se ha señalado a la enfermedad periodontal; pudiendo ser más severa y refractaria al tratamiento que en sujetos sanos.

Objetivos: Determinar la prevalencia de gingivitis y periodontitis así como el índice periodontal de necesidad de tratamiento de las comunidades en población diabética comparada con una control. Analizar las características histológicas en encía de pacientes diabéticos.

Diseño del estudio: La muestra del estudio fue de 74 sujetos control y 70 diabéticos. Evaluamos los siguientes parámetros: estado gingival según el criterio de Löe y Silness, profundidad de sondaje, pérdida de inserción, recesión gingival e índice periodontal de necesidad de tratamiento de las comunidades. Realizamos también biopsias de encía en 42 pacientes diabéticos y 29 controles para estudios histológicos.

Resultados: Encontramos un índice de gingivitis, una pérdida de inserción y una recesión gingival estadísticamente más elevadas en pacientes diabéticos respecto a la población control, no ocurriendo lo mismo con la profundidad de sondaje. No hallamos diferencias
significativas en el índice CPITN de acuerdo al tipo de diabetes mellitus, control metabólico o duración de la enfermedad. El estudio de las biopsias no mostró cambios significativos en la encía de pacientes diabéticos frente a la población control.

Conclusiones: El índice de gingivitis fue más elevado en población diabética. Tras el examen de las necesidades de tratamiento, observamos cómo los pacientes diabéticos precisaron de un tratamiento más complejo.

Palabras Clave: Diabetes mellitus, índice gingival, enfermedad periodontal.

INTRODUCCION

La relación diabetes-enfermedad gingival ha sido ampliamente discutida en la literatura. Es generalmente admitido que la diabetes por sí misma no va a dar lugar a la aparición de una enfermedad gingival aunque sí va a favorecer la modificación del terreno gingivo-periodontal, facilitando un empeoramiento del cuadro clínico cuando se presenta la placa bacteriana como factor iniciador de la enfermedad (1-3). Algunos autores señalan cómo las encías de los diabéticos no tratados suelen presentar un color rojo intenso, los tejidos gingivales tienen aspecto edematoso y a veces están algo hipertrofiados, incluso es típica la supuración dolorosa de los bordes gingivales y de las papilas interdentarias (4). Esta asociación diabetes mal controlada-aumento de gingivitis y sangrado es señalada en más estudios (5, 6); otros, como Rosenthal (7) y Rylander y cols. (8) observan cómo la presencia de complicaciones tardías también podrían contribuir al aumento de inflamación gingival.

Un grado avanzado de gingivitis puede desencadenar la existencia de una enfermedad periodontal. Dicha enfermedad puede ser especialmente problemática en pacientes diabéticos, ya que es más prevalente, más severa y progresa más rápidamente que en la población normal (9); de ahí, que su prevención sea más importante en personas diabéticas que en no diabéticas (10, 11):

Articulo 33

Diabète et maladies parondontales

Diabetes and periodontal diseases.

Résumé

Le diabète et les maladies parodontales sont deux pathologies chroniques dont la prévalence mondiale est élevée et qui entretiennent des relations cliniques et biologiques complexes. L'augmentation de l'incidence et de la sévérité des parodontites chez les diabétiques est prouvée par de nombreuses études épidémiologiques. Les spécificités du traitement parodontal chez le diabétique sont liées à l'immunodépression qui engendre des retards de cicatrisation mais son efficacité est démontrée. Cependant les mécanismes pathogéniques sont encore loin d'être parfaitement élucidés. Depuis quelques années, la relation inverse entre parodontites et diabète a été l'objet de nombreuses recherches.
De récentes revues systématiques indiquent que les parodontites augmentent l'incidence, le contrôle et les complications du diabète et que le traitement parodontal classique (détartrage-surfaçage) diminue le taux d'hémoglobine glyquée de 0,4 %. Là encore, les mécanismes biologiques sous-jacents restent à démontrer même si l'inflammation et le stress oxydant semblent impliqués.

Abstract

Diabetes and periodontal diseases are two chronic diseases with a high global prevalence and with complex clinical and biological relationships. Many epidemiological studies have shown an increased incidence and severity of periodontitis in diabetics. Immunosuppression in diabetics explains delay healing and specificity of periodontal therapy in those patients, but effectiveness of the treatment has been demonstrated. The pathogenic mechanisms are still far from being fully elucidated. In recent years, the inverse relationship between periodontitis and diabetes has been the subject of many researches. Recent systematic reviews indicate that periodontitis is responsible for increasing the incidence, control and complications of diabetes and that conventional periodontal treatment (scaling and root planning) reduces glycated haemoglobin of 0.4%. The biological mechanisms implicated remain to be analysed however it appears that inflammation and oxidative stress are involved.

MOTS-CLEFS :
- Maladies parodontales, parodontites, diabète, inflammation

KEYWORDS:
- *Periodontal diseases, periodontitis, diabetes, inflammation.*

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Articulo 34

Lasers Med Sci (2016) 31:1633–1640
DOI 10.1007/s10103-016-2030-8

ORIGINAL ARTICLE

Local adjunct effect of antimicrobial photodynamic therapy for the treatment of chronic periodontitis in type 2 diabetics: split-mouth double-blind randomized controlled clinical trial

Nídia Cristina Castro dos Santos[1] · Naira Maria Rebelatto Bechara Andere[1] · Cássia Fernandes Araujo[1] · Andrea Carvalho de Marco[1] · Lúcio Murilo dos Santos[2] · Maria Aparecida Neves Jardini[1] · Mauro Pedrine Santamaria[1]

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Abstract Diabetes has become a global epidemic. Its complications can have a significant impact on quality of life, longevity, and public health costs. The presence of diabetes might impair the prognosis of periodontal treatments due to its negative influence on wound healing. Antimicrobial photodynamic therapy (aPDT) is a local approach that can promote bacterial decontamination in periodontal pockets. The aim of this study was to investigate the local effect of adjunct aPDT to ultrasonic periodontal debridement (UPD) and compare it to UD only for the treatment of chronic periodontitis in type 2 diabetic patients. Twenty type 2 diabetic patients with moderate to severe generalized chronic periodontitis were selected. Two periodontal pockets with probing depth (PD) and clinical attachment level (CAL) ≥5 mm received UPD only (UPD group) or UPD plus adjunct aPDT (UPD + aPDT group). Periodontal clinical measures were collected and compared at baseline and 30, 90, and 180 days. After 180 days of follow-up, there were statistically significant reductions in PD from 5.75 ± 0.91 to 3.47 ± 0.97 mm in the UPD group and from 6.15 ± 1.27 to 3.71 ± 1.63 mm in the UPD + aPDT group. However, intergroup analysis did not reveal statistically significant differences in any of the evaluated clinical parameters ($p > 0.05$). The adjunct application of aPDT to UPD did not present additional benefits for the treatment of chronic periodontitis in type 2 diabetic patients. The ClinicalTrials.gov identifier of the present study is NCT02627534.

Keywords Diabetes mellitus · Chronic periodontitis · Periodontal pocket · Antimicrobial therapy · Photodynamic therapy · Low-level laser therapy

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Introduction

Diabetes mellitus (DM) has emerged as a global epidemic. Its complications may significantly impair quality of life, longevity, and public health care costs [1]. The International Diabetes Federation (IDF) estimates that by 2040, 642 million people will suffer from diabetes, or approximately 10 % of the world's adult population [2]. The presence of diabetes may lead to other health problems that can have a direct impact on quality of life. Among these, the most common diabetes complications are neuropathy, nephropathy, retinopathy, cardiovascular disease, and periodontal diseases.

Periodontal diseases (PDs) are characterized by inflammation in periodontal tissues, initiated by dental biofilm, that lead to the destruction of periodontal tissues and tooth loss. It is well known that diabetes increases the risk for the development and progression of periodontal diseases [1]. Type 2 diabetic individuals have a higher prevalence and severity of chronic periodontitis than normoglycemic individuals, besides having worse treatment prognoses [3].

Periodontal therapy aims at removing supra- and subgingival dental biofilm to reduce periodontal inflammatory burden, re-establish tissue homeostasis, and stop the progression of periodontal diseases. Mechanical periodontal therapy is the gold standard treatment modality for chronic

Articulo 35

Effects of Periodontal Therapy on Metabolic Control in Patients With Type 2 Diabetes Mellitus and Periodontal Disease

A Meta-Analysis

Tze-Fang Wang, MSN, I-An Jen, MD, Chyuan Chou, DDS, Dr. PH, and Yen-Ping Lei, PhD

Abstract: Epidemiologic studies have reported increased incidence, prevalence and acuity of periodontitis in adults with diabetes and some have also suggested that treating periodontal disease may improve glycemic control in diabetic patients.

This meta-analysis was conducted to evaluate the effects of different periodontal therapies on metabolic control in patients with type 2 diabetes mellitus (T2DM) and periodontal disease.

We searched the Medline, EMBASE and Cochrane Library (Central) databases up to January 2014 for relevant studies pertaining to periodontal treatments and glycemic control in adults with T2DM. The search terms were periodontal treatment/periodontal therapy, diabetes/diabetes mellitus, periodontitis/periodontal and glycemic control. The primary outcome measure taken from the included studies was glycated hemoglobin (HbA1c).

We compared differences in patients' pre- and post-intervention HbA1c results between a treatment group receiving scaling and root planing (SRP) combined with administration of oral doxycycline (n = 71) and controls receiving SRP alone or SRP plus placebo (n = 72). Meta-analysis was performed using Comprehensive Meta Analysis software.

Nineteen randomized controlled trials (RCTs) were identified. Four trials involving a total of 143 patients with T2DM and periodontal disease were determined to be eligible for analysis. Data of 1 study were not retained for meta-analysis because HbA1c results were recorded as median with IQR. Meta-analysis of the included 3 studies revealed no significant differences in HbA1c results between the periodontal treatment group (n = 71) and control group (n = 72) (HbA1c SMD = −0.238, 95% CI = −0.616 to 0.140; $P = 0.217$).

Systemic doxycycline added to SRP does not significantly improve metabolic control in patients with T2DM and chronic periodontitis. Current evidence is insufficient to support a significant association between periodontal therapy and metabolic control in this patient population. However, evidence suggests that periodontal therapy itself improves metabolic control and reinforces that T2DM is a risk factor for periodontitis.

(*Medicine* 93(28):e292)

Abbreviations: HbA1c = glycated hemoglobin, PD = periodontal disease, RCT = randomized controlled trial, SMD = standardized mean difference, SRP = scaling and root planing, T2DM = type 2 diabetes mellitus.

INTRODUCTION

Periodontal disease (PD) is a chronic inflammatory disease that destroys the gingiva or tooth-supporting tissues. It is one of the most prevalent chronic infections in adults between ages 30 and 90 years in the United States and the most prevalent dental disease in people with diabetes, affecting up to 22% of diabetic patients.[1] PD is reported to affect about 90% of people globally.[2] The 2 major forms of PD, gingivitis and periodontitis, are the result of bacterial plaque, which ultimately destroys gingival tissue and periodontal attachment apparatus.[3] Although tooth-adherent microorganisms initiate PD, the individual inflammatory response along with concomitant chronic disease such as cardiovascular disease, chronic pulmonary disorders and diabetes, is responsible for the chronic nature of the disease and eventual breakdown of tissue. These conditions suggest that type 2 diabetes mellitus (T2DM) is a risk factor for periodontitis.[1] Epidemiologic studies over the years have consistently reported that increased incidence, prevalence and acuity of periodontitis is found among adults with T2DM.[4] Incidence of periodontitis increases as diabetic patients age and is both more frequent and more severe in T2DM patients with advanced systemic complications.[5]

Studies of diabetes patients with PD have examined different treatments for gingivitis and periodontitis that are targeted toward reducing oral bacteria and associated calculus. Patients with gingivitis without concomitant disease that influences oral health, may respond well to simply improving personal plaque control using a mix of mechanical and hygienic processes.[6] However, self-treatment alone is inconsistent and seldom results in maintaining plaque-free status, so professional reinforcement is usually advised.[6] Treatment of periodontitis is directed toward removing pathogenic bacteria and preventing recolonization; correcting modifiable risk factors such as smoking, alcohol abuse,

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The authors declare that they have no conflict of interest.

Articulo 36

International Journal of *Environmental Research and Public Health*

MDPI

Article

Periodontal Treatment Experience Associated with Oral Health-Related Quality of Life in Patients with Poor Glycemic Control in Type 2 Diabetes: A Case-Control Study

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Abstract: Severe periodontitis is a risk factor for poor glycemic control. The appropriate medical treatment and plaque control of periodontitis positively affects blood-sugar control in diabetes patients. We aimed to identify the factors associated with glycemic control and examine the periodontal treatment (PT) experience and oral health-related quality of life (OHQoL) for patients with poor glycemic control in type 2 diabetes mellitus (T2DM). This multicenter case–control study recruited 242 patients with poor glycemic control and 198 patients with good glycemic control. We collected patients' information through face-to-face interviews using a structured questionnaire. The Oral Health Impact Profile-14 (OHIP-14) was used to measure OHQoL. Based on PT status, the patients were classified into three groups: a non-periodontal disease group, a PT group, and a non-PT (NPT) group. Regression models were used to analyze the data. No interdental cleaning (adjusted odds ratio (aOR) = 1.78) and positive attitudes toward periodontal health (aOR = 1.11) were significantly more likely to be associated with poor glycemic control in patients with T2DM. The PT group had a significantly lower OHIP-14 score than the NPT group (6.05 vs. 9.02, $p < 0.001$), indicating a better OHQoL among patients with poorly controlled T2DM. However, the OHQoL did not differ significantly in patients with well-controlled T2DM between the PT and NPT groups. This suggested that diabetic patients with poor glycemic control must improve periodontal care practices and receive proper PT, if necessary, to improve their OHQoL.

Keywords: Glycemic control; oral health-related quality of life; periodontal care behavior; periodontal treatment experience

Articulo 37

J Clin Periodontol 2013; 40 (Suppl. 14): S153–S163 doi: 10.1111/jcpe.12084

Journal of Clinical Periodontology

Evidence that periodontal treatment improves diabetes outcomes: a systematic review and meta-analysis

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Engebretson S, Kocher T. Evidence that periodontal treatment improves diabetes outcomes: a systematic review and meta-analysis. J Clin Periodontol 2013; 40 (Suppl. 14): S153–S163. doi: 10.1111/jcpe.12084.

Abstract

Context: The effect of periodontal therapy on diabetes outcomes has not been established.

Objective: This update examines the effect of periodontal treatment on diabetes outcomes.

Data sources: Literature since October 2009 using MEDLINE.

Study eligibility criteria: Published RCTs including periodontal therapy for diabetic subjects, a metabolic outcome, an untreated control group, and follow-up of 3 months.

Articulo 38

Cochrane Database of Systematic Reviews | Review - Intervention

Treatment of periodontal disease for glycaemic control in people with diabetes mellitus

Terry C Simpson, Jo C Weldon, Helen V Worthington, Ian Needleman, Sarah H Wild, David R Moles, Brian Stevenson, Susan Furness, Zipporah Iheozor-Ejiofor Authors' declarations of interest

Version published: 06 November 2015 Version history

https://doi.org/10.1002/14651858.CD004714.pub3

Collapse all Expand all

Abstract

Available in English | Español

Background

Glycaemic control is a key issue in the care of people with diabetes mellitus (DM). Periodontal disease is the inflammation and destruction of the underlying supporting tissues of the teeth. Some studies have suggested a bidirectional relationship between glycaemic control and periodontal disease. This review updates the previous version published in 2010.

Objectives

The objective is to investigate the effect of periodontal therapy on glycaemic control in people with diabetes mellitus.

Articulo 40

PHYTOTHERAPY RESEARCH
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(wileyonlinelibrary.com) **DOI**: 10.1002/ptr.5737

The Impact of Resveratrol Supplementation on Blood Glucose, Insulin, Insulin Resistance, Triglyceride, and Periodontal Markers in Type 2 Diabetic Patients with Chronic Periodontitis

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The aim of this study was to investigate the impact of resveratrol supplementation along with non-surgical periodontal treatment on blood glucose, insulin, insulin resistance, triglyceride (TG), and periodontal markers in patients with type 2 diabetes with periodontal disease. In this double-blind clinical trial study, 43 patients with diabetes with chronic periodontitis were participated. Subjects were randomly allocated to intervention and control groups. The intervention and control groups received either 480 mg/day of resveratrol or placebo capsules (two pills) for 4 weeks. Fasting blood glucose, insulin, insulin resistance (homeostasis model assessment of insulin resistance), TGs, and pocket depth were measured in all subjects' pre-intervention and post-intervention. The

Articulo 41

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The Review of DIABETIC STUDIES

REVIEW

Resveratrol and Diabetes

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■ Abstract

Resveratrol is a stilbene compound, and a phytoalexin, synthesized by plants in response to stressful stimuli, usually caused by infection. It is abundantly present in red wine, ports and sherries, red grapes, blueberries, peanuts, itadori tea, as well as hops, pistachios, and in grape and cranberry juices. The anti-hyperglycemic effects of resveratrol seem to be the result of an increased action of the glucose transporter in the cytoplasmic membrane. Studies on rats with streptozotocin-induced diabetes have demonstrated that the expression of the insulin-dependent glucose transporter, GLUT4, is increased after resveratrol ingestion. Also, resveratrol enhances adiponectin levels, which could be one of the potential mechanisms by which it improves insulin sensitivity. Another important observation is that resveratrol induces the secretion of the gut incretin hormone, glucagon-like peptide-1. Resveratrol is also reported to activate Sir2 (silent information regulatory 2), a SIRT1 homolog, thus mimicking the benefits of calorie restriction. It produces a wide variety of effects in mammalian cells, including activation of AMP-activated protein kinase, which is involved in some of the same metabolic pathways as SIRT1, which may influence other mechanisms via the involvement of nuclear factor kappa B (NF-κB). In the near future, resveratrol-based therapies with either resveratrol or its analogs that have better bioavailability could be useful in the treatment of diabetes and its complications, either alone or in combination with other anti-diabetic drugs.

Keywords: diabetes · FOXO1 · glucose transport · GLUT4 · mitochondrial function · AMPK · SIRT1 · resveratrol

Introduction

Resveratrol (RSV), or 3,5,4-trihydroxystilbene, is a stilbene compound, and a phytoalexin, synthesized by plants in response to stressful stimuli, usually to infection. In addition to its presence in red wine, ports, and sherries, it is also found in red grapes, blueberries, peanuts, itadori tea, hops, pistachios, and in grape and cranberry juices [1-3]. RSV exerts beneficial effects in humans and may be helpful in preventing and treating metabolic diseases such as obesity and diabetes mellitus [4-5].

Anti-hyperglycemic action of RSV

RSV has anti-hyperglycemic effects in diabetic animals, which is associated with its stimulatory action on intracellular glucose transport. In the presence of RSV, glucose uptake is increased by different cells isolated from diabetic rats. Interestingly, in experiments on isolated cells, RSV has been able to stimulate glucose uptake in the absence of insulin [6-7]. The stimulation of glucose uptake induced by RSV seems to be the result of an increased action of the glucose transporter in the cytoplasmic membrane. Studies in rats with streptozotocin-induced diabetes have demonstrated that the expression of the insulin-dependent glucose transporter, GLUT4, after resveratrol ingestion is increased, compared with diabetic animals which were not given RSV [8-10]. It should be mentioned, however, that in some experiments in rats with streptozotocin-induced diabetes, RSV appeared to be ineffective and failed to decrease blood glucose [11-12].

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Effect of Resveratrol on biofilm formation and virulence factor gene expression of *Porphyromonas gingivalis* in periodontal disease

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Periodontal disease is an oral inflammatory disease that destroys the tooth supporting periodontal tissues resulting in tooth loss. *Porphyromonas gingivalis* is a keystone pathogen that plays a significant role in periodontitis. In previous studies, resveratrol has shown significant results by targeting inflammatory and adhesive markers. Virulence factors of *P. gingivalis* play an important role in the bacterial adhesion and colonization. In this study, we aimed to demonstrate the anti-biofilm and anti-bacterial activity of resveratrol and also study the effect of resveratrol on the expression of virulence factor genes of *P. gingivalis* using reverse transcriptase polymerase chain reaction (RT-PCR). The anti-microbial and anti-biofilm activity of resveratrol on *P. gingivalis* was carried out by broth microdilution assay and biofilm adhesion reduction–crystal violet assay, respectively. We carried out the gene expression analysis by RT-PCR with the *P. gingivalis* treated compound to analyze the change in the expression of virulence factors: fimbriae and gingipain. Minimal inhibitory concentrations (MIC) of resveratrol against *P. gingivalis* and other clinical strains are in the range of 78.12–156.25 μg/mL. Resveratrol dose-dependently prevented the biofilm formation and also attenuated the virulence of *P. gingivalis* by reducing the expression of virulence factor genes such as fimbriae (type II and IV) and proteinases (kgp and rgpA). Resveratrol demonstrated superior anti-bacterial and anti-biofilm activity against *P. gingivalis*. There was significant reduction in the expression of fimbriae and gingipain with the resveratrol-treated compound. The results suggest that resveratrol, due to its multiple actions, may become a simple and inexpensive therapeutic strategy for treating periodontal disease.

Key words: Periodontitis; resveratrol; biofilm; fimbriae; virulence; RT-PCR.

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Periodontitis is a chronic disease of oral health which comprises of the inflammation of gum, leading to the destruction of bone and connective tissue. Oral bacteria trigger inflammatory responses by attaching themselves to the tooth surface, leading to the destruction of supporting tissues and alveolar bone (1). Periodontal disease is prevalent in both developed and underdeveloped countries. According to the recent data by the Centers for Disease Control and Prevention (CDC), half of the citizens of the USA aged 30 or more were found to have periodontitis. Worldwide, about 35% of adults over the age of 30 and more than 50% of adults over the age of 50 were found to have chronic periodontitis (2).

The oral ecological niche is inhabited by over 700 bacterial species (3). The bacteria that are responsible for the progression of the disease are a group of bacteria which includes *Porphyromonas gingivalis*, *Treponema denticola* and *Tannerella forsythia*, *Aggregatibacter actinomycetemcomitans*, etc. *P. gingivalis* is a gram-negative black pigmented anaerobic bacterium, considered as a 'keystone' pathogen in the disease (4). The pathogenic ability of *P. gingivalis* is due to its multiple virulence factors which help the bacteria in colonization, biofilm formation and destruction of epithelial cells (5). *P. gingivalis* forms a biofilm on the calcified

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ORIGINAL ARTICLE

WILEY molecular oral microbiology

Resveratrol attenuates the pathogenic and inflammatory properties of *Porphyromonas gingivalis*

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Porphyromonas gingivalis has been strongly associated with chronic periodontitis, which affects tooth-supporting tissues. This Gram-negative anaerobic bacterium produces a repertoire of virulence factors that modulate tissue destruction directly or indirectly by the induction of inflammatory processes. The aim of this study was to investigate the effects of resveratrol, a major polyphenol found in grapes and wine, on the growth and virulence properties of *P. gingivalis* as well as on gingival keratinocyte tight junction integrity and the host inflammatory response. Resveratrol exhibited antibacterial activity that may result from damage to the bacterial cell membrane. Resveratrol also killed a pre-formed *P. gingivalis* biofilm and reduced bacterial adherence to matrix proteins. In addition, resveratrol had a protective effect on the integrity of the keratinocyte tight junctions by inhibiting its breakdown by *P. gingivalis*. This may be related to the ability of resveratrol to inhibit the protease activities of *P. gingivalis*. Lastly, resveratrol reduced *P. gingivalis*-mediated activation of the NF-κB signaling pathway and attenuated TREM-1 gene expression as well as soluble TREM-1 secretion in monocytes. The effect on NF-κB activation likely results from the ability of resveratrol to act as a PPAR-γ agonist. In summary, the antibacterial, anti-adherence, and antiprotease properties of resveratrol, as well as its ability to protect the gingival keratinocyte barrier and attenuate the inflammatory response in monocytes suggest that it may be a promising novel therapeutic agent for treating periodontal disease.

KEYWORDS
oral microbiology, periodontal disease, *Porphyromonas*

1 | INTRODUCTION

Periodontitis is an inflammatory disorder of the periodontium initiated by specific bacterial species and is characterized by the destruction of supporting connective tissue and, in severe cases, the exfoliation of teeth. *Porphyromonas gingivalis*, a Gram-negative anaerobic bacterium, has been identified as the keystone species in the development and progression of chronic periodontitis (Hajishengallis, Darveau, & Curtis, 2012). This dysbiotic bacteria expresses a large array of virulence factors, including adhesins, cysteine proteinases, and lipopolysaccharide (Bostanci & Belibasakis, 2012a; Enersen, Nakano, & Amano, 2013; Guo, Nguyen, & Potempa, 2010; Jain & Darveau, 2010). While fimbriae are considered to be critical determinants for the adhesion of the bacteria to host cells and subsequently their invasion, cysteine proteinases, also known as gingipains, have been suggested to play key roles related to evasion of the host immune defense and tissue destruction (Bostanci & Belibasakis, 2012a; Enersen et al., 2013; Mysak et al., 2014). *Porphyromonas gingivalis* can also modulate host cell cytokine signaling networks (Bodet, Chandad, & Grenier, 2006; Bostanci et al., 2013; Hajishengallis, 2011) and dysregulate the production of proinflammatory mediators that can mediate tissue destruction and alveolar bone resorption (Hajishengallis & Lamont, 2014).

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Issue: *Resveratrol and Health*
REVIEW

Therapeutic applications of resveratrol and its derivatives on periodontitis

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Periodontitis is an inflammatory disease of the supporting tissues of the teeth induced by periodontopathic bacteria that results in the progressive destruction of periodontal tissues. Treatment of periodontitis is painful and time-consuming. Recently, herbal medicines have been considered for use in treating inflammation-related diseases, including periodontitis. Resveratrol and its derivative 2,3,5,4′-tetrahydroxystilbene-2-*O*-β-glucoside (THSG), a polyphenol extracted from *Polygonum multiflorum*, have anti-inflammatory properties and other medical benefits. Here, we highlight the importance of resveratrol and its glycosylated derivative as possible complementary treatments for periodontitis and their potential for development as innovative therapeutic strategies. In addition, we present evidence and discuss the mechanisms of action of resveratrol and THSG on periodontitis, focusing on *Porphyromonas gingivalis*–induced inflammatory responses in human gingival fibroblasts and animal modeling of ligature-induced periodontitis. We also illuminate the signal transduction pathways and the cytokines involved.

Keywords: resveratrol; periodontitis; oxidative stress; inflammation; antioxidant

Introduction

Periodontitis is a chronic inflammatory and infectious disease related to specific bacteria that results in the destruction of supporting structures of the teeth, such as alveolar bone and connective tissues. Regression of this destructive disease is dependent on an irregular host response to subgingival plaque formation. The formation of plaque allows the growth of anaerobic bacteria, which eventually leads to the recruitment and activation of neutrophils.[1] Therefore, microbial plaque is the primary etiology and initiates the host immune response, which induces the signs of periodontitis.[2] To date, certain surgical and nonsurgical therapeutic strategies have been selected and used to treat teeth with periodontitis; however, there are few medications for periodontitis therapy. Herbal medicines have been used to treat inflammation-related diseases and were recently considered for the prevention and treatment of periodontitis. Using evidence from

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