GRADUATION PROJECT

Degree in Dentistry

ADHESION OVER THE DENTIN, CURRENT PROCEDURES

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ABSTRACT

Introduction: Adhesion is a crucial dental procedure that has been studied for many years and is still under investigation for improvement. The adhesive technique has been modified and it is very interesting to explore the different adhesives studied until nowadays and the challenges that have to be overcome when bonding dental restorations. **Objectives:** To evaluate the challenges to face for adhesion over the dentin and compare the different generations dental adhesives. Evaluate bond strength, sealing ability, nanoleakage of different adhesives, and also if survival rate and marginal integrity of the restorations were influenced by the adhesive used. **Material and methods:** The literature review was conducted through two scientific databases: Medline and Dentistry and Oral Science Source. Articles taken into consideration were from 2012 to 2022, free full text available, and were written in English. Were excluded studies with artificial samples, duplicates, or from non-impact journal. **Results:** Self-etch have been invented to overcome different clinical problems. Adhesives can be applied using different techniques and have varying results in terms of bond strength, and sealing ability, with the 3-step etch and rinse adhesives being the “gold standard”. Have been shown that the excessive presence of water can hinder adhesion. Marginal gaps are more often found on dentin than enamel. **Conclusions:** Post-operative sensibility, clinical time, operator susceptibility, and longevity of the restorations were the biggest problems to face. Studies showed that the 3-steps etch and rinse adhesive are still the “golden standard” for bond strength and marginal integrity but the self-etch adhesives are trying to match their performance by implementing functional monomers in the composition. The only MMPs inhibitors suggested by the literature at this moment is chlorhexidine 2%.

Keywords: dentistry, dentin, bond strength, enamel, adhesion

RESUMEN

Introduccion: La adhesión es un procedimiento dental crucial, estudiado durante muchos años y aún está bajo investigación. La técnica ha sido modificada y es interesante estudiar diferentes adhesivos y los problemas que hay que superar. **Objectivos:** Evaluar los problemas para la adhesión sobre dentina y comparar diferentes generaciones de adhesivos. Evaluar la fuerza de adhesion, la capacidad de sellado, la nanofiltración de diferentes adhesivos y si la tasa de supervivencia y la integridad marginal de las restauraciones se vieron afectadas por el adhesivo. **Material y metodos:** La revisión bibliográfica se realizó con dos bases de datos científicas: Medline y Dentistry and Oral Science Source. Los artículos que se tomaron en consideración fueron de 2012 a 2022, disponibles en texto completo gratuito y escritos en inglés. Se excluyeron estudios con muestras artificiales, duplicados o de revista sin impacto. **Resultado:** Se han inventado los adhesivos de autograbado para superar varios problemas clínicos. Los adhesivos se aplican utilizando diferentes técnicas y tienen resultados variables en términos de fuerza de adhesion y capacidad de sellado, siendo los adhesivos de grabado y lavado de 3 pasos el “gold standard”. Se demuestra que la presencia excesiva de agua puede dificultar la adhesion. La integridad marginal se encuentra mas en el esmalte que en la dentina. **Conclusiones:** La sensibilidad postoperatoria, el tiempo clínico, la susceptibilidad del operador y la longevidad de las restauraciones fueron los mayores problemas. Los estudios demostraron que el adhesivo de grabado y lavado de tres pasos es el "gold standard" para la fuerza de adhesion y la integridad marginal, pero los adhesivos de autograbado están tratando de igualar su rendimiento mediante la implementación de monómeros funcionales en la composición. El único inhibidor de las MMP sugerido por la literatura ahora es la clorhexidina al 2%.

Palabras clave: odontología, dentina, fuerza de union, esmalte, adhesión

INDEX

- **1. INTRODUCTION**

One of the most crucial dental techniques in dentistry is adhesion. Over the years there have been many studies and many modifications to the adhesive and the technique, both from the point of view of the characteristics and the method of application. Is interesting to study the different generations and the methods of application of the adhesives and also the many difficulties that have to be overcome when bonding restoration on the different substrates (1).

- 1.1. History of adhesion

More than 60 years ago, dental adhesives were first used on dental tissue (2). Since then, different adhesive restoration techniques have been successfully used in restorative dentistry. It is well established that using the right adhesive procedure helps to minimize marginal stains and recurrent caries as well as reduce postoperative sensitivity and enable effective cavity sealing (3). The original adhesive in dentistry, which used dentin as substrate for adhesion rather than enamel, was invented in the year 1949 by a Swiss scientist Dr. Hagger, a Swiss scientist. Hagger obtained a brevet, in 1951, for a "Cavity Seal®" substance which had to be implemented along with the "Sevriton®" which was a chemically curing resin. This item, which later will be known as "Sevriton Cavity Seal®" was composed of an adhesive known as glycerolphosphoric acid dimethacrylate that was polymerized with the help of an initiator (1). This adhesive depends on acidic monomers that can etch tooth surfaces and interact with them in order to create chemical and physical interactions between the restoration and the tooth. This creates a layer that later would be known as the hybrid layer (2). A year later, Mclean and Kramer reported that the "Sevriton Cavity Seal®" adhered to the tooth chemically. It was the initial account of dentin modifications brought on by an acidic

monomer, this was the precursor of the hybrid layer (2). The adhesive contains a particular molecule, which is the phosphate monomer that Dr. Buonocore and his team later identified as glycerol phosphoric acid dimethacrylate (GPDM), which is part of small number of modern dental adhesives (1). 1955 was another historical milestone for adhesion. In fact, Dr. Buonocore implemented a new technique to help the application of adhesive on the teeth. The technique in question took inspiration from a process used to make the varnish adhere over metals. Dr. Buonocore utilized 85% phosphoric acid to make the surface of the teeth more porous and with this, the adhesive can penetrate better the tooth surface and improve the quality and strength of the adhesion. More than 65 years later this is considered the best method to help adhere composite or other dental supplies over the teeth (1). After acid etching procedure by Buonocore, a progressive abandonment of the theory of mechanical retention of the restoration has been seen, and instead it is aimed more towards a micromechanical and chemical bonding of the rehabilitations over the teeth (4). Another advance in adhesive dentistry happened in 1960. This year Rafael Bowen and Mario Rodriguez published a study where were displayed the tensile strength of different materials. Is important to highlight that one of these materials was a new silica-resin composed of vinyl silane and glycidyl methacrylate and bisphenol A in which the function of the silane is basically to improve the union between the inorganic part to the bisphenol A-glycidyl methacrylate (Bis-GMA). Some years later, in 1964 was commercialize the first composite resin (Addent 3M®) after that, the composition was fully developed a year before. Since then, the biggest modifications to the composite were made only regarding the size of the filler particles and not regarding the part of the matrix (1). In 1968 a crucial discovery was made. Two laboratory technicians working for the UK government, Alan Wilson and Brian Kent bring to light a new material called glass ionomer cement (GIC) (1). It is a self-etching material that was then launched on the market some years later in

Europe, precisely in 1975 (1). In 1979 Takao Fusayama stated that the act of condition the entire tooth with orthophosphoric acid at 40% for sixty seconds improves substantially the union with the dental material defeating the idea that etching the dentine was actually dangerous for the dentin, in fact, it was believed that this procedure could cause irreversible pulp damage. Nobou Nakabayashi and his research team discover in 1982 the hybrid layer in dentin(1,2). They found with the scanning electron microscope (SEM), a "demineralization-resistant zone", after that this substrate was treated with 10% citric acid, 3% ferric chloride for thirty seconds and appliying methacryloxyethyltrimellitate anhydride (META) cured with tri-n-butyl borane. They also recognize the need to use two different types of molecules to improve adhesion over dental tissues. This two molecules have to be one hydrophilic and the other one has to be hydrophobic to help dentin penetration thus helping adhesion (1). To introduce the most recent developments in the field of adhesion in dentistry it is important to talk about the concept of self-etch adhesive (5). Self-etch adhesives were introduced to try to reduce dentinal sensibility and also to reduce the time of the clinical procedure. In fact, with this new system of adhesive the etching with orthophosphoric acid is not required since the hydrophilic resin is accompanied by the acid resin. These adhesives are grouped depending upon pH : (pH≤1), (pH=1.5), and (pH≥2) (2). The first ones are the strong ones and they are not very used due to their excessive acidity which leads to an unstable dentinal adhesion. Strong self-etch adhesives have other problems: collagen fibrils are not supported by minerals and this lead to prevents chemical bonding. Additionally, the resin did not become hydrophobic since the light cannot polymerize adequately. Therefore the adhesive remained hydrophilic, and was more susceptible to be deteriorate. The second ones are the mild ones that conditioned just the superficial layer of the dentin, leaving some hydroxyapatite crystal to allow chemical bonding (1). The interesting difference with etch and rinse adhesives is that the self-etch ones

do not eliminate the smear layer, formed of cut debris, saliva, and organic and inorganic components. This layer is removed in etch and rinse procedures to unplug the dentinal tubules and the dentinal substrate in general to allow the penetration of the hydrophilic resin. The procedure of unplugging the dentinal tubules allows the dentinal fluid to exit from the tubules and can have the adverse effect of causing post-operatory hypersensibility. Since the self-etch adhesive does not remove the smear layer, the degree of resin penetration is less. Removing less smear layer brings to a direct conclusion: the hybrid layer that is going to be produced will be thinner than the one produced from the action of the etch and rinse adhesive thus the strength of the adhesive (2). This problem is partially solved thanks to chemical bonding that is possible to achieve as a result of the presence of residual hydroxyapatite crystal unconditioned in the dentin or also with the selective etching of the enamel. Another consequence of not removing smear plugs is the reduction or the absence of post-operatory sensibility (6). The most recent milestone is the concept of adhesion decalcification. It was introduced in 2001 by Yoshida and Yoshioka and it is still valid. This concept is based on the formation of stable bond between calcium in the hydroxyapatite crystals (1). Etch and rinse adhesives are based on the decalcification pathway, since the molecules in their composition (citric and maleic acid) form very unstable bonds with calcium and this behavior make these substances optimal for the etching of the surface. On the other hand, mild self-etch adhesives based on some molecules such as oxalic acid or polyalkenoic acid. Mild elf-etch adhesives follow an adhesion route but still cause minimal decalcification over the underlying tissues that is beneficial. The stability of the bonds allows to block dentinal tubules thus the post-operative sensibility is reduced to the minimum (1,5). The latest adhesive generation is commonly known as universal adhesives. This new generation has been introduced with the aim of satisfying the requirements of dentists in daily practice having an adhesive that

could be reliable in term of adhesion and easy to use (2). The challenge here is to try to reduce the steps necessary for adhesion, trying to limit the error of the operator, but also without having a reduction of the bond strength. This new type of adhesive is under investigation and in the future will be published different articles with more accurate results over the long lasting bond strength (7). They contain a primer (hydrophilic resin) and adhesive resin (5). Universal adhesives are chosen because of their ease of use and their versatility; in fact they can be used as etch and rinse or self-etch adhesives and so can suit different scenarios (8). Universal adhesives used to not contain the hydrophobic resin and for this particular reason they suffer incredibly hydrolytic degradation. This hydrophobic resin has been later added to the universal adhesive procedure but the improvements seen in 6 months in vitro studies have not been confirmed when the adhesive was applied in clinic. These adhesives are easy to use also because is not necessary to maintain the dentin moist when using etch and rinse technique. Another advantage is that when used in self etching mode the scrubbing movement increase enamel bond strength (1). Even though manufacturers try to support this hypothesis, in reality this information is still not well documented in the literature and the magnitude necessary to be applied when rubbing universal adhesives has not been studied (7). When using universal adhesives, is not recommended etching the dentin because universal adhesives will not seal correctly and therefore the margins of the restorations will tend to discolorate. For this reason is necessary to selective etch the enamel and this extra step increases the working time (1). Usually if the self-etch mode is used, the selective etching of the enamel is critical, because the self-etch mode is not sufficient to achieve a long lasting adhesion without risk of marginal discoloration and discrepancies caused by the low degree of adhesion over the enamel (8). After the polymerization phase, the situation is critical because these types of adhesives may act as a permeable membrane that will cause the degradation of the hybrid layer

over time due to the presence of water at the interface between resin and dentin. The water could remain trapped inside interface because it has not been evaporated correctly (1). Universal adhesives have in their composition a molecule called Methacryloyloxydecyl Dihydrogen phosphate (MDP) which is a hydrophilic molecule with mild-etching characteristic that allows universal adhesives to be used with different etching techniques. In their composition are found different molecules such as hydroxyethul methacrylate (HEMA) which has a hydrophilic characteristic, decandioldimethacrylite (D3MA) with hydrophobic properties and bis-GMA; the combination of them permit these adhesive to effectively create a bond between the hydrophilic tooth substrate and hydrophobic restoration (2). Bonding agents are divided into two group based on:

1) From first to eighth generation (5).

2) By number of steps which divides the adhesives based on the fact if they need a previous step to condition the dentin with acids or if the acid is included in the adhesive. This classification is explained in Figure 1 (1).

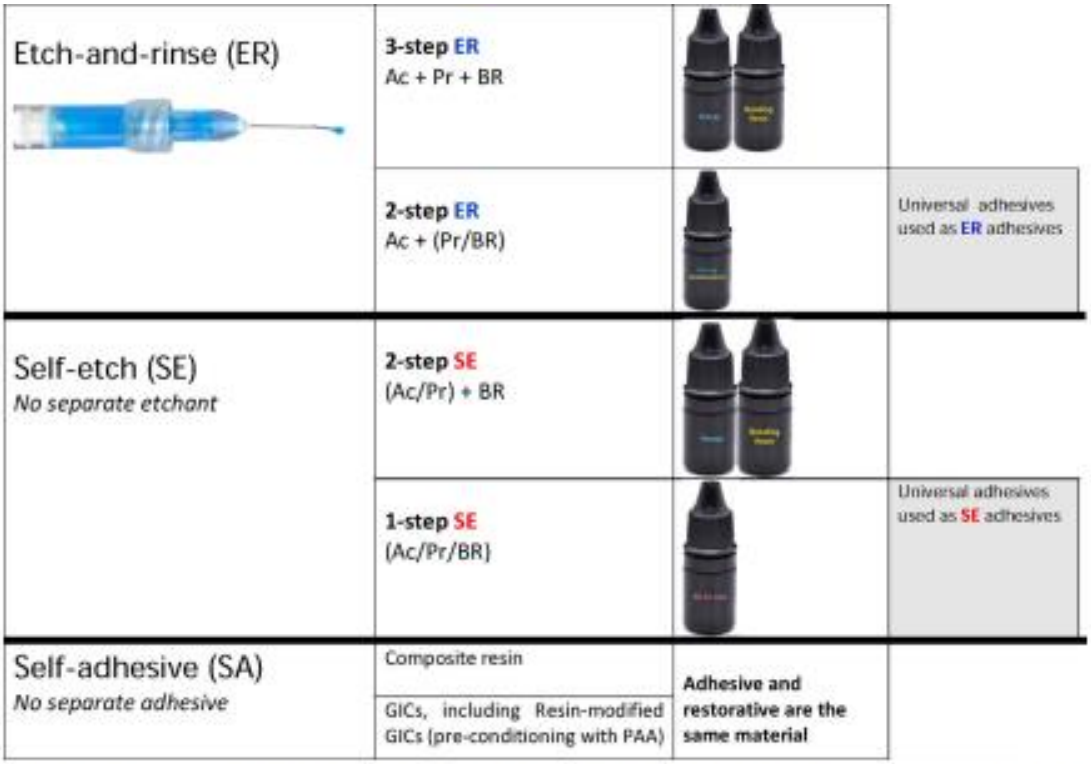

Figure 1. Classification by number of steps (1).

Adhesives have the function to bind restorative materials to teeth. Teeth are composed by different tissues such as enamel and dentin and adhesive protocols change depending on the substrate we want to adhere to. Enamel and dentin include in their composition inorganic matters but in different percentage (1); The enamel contains 4% of water and residual organic content, 96% is the percentage of inorganic matter. The dentin contains also inorganic matter but in a lower percentage because a larger part is occupied by the organic matter and water. The most predominant as organic matter is collagen type I. Due to these characteristics and the presence of smear layer and also due to its heterogeneous nature, adhesion over dentin is more challenging than adhesion over enamel (4,9).

- 1.2 Adhesion over the enamel

In order to achieve optimal long-term adhesion of different restoration materials it is important to understand how enamel and dentin are formed since a different composition implies a different approach for adhesion. Enamel is the toughest component of the human organism (10). The enamel is a dry substrate that does not contain vital structures. For all its characteristics is considered that the adhesion is easier to reach at the level of the enamel, that is considered almost the ideal substrate to adhere to (1). It covers the whole crown of the tooth covering both dentin and cementum (11). This substrate, which is the one that give resistence and strength to the tooth, is formed during odontogenesis. It is made up mostly of inorganic matter (96%). This part, besides calcium, phosphate, zinc, copper and magnesium, are present crystals of hydroxyapatite which are arranged in an organized way. The smallest unit of enamel are crystallites oriented in three dimensions. The relationship between the hydroxyapatite crystals forms the rods or prism. The rest of crystals that surround each rod are called interred enamel. As a matter of fact enamel is a poor substrate for adhesion due to its characteristics as the smooth surface, the low surface energy, the presence of the organic pellicle and due to the presence of saliva that makes its surface is constantly wet. For these reasons, to make the enamel an optimal adhesive substrate it is important to make the environment dry and free of contaminations. This is reachable with the use of different types of isolation techniques and also its surface has to be conditioned with ortophosphoric acid or prepared with high speed diamond burs. All these procedures have the objective to make the enamel more receptive to adhesive thanks to the increment of the surface energy. The space between the crystals (4%) is mainly composed of water and organic matter which are still needed for proper functioning of this substrate. The organic part is made of cells, fibers and proteins being the latter the most important ones. The function of water is basically permit diffusion of different

components and has an active role in the demineralization - remineralization process (10,11).

- 1.3 Adhesion over the dentin

Dentin is still a mineralized matrix but less than the enamel (12). In fact it is composed of 70% mineral, 20% organic matrix and 10% water (1). Dentin bonding has always been challenging due to different characteristics explained before (12). It is a vital porous, flexible, and without blood supply and has a heterogeneous composition, it is less calcified. The dentin presents metalloproteinase, which is a proteolytic enzyme able to degradate proteins and the hybrid layer and we have to take it into account when it comes to evaluating the success of restorations, and also the dentin present an important water content (3). Its structure changes throughout years due to aging, caries or operative procedures but in general it has a particular tubular structure filled with low pressure liquid and odontoblastic process. Dentin structure presents intertubular dentin and peritubular dentin. The former contains more collagen than the latter which is more calcified and is present in between tubules (13). The dentin protects the pulp, and thanks to the presence of water, it absorbs the loads coming from the enamel during function to avoid tooth fractures. Structure changes from the deepest part near the pulp, to the most superficial at the level of dentin-enamel junction. The number and size of the tubules increase near the pulp. The number of dentinal tubules in superficial dentin is around (15,000/mm2) instead near to the pulp are around (65,000/mm2). Tubules number ranges from about 42,400/mm2 to 8,200/mm2 from coronal to apical. Size varies also from 0.8 μm in the coronal to 2 μm near the pulp. This results in a decrease in the collagen fibers, from superficial to deep dentin (3). Dentin also present hydroxyapatite crystals but they are arranged in a different way than the enamel since in the dentin they are placed randomly in an organic matrix (13). Another

important difference compared to enamel is that the dentin presented a smear layer. It is a thin layer of cut debris where traces of dentin, saliva, odontoblast, collagen, organic and inorganic components can be found. The presence of this layer decrease dentin permeability and surface wettability (1).

- 1.4 Mechanism of adhesion over enamel and dentin

The most efficient method for achieving durable bond in enamel is still the etch-and-rinse method, which selective dissolve of hydroxyapatite crystals (6). When applying adhesive, two types of resin tags are created: macro-tags and micro-tags. The former fill the interrod enamel and are less in number, while the latter result from resin infiltration in the micro porosity over the prisms and are more in number. Micro-tags are the ones who helps the adhesion more since they have a wider surface because they are more present on the surface (2). To help remove the smear layer, created after the removal of the caries, orthophosphoric acid is used. The conditioning of dentin helps to increase the surface energy and expose the scaffold of collagen fibrils thanks to the decalcification of the inter and peritubular dentin. The intertubular dentin is dissolved and the scaffold of collagen fibril is expose at 3-4µ in depth. The peritubular dentin decalcification by the penetration of the acid into the tubules allows walls calcification 4-5µ in depth. This structure will allow the infiltration of the hydrophilic resin that will create a hybrid layer. This layer; discovered by Nakabayashi, Kojima and Masuhara in 1982; is an interdiffusion area created from the combination of hydrophilic resin and the collagen fiber (6). The resin replaces the hydroxyapatite crystals and the water created an interlock system. The better is the quality of this layer the better will be the strength and the durability of the bonding with the restoration. To improve the quality of this layer the collagen fibers should be a little bit wet to avoid their collapse to allow a better resin infiltration. Concomitant with hybridization, the resin is able to go inside dentinal

tubules to improve retention. According to Van Meerbeek in 1993 this interdiffusion area is divided in 3 layers: superficial, intermediate and deep layer. The first has in the composition mostly resin and it is in contact with the hydrophobic resin; the second is the real hybrid layer and, in the third layer, is seen a less decalcification and gaps can be found where the resin does not reach all the decalcified structure (6).

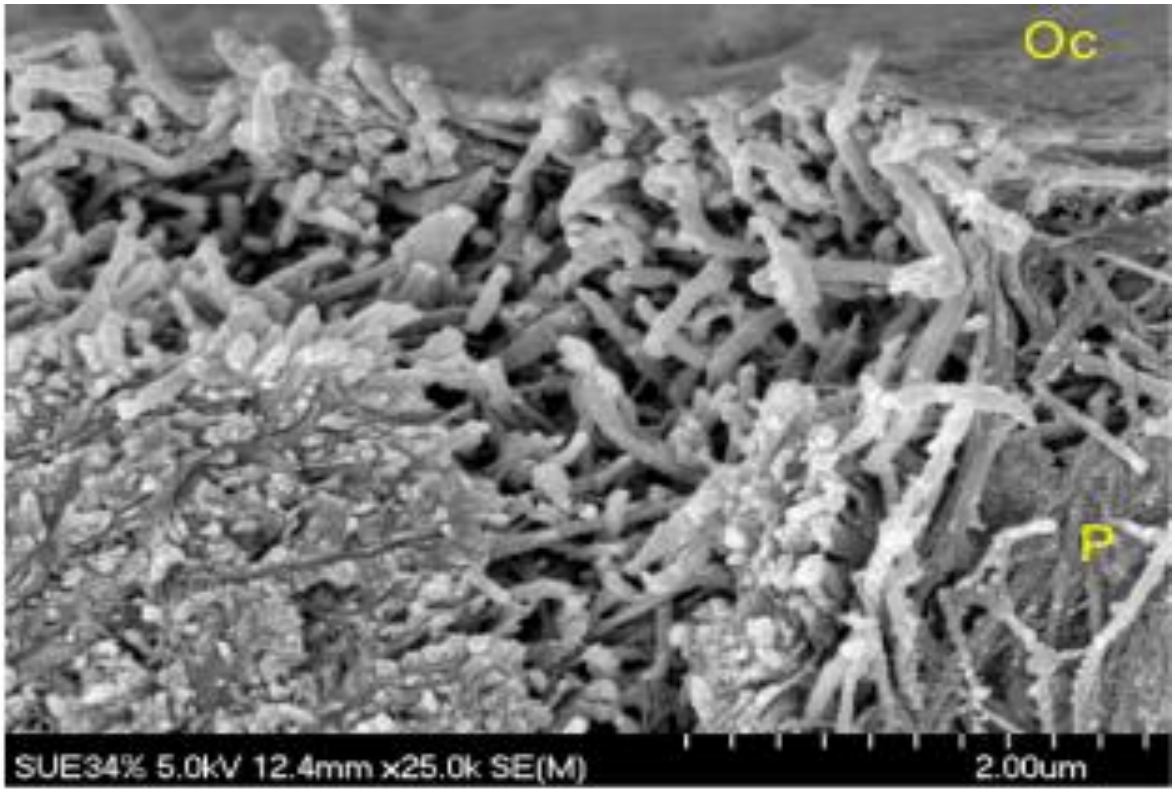

Figure 2. The areas between the collagen fibrils are filled with water once the etchant has been rinsed *(14)*

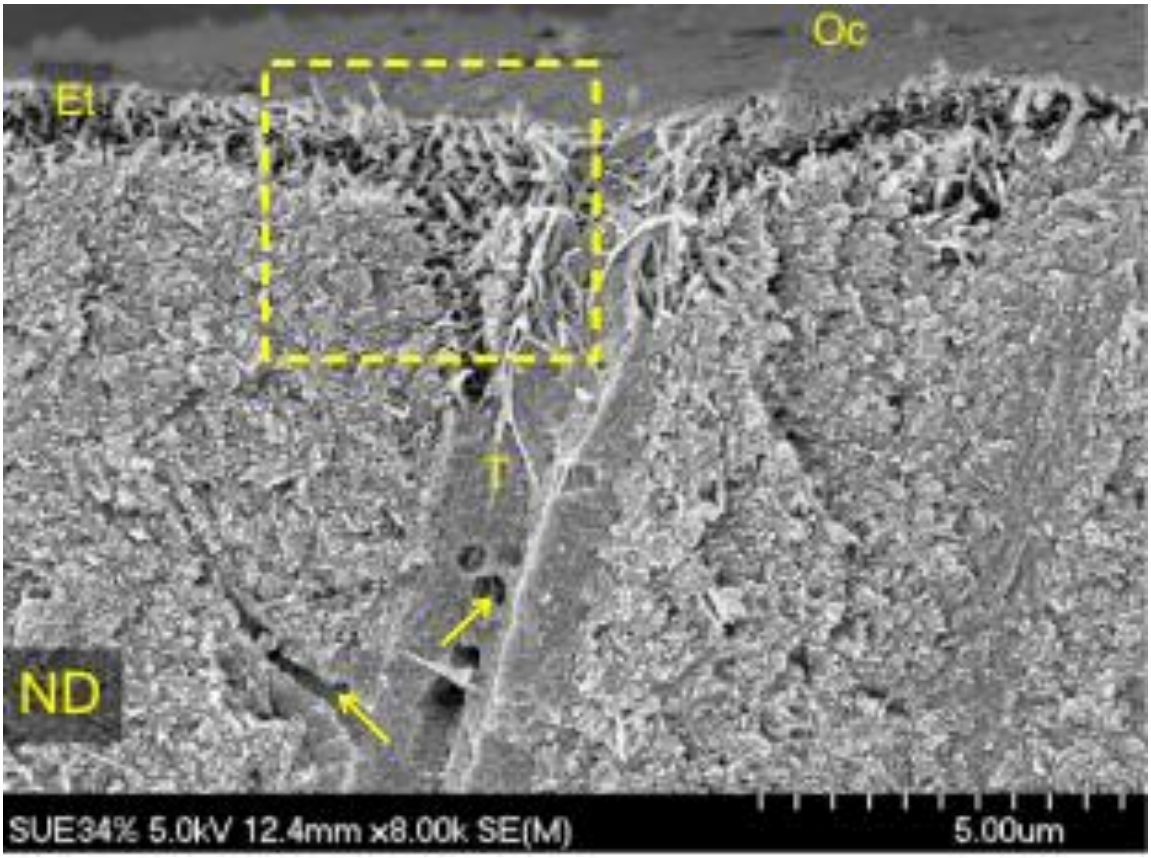

Figure 3. Etched dentin with 34% orthophosphoric acid for 15 seconds. Oc = occlusal surface; Et = etched dentin with collagen fibers; T = tubule; ND = normal dentin (14).

- 1.5 Challenges of adhesion to dentin

In opposition to enamel, dentin is a much more wet, contains organic components and adhesion over it has always been challenging and not very predictable (1). Adhesion of restorative materials is affected by different factors, for example patient's age, location of the tooth, depth of the cavity, sclerotic and/or carious dentin, radicular dentin or coronal dentin, isolation, dentist's experience, fluid in the internal structure of the dentin. Mineral deposition in the dentin increase after some stimuli such as a caries. This lead to a reduction of the permeability of the substrate and for instance the adhesion will be much more difficult. Other important factor is the presence of matrix metalloproteinase (MMP) that can hinder adhesion because it degrades over time the hybrid layer and therefore lower the durability of the

restoration (15). To try to overcome this problem different solutions are being currently studied. One of the options is to apply chlorhexidine 2% but most of results were conflicting and further investigations are needed (9). Since MMPs destroy the collagen of the extracellular matrix by adding water, is possible to try to inactivate MMPs by replacing the water with ethanol, to try to prolong the duration time of the restorations. This technique, known as ethanol wet-bonding, seems very promising but, increase the working time and most importantly can end up in reducing adhesive infiltration in the substrate, since it cause a collapse of the collagen fibrils (14). There are also some risk factors which are constant concerns of many researchers: pH of the medium, hydrophilicity of the adhesive. Also the position on the tooth where it is going to be placed in the restoration is very important and can influence the long term durability of the restoration (3). For example, in non-carious cervical lesion (NCCL), there is no retentive cavity and the margins of the cavity are on dentin and cementum which are not favorable for adhesion. In addition, the dentin present in this type of cavity is sclerotic and the more sclerotic is the dentin, the more difficult is adhesion (15). Dentin permeability is affected by a variety of elements. For example, the vasoconstrictors in local anesthetics have the ability to reduce the pressure exerted by the pulp and dentin liquid flows inside the tubules. Other factors that modify dentin permeability are the radius and length of the dentinal tubules, the viscosity of dentinal fluid, and the pressure gradient (6). Limited investigations are conducted about the preservation of collagen network of the dentin with some nontoxic cross-linking agents that reduce degradation of the bond over time and can also improve increase mechanical qualities (6,9). The concept is based on the fact that collagen fibers form cross-links and this help against enzymatic degradation and also help having a good tensile property. For the purpose of replacing and reinforcing these natural cross-links, it has been studied the effect of the glutaraldehyde, that can enhance collagen stability

but due to its toxicity it has been discarded, and proanthocyanidins (PA) which are chemical compounds without toxicity that help stabilize the links between type-1 collagen fibers through covalent, ionic and hydrogen bonding (6). It has been proved that application of a hydrophobic coat helps to stop the diffusion of water through the hybrid layer that is the main cause of the degradation of the dentin-adhesive interface and also increase the thickness of the adhesive layer that is known to reduce polymerization stresses. In the literature is showed that remaining solvent into the resin can affect negatively the quality and the lasting of the restoration. To overcome this problem, they suggest that warm air-drying is necessary to improve the adhesion (6,13). The air-drying time required vary depending on the type of solvent and the distance of the air syringe from the dentin. Over-dry dentin is scientifically proven, in different articles, to decrease adhesion since the collagen surrounding the tubules tend to collapse and therefore is difficult, for the adhesive, to impregnate the dentin (2,14). One of the peculiarities of dentin is that it has in its composition water. Water helps to maintain the structure of collagen fibrils, avoiding its collapse. Maintaining this three dimensions (3D) structure will allow the hydrophilic resin to infiltrate better and to have a more desirable hybrid layer. Mantain the dentin moist during the process of adhesion is called wet-bonding technique (14). This technique is very useful mostly when using ethanol-based adhesives. Ethanol is able to replace water so is able to maintain the structure of the collagen fibrils and therefore it makes this zone to be infiltrated by the resin. The main disadvantage of this technique is its subjectivity: the degree of wetness and dryness depends on the operator and is also known that an overwet or overdry dentin affects the performance of the adhesive (5). When the preparation is very deep in the dentin other problems arise. For a better interaction with the deep dentin, studies show a better diffusion of the adhesive through the dentin when the operator applies the adhesive actively (6). The substrate of adhesion is extremely important

to understand the durability of the restoration. For example an eroded substrate, such as dentin, can be considered a difficult substarte to adhere to. On the other hand, eroded enamel seems to facilitate adhesion since the erosion makes the substrate more porous and therefore the resin penetration and retention is facilitated. On the contrary, is more difficult bond to eroded dentin because the hypermineralized layer occlude the tubules and this leads to an impregnation of poor quality. In eroded dentin, the minerals present in its composition are dissolved, so there is a much thicker layer of organic material that leads to a tag formation of under 3 μm. In sound dentin these tags are around 9 and 15 μm (9). A great importance is given to the smear layer that is a crucial concept to understand regarding adhesion. Its presence hinders adhesion and its removal helps the infiltration of the adhesive though the collagen fibers forming a better hybrid layer and therefore a better adhesion (3). To enhance the diffusion of the hydrophilic resin into the dentin, some solvents are in the adhesives. Typical solvents are water, ethanol, and acetone (1). During the procedure for adhesion, it is crucial to evaporate these solvents because their excessive presence during the polymerization weakens the strength of the bonding (6). Other additives to the adhesives are photoinitiators such as camphorquinone that can be light-curing or self-curing, catalysts to accelerate chemical reactions, and also inorganic fillers, needed to compensate the shrinkage of polymerization (2,5).

- **2. OBJECTIVES**

Main objective: To compare the different techniques and different generations of dental adhesives

Secondary objectives:

- To evaluate the challenges to face for adhesion over the dentin

- To compare the bond strength, nanoleakage, sealing ability, retention rate, and marginal integrity of restorations using different adhesives.

- **3. MATERIAL AND METHODS**

A literature review was conducted on the 5th of December 2022 and the databases used were Medline and Dentistry and Oral Science Source. All the articles displayed were published between 2012 and 2022. The inclusion criteria identify articles that are in English, free full text and not older than 10 years. The exclusion criteria are: duplicate articles, articles from non-impact journals, studies that used artificial specimients and some were excluded due to title and abstract or due to full text reading because the articles covered topics not related to the objectives of this review. The terms used for this research are: dentistry [meSH Term] AND dentin [meSH Term] AND dental bonding [meSH Term] AND dentin-bonding agent [meSH Term] AND adhesion.

- **4. RESULTS**

- 4.1 Prisma flow chart

The articles of this review have been selected following a PRISMA flow chart

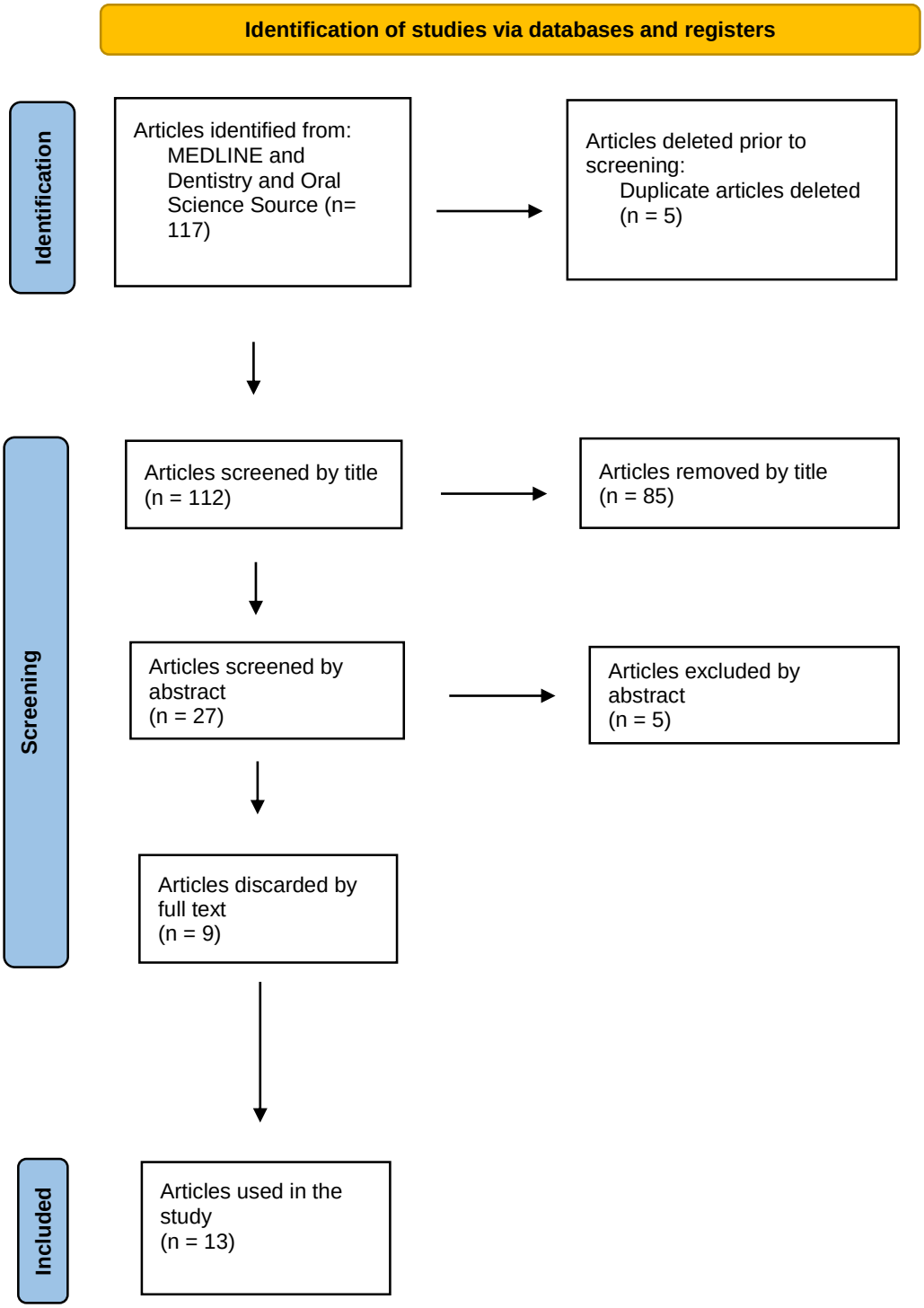

Figure 4. Prisma flow chart

Below a summary table was created with the articles included in this review.

Author, year (reference)	Sealers evaluated	Control/s	Technique used	Focus of the article
Peumans et al. (2018) (16)	HEMA-free 1-step G-Bond®	3-steps etch and rinse Optibond FL®	A total of fifty-two patients with a minimum of two non-carious cervical lesions participate in the study. NCCL 1-step self etch G-Bond® or 3-steps etch and rinse Optibond FL®. All the procedures were conducted by expert dentists, and every step was monitored to guarantee consistency	Retention, marginal integrity, marginal discoloration
Bacelar-Sà et al. (2017) (17)	G-aenial Bond®, BeautiBond® HEMA-free and All-Bond 3®	Adper Single Bond 2® (HEMA)	All bonding agents have been used following companies' recommendations	Dentin sealing, micropermeability and bond strength
Saikaew et al. (2021) (18)	Dentin conditioned with superfine or regular diamond burs; adhesives such as Clearfil SE Bond 2®, Scotchbond Universal® and G-Premio Bond®; applying adhesives actively or passively	-	84 premolars divided: 1) dentin conditioned with superfine or regular diamond burs 2) three adhesives 3) two modality of application. 6 teeth per group analyzed for bond strength testing	Bond strength differences between different adhesives and different application modes
Hosaka et al. (2021) (19)	One-step self etch adhesive	Two-step self etch adhesive	42 experienced restorative dentistry specialists participated in the placement of restorations at different clinics. The dentists had the possibility of use or not a dye to detect caries and use or not complete isolation. They could choose also the adhesive system but were obliged to follow the manufacturers' recommendations	Compare mid-term clinical effectiveness of direct composite restorations using one-step or two-step self-etch adhesives

Deepa et al., (2014) (20)	Clearfil SE Bond®-6th generation and G-Bond®-7th generation	XP Bond®-5th generation (one bottle total etch system)	Bond strength of the composite restorations was analyzed after restoration bonding over the samples	Microshear bond strength
Kaczor et al., (2017) (21)	Scotchbond universal®, All-bond universal®, G-bond plus®, Prime&Bond elect®, Peak universal®, Clearfil universal bond®, Futurabond U®	-	The articles of this review were screened through PubMed/MEDLINE, Web of Science, Scopus and Science Direct electronic databases	Nanoleakage of universal adhesives
Chowdhurry et al., (2019) (22)	One-step universal adhesive G-Premio Bond®, Scotchbond Universal®	Two-step self-etch adhesive Clearfil Megabond 2®	The experiment involved 60 human third molars that were extracted, and an additional 24 third molars were specifically prepared for studying the interaction between the resin-dentin interface and adhesive-smear layer	Bond strength
Ricci et al., (2015) (23)	1-step self-etch adhesives and 2-step self-etch adhesives	3-step etch and rinse adhesives	-	-
Sezinando et al., (2012) (24)	OptiBond FL®, OptiBond SOLO plus®, OptiBond XTR® and OptiBond ALL-inOne®	-	48 human third molars were assigned to four groups of teeth and in each group a different adhesive was used. Each adhesive was assigned to one of the three aging condition: 1) distilled water for 24 hours, 2) thermocycled for 20.000 cycles, and 3) distilled water for 6 months	Bond strength

Table 1. Results selected in this review.

Bacelar-Sà et al., (2017) (25)	Dentin treated with cross-linking agents (5% glutaraldehyde and 6.5% proanthocyanidin) for 10 minutes	Dentin kept untreated	60 third molars stored in thymol-saturated solution at 4° C and used within three months after the extraction	Dentin sealing and bond bond strength
Bortolotto et al., (2012) (26)	Five etch and rinse and seven self-etch adhesive systems with their corresponding composites.	-	Assesing margin behavior of 12 contemporary restorative systems in class V restorations with margins located on enamel and dentin after mechanical loading and water storage.	Marginal integrity
Coelho et al., (2021) (27)	Chlorhexidine, EDTA, ethanol, lasers, fluoridated agents, sodium hypochlorite used as cavity disinfectants	-	The research was conducted using Cochrane Library, PubMed, and Web of Science. There were used the results from in vitro and in situ studies. Quality assessment of the review done with Revised Cochrane risk-of-bias tool.	Bond strength and MMPs inhibitors
Maciel et al., (2020) (28)	Teeth prepared with electric current (50Ma)	Teeth not prepared with electric current (conventional application)	Teeth divided into 12 groups and three adhesive systems were used: two-step etch-and-rinse, two-step self-etch and one-step self-etch	Bond strength

- **5. DISCUSSION**

- 5.1 Bond strength

According to the study of Bacelar-Sà et al. bond strength is better in situations in which acid etching is used because it creates a thicker hybrid layer and also longer resin tags (17). Adper Single Bond 2® (HEMA-containing etch and rinse 2-steps one bottle) and All-Bond 3® (universal adhesive) are the ones that had better results for bond strength and both used acid etching previous their application. G-aenial Bond® and Beautibond® showed the worst results. The results are similar to both 24 hours and a 1 year follow up in water storage (17). The orthophosphoric acid, when used for too much time before applying adhesives, it can demineralize too much the dentin and therefore instead of helping the strength of the adhesion it is making it worse because the acid destroys too much the dentinal tubules, letting out too much water (25). In the study of Sezinando et al., after 24 hours and 6 months of water storage, the best results in terms of bond strength is found in teeth with a 2-steps self-etch adhesive (OptiBond XTR®). This is in contrast with the findings of the authors of the study Bacelar-Sà et al. since in the last study the best results are achieved with a self-etch adhesive and not with an etch and rinse one (17,24). The best adhesive after thermo cyclic fatigue is still OptiBond XTR® (24). This can be explained because self-etch adhesives adhere to the substrate mechanically and also chemically, thanks to the presence of the 10-MDP molecule. This last part is the reason why, these days, 2-steps self-etch adhesives, with a separate hydrophobic resin application, can have equal and often better results than the etch and rinse adhesives (24). The study of Van Landuyt et al. found better results when using OptiBond FL® than for example All-in-One®. This is in contrast with the study of Sezinando et al., and this can underline the fact that it is an adhesive very susceptible

to the ability of the operator (24). In the literature, have been used different methods to improve the bond strength of the restorations. As a matter of facts, in the study of Maciel at al. is explained how is possible to increase bond strength with the use of electric current (28). To improve the results of the bond strength the study of Maciel et al. utilizes an electric field. The electric current helps the monomer of adhesives to penetrate better into the demineralized dentin. The results are improved if self-etch adhesives are utilized because they are composed of more polar molecules but the still the differences with etch and rinse adhesives were not statistically significant in this particular study (28). All the results of this study are at 24 hours so further studies are necessary to understand better the long-term results of this experiment (28). In the study of Saikaew et al. the active application brings good results in terms of bond strength in both situations: when the dentin is prepared with a regular diamond bur and also when the dentin is prepared with a superfine diamond bur (18). This means that the results are not influenced by the bur utilized in this experiment (18). The active application, in the study of Saikaew et al., of the adhesives helps to remove the smear layer which is the same principle at the base of utilizing the orthophosphoric acid in the study of Bacelar-Sà et al. (17,18). To support this thesis, for example, Clearfil Megabond 2® would have benefited, in terms of bond strength, of an active application (18). Other than removing the smear layer, active application of the adhesives, helps the evaporation of the solvent creating more resin tags (18). In fact, supporting the thesis of the study of Bacelar-Sà et al. and Maciel et al., the active application improves more the self-etch adhesives than the etch and rinse ones, because in these cases the smear layer is already been removed by the application of the orthophosphoric acid (18). Regarding the influence of the the smear layer, the study of Chowdhury et al. showed that changing the bur for preparing the dentin changes the quantity of the remaining smear layer, but that, as is said in the study of Saikaew et al., is not statistically

significant in these two particular studies (18,22). The presence of water is a problem when adhering to dentin since it promotes hydrolytic degradation as stated by the study of Hosaka et al. (19). Following the results of his study, 2 steps self-etch adhesives performed better than the 1 step self-etch adhesives because of the excessive hydrophilicity that promotes hydrophilic degradation (19). In fact in the study of Deepa et al., higher values of bond strength are seen in the coronal dentin than in pulpar dentin due to the morphological characteristic of the dentin. As a matter of fact, in the pulpar dentin is present more water than the coronal dentin. Supporting the findings of study of Hosaka et al., adhesives that contain more hydrophilic molecules have more problems adhering to the dentinal substrate (19). To support this finding is possible to say that all in one system showed lower values of bond strength in both pulpar and coronal dentin due to the fact that this system is very hydrophilic (20). The results are in contrast when talking about the presence of the smear layer. In the study of Chowdhury et al., the thickness of the smear layer does not influence adhesion (22). In the study of Saikaew et al., the results showed that the ability to remove the smear layer positively affects the bond strength since the etch and rinse adhesives showed better results (18). As mentioned by some authors, the presence of excessive water in the dentin-adhesive interphase is known to hinder adhesion (19,25). As a matter of fact, to avoid the excessive presence of water in the interphase adhesive-dentin, is better that adhesives with more hydrophilic molecules are applied two times so water is removed from the substrate and this is considered positive seeing the results (22). Adhesives with hydrophilic tendency usually contain the HEMA molecule, which helps the adhesive to impregnate the substrate better according to the study of Chowdhury et al., and its absence makes the adhesion weaker (22). This is in contrast to what is found in the study of Bacelar-Sà et al. since the presence or absence of HEMA does not influence the bond strength both at 24 hours and at 1 year (25). According to the authors of

Chowdhury et al., the presence of HEMA in the adhesive Scotchbond Universal® helps this adhesive to perform better in terms of bond strength than G-Premio Bond®, which does not contain the HEMA molecule (22). This is in agreement with the findings of the study of Bacelar-Sà et al. in which HEMA-free adhesive (G-Aenial®) showed lower bond strength than Prime and Bond Elect® and Scotchbond Universal® (both HEMA-containing) even though in this case the dentin was modified with collagen cross-linkers agents, which improve collagen resistance to degradation over time (25).

- 5.2 Nanoleakage

Scotchbond® is a universal adhesive and with 10-MDP monomer it helps reduce nanoleakage (25). This in accordance with the results of the study of Kaczor et al. that suggested MDP molecule, and in general, all the functional monomers, help reduce nanoleakage because they reduce the dissolution rate of the resin-dentin interface (21). When applying G-Premio Bond (universal adhesive) in two applications it helps reduce nanoleakage (22). This is the same as the study of Kaczor et al., in which it has been shown that, for 1-step self-etch adhesives, increasing the time and surface of contact between dentin and adhesive reduces nanoleakage and increases bond strength (21). This is also suggested by the study of Munoz et al. (29).The study of Kaczor et al. also showed that etch and rinse adhesives have lesser nanoleakage than self-etch adhesives but this last category is able to recover the gap thanks to the presence of 10-MDP or other functional monomers (21).

- 5.3 Sealing ability

Dentin sealing is the act of applying a layer of adhesive to seal the dentin and to avoid future contamination or post-operatory sensitivity and, therefore, increase the durability of the natural tooth in the mouth of the patient (17).

The best results in term of dentin sealing were reached by Adper Single Bond 2® (HEMA-containing) and All-Bond 3® (HEMA-free) both at 24 hours and at 1 year and perfect results were reached by G-aenial Bond® (HEMA-free) at 24 hours (17). This shows that it makes no difference, for the authors, if the adhesive contains the HEMA molecule or not (17). For the authors, maybe the presence of nanofillers, in the composition of Adper Single Bond 2®, helps the adhesive to reach the same results of All-Bond 3® which was expected to produce better results, since it does not contain HEMA in the last bottle (25). These are the same results found in the study of another article made by the same author in 2017 in which, at 6 months, no differences were seen in terms of dentin sealing (25). The results are the same in the two articles even though the dentin in the study of the 2017 was prepared with proanthocyanidin extract or glutaraldehyde. The choice of these two collagen cross-linkers agents does not influence both bond strength and dentin sealing (25). The drop of sealing of G-aenial Bond® is due to its tendency to behave as a permeable membrane and therefore this adhesive tends to lose the ability to seal the dentin. This finding is supported also by the study of Tay et al. (25,30).

- 5.4 Retention rate

To increase the durability there are longitudinal in vitro studies that let us know that the gold standard for adhesives is still the 3-steps etch-and-rinse adhesives (23). For example, Optibond FL® showed a better retention rate than G-Bond® (16). Adhere on sclerotic dentin could be difficult and some adhesives may work better than others (16). It is clear that adhesives that need previous etching with orthophosphoric acid are more likely to succeed in these situations (16). In the study of Peumans M et al. there were compared HEMA-free 1-step self-etch G-Bond® and 3-steps etch-and-rinse Optibond FL® for NCCLs with a retention rate of 89,7% for both adhesives. Instead in the literature it is found that at 5 years, retention rate is a little bit higher

for G-Bond®. The results were 97,4% for the study of Burrow et al. but the enamel was previously etched and this technique increased the retention rate (16,31). Have not been found differences between 1 and 2 steps self etch adhesives in the study of Hosaka et al. (19). The study of Sezinando et al. shows how retention rate for OptiBond SOLO®, which is a 2-steps etch-and-rinse adhesive, provides acceptable clinical results at 8 years fo NCCLS (69%) and just 59% with Prime and Bond 2.1® which is an universal adhesive (24). The clinical trial by van Dijken et al. recorded a retention rate at 5 years of 92,1% (32). Another study, recorded retention rate at 13-years, and it was found that the retention rate for Optibond FL® was higher than G-Bond® and it was 94% (28). To increase the retention rate of the restorations, also the use of complete isolation has been taken into account because it is suppose to keep the working field free of contaminations and humidity, leaving a better substrate to adhere to (16,19). In both studies of Hosaka et al. and Peumans M et al. no statistically significant differences, regarding survival rate, have been found regarding the use of rubber dams for complete isolation (16,19). The results of the study of Manh et al., instead, showed a positive correlation between the use of rubber dam and the increase of retention rate (31).

- 5.5 Marginal integrity

In recent years, direct composite restorations are becoming the first choice of treatment (26). To assure that the treatment lasts long enough it is important to use the best adhesive for each situation depending on the fact if the margins of the restoration are on the enamel or on the dentin. This will help the retention and the resistance to cyclic fatigue of the restoration. Following the results of the study of Bortolotto et al., the highest score of marginal integrity was observed in a three-steps etch and rinse adhesive (Optibond FL®) and a one-step self-etching adhesive (G Bond®) in both enamel and dentin (26). No differences between Optibond FL® and

G Bond® were shown in the study of Blunk and Zaslansky et al. for class I restorations (33). The results found in this study, regarding Optibond FL®, are supported also by the studies of Peumans M et al. (34), and Banu Ermis R et al. (35), found more perfect restoration margins at the level of the enamel rather than at the level of the dentin (26). This result is in contrast with Scotchbond 1XT® which showed that the margin of the restorations were more intact at the level of the dentin (26). Optibond FL® was the only one that showed the same results both in dentin and enamel. Instead, for the self-etch group, no differences were found. In general, in this study has seen an increase of 32% and 28% of marginal gaps on enamel and dentin after one year of water storage. This is in accordance with another study that also showed a 50% decrease of bond strength (36). This supports the findings of this study that also enamel-resin interfaces are prone to degradation. Another study that proposes the same idea is the one of Foxton at al. (37). The trend observed in these studies is that etch and rinse adhesives showed more marginal integrity on enamel and self-etch adhesives showed better marginal integrity over dentin (26,36). This is in accordance with the result of the study of Hosaka et al. which found more marginal gaps when applying mild acidic adhesives, but the problem can be solved by etching selectively the enamel, prior to the application of the adhesive (19). The results of this study and ones published by Chiang et al. supports the same hypothesis: the competition between enamel and dentin adhesion (38). This means that if the adhesive is not bond effectively, the subsequent restoration will tend to shrink toward the strongest bond. The comparisons between iBond and G Bond is very interesting because they only differ for the glutaraldehyde contained in G Bond but in different studies, iBond performs better than G Bond in terms of marginal integrity. This result is the same for several studies (33,39,40). All the authors gave no explanation regarding these results, so further studies are needed to understand if the glutaraldehyde has a negative effect on adhesion over enamel (31).

- 5.6 Marginal discoloration

Marginal discoloration is linked to marginal integrity and following the results of the study of Peumans M et al., polishing the margins of the restoration can help the restoration from the point of view of the aesthetic and durability. In this study, margin discoloration results were the same for both GB and OFL if the operator was an expert, but if the adhesive was applied by dental students with less experience, better results are seen with OFL than GB. In this study, in general, marginal discoloration was seen more with GB (95,3%) than OFL (65,4%) on enamel (16). To overcome this problem, in a 13 year clinical trial conducted by Peumans M et al. (41), less marginal discoloration on enamel was seen if the enamel was previously selectively etched. This was also confirmed in a systematic review of Szesz A et al. (42). No differences were found on the dentin side in these studies (41,42).

- 5.7 Matrix metalloproteinases inhibitors

In dentistry some inhibitors of the MMPs are being used to try to improve bond strength of the restorations (27). Chlorhexidine is the one that is being studied and also utilized the most among this category of MMPs inhibitors (27). The study of Coelho et al. showed the percentage of chlorhexidine most used and the one which gave better results in the majority of the studies analyzed (27). Indeed, is possible to state that chlorhexidine maintains or increases bond strength and only a minor portion of authors reported a negative effect on bond strength. In the case in which chlorhexidine was used before applying a self-etch system, for the majority of the authors, the bond strength decreases. Only in the study of Elkassas et al., it was found that the bond strength diminished when using an etch and rinse adhesive system (43). With regard to universal adhesive systems, has been found positive results regarding bond strength in the study of Say et al. (44) and Campos et al. (45).

Instead, no differences were found, between etch and rinse and self-etch systems, in the study of Akturk et al. (46). Another protocol is being studied and is the use of sodium hypochlorite to inhibit MMPs but the results are discordant. In the study of Kunawarote et al. (47) is possible to appreciate positive results regarding bond strength but the study of Aguilera et al. (48) did not find differences in both superficial and deep dentin. The study of Kunawarote et al. also showed that, if the operator utilizes sodium hypochlorite between 0,5% and 10% solutions for more than 30 seconds, the adhesive forces are affected negatively (47). Another protocol under investigation is the use of different laser irradiations that, theoretically should minimize the access of bacteria to the pulp but in reality, the results are not consistent so further studies are needed (27).

- **6. CONCLUSIONS**

- Different generations and techniques were developed over time allowing adhesives to be applied in different modalities: etch and rinse adhesives, without etching, or etching selectively. In the first group, the adhesion techniques can be 3-steps or 2-steps, depending if the adhesives are contained in one or two bottles. In the second group, self-etch adhesives can be applied directly over the dentin, or is necessary to mix two bottles of adhesives before application. The newest adhesives are called universal, so they can be applied directly on the tooth or applied after selectively etching the enamel to improve bond strength.
- Over the years there were developed new adhesives and techniques to overcome the problems to adhere to dentin. To avoid post-operative sensibility, the manufacturers developed self-etch adhesives with which there is no need to etch the dentin. Therefore, the dentin is not too demineralized and the smear plugs still help to protect the dentin.
- Self-etch adhesives and also universal adhesives were also introduced to try to reduce clinical time and the errors of the operator without giving up on the quality of adhesion. The other problem faced when using self-etch adhesives is the formation of a thinner hybrid layer which decreases the life of the restoration. This is due to the presence of the smear layer which is not removed but the problem is partially solved with the functional monomers. Authors suggest using adhesives actively to increase the diffusion of the adhesive in dentin but mostly in its part close to the pulp since is a more wet substrate than superficial dentin.
- In achieving maximum bond strength, the gold standard is still the 3-steps etch and rinse adhesives but the addition of functional monomers in the composition of self-etch adhesives, application of electric current, and some precautions help reduce the gap in terms of bond strength and nanoleakage.

- Has been found that the thickness of the smear layer can influence the bond strength significantly only when self-etch adhesives with a mild pH are used.
- The number of steps used is important to improve bond strength since the application of an extra hydrophobic layer of adhesive enhances bond strength.
- Regarding MMPs inhibitors, the only positive consistent results were found only about bond strength, when using chlorhexidine. Instead, the use of sodium hypochlorite or laser irradiation should be avoided due to the lack of consistent scientific evidence.
- Is important to understand that the excessive hydrophilicity of the adhesive and the excessive presence of water in the substrate hinders adhesion but HEMA-free adhesives (less hydrophilic) show less bond strength but same percentage of dentin sealing. In different studies, this results seem to be contradictory.
- Aesthetic these days is very important so marginal discoloration and integrity of the restoration has a crucial role in today's dentistry and for this purpose, the best adhesives still are the 3-steps etch and rinse adhesives.
- New functional molecules like MDP, together with double application of the adhesives seem to help reduce nanoleakage of self-etch adhesives but further studies are needed.
- A lot of articles state that the 3-steps etch and rinse adhesives perform better in terms of retention rate but in the literature results seem to be conflicting.

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- **8. ANNEXES**

- 8.1. Abbreviations

GPDM = glycerol phosphoric acid dimethacrylate

Bis-GMA = bisphenol A-glycidyl methacrylate

GIC = glass ionomer cement

SEM = scanning electron microscope

4-META = 4 methacryloxyethyltrimellitate anhydride

MDP = methacryloyloxydecyl dihydrogen phosphate

HEMA = hydroxyethul methacrylate

D3MA = decandioldimethacrylite

mm = millimeters

μm = micrometers

μ = micron

Oc = occlusal surface

Et = etched dentin

T = tububle

No = normal dentin

MMP = matrix metalloproteinase

NCCL = non-carious cervical lesion

PA = proanthocyanidins

3D = three dimensions

° C = celsius

Ma = milliampere

- 8.2 Figures

-Figure 1. Classification by number of steps (1)

-Figure 2. The areas between the collagen fibrils are filled with water once the etchant has been rinsed (14)

-Figure 3. Etched dentin with 34% orthophosphoric acid for 15 seconds. Oc = occlusal surface; Et = etched dentin with collagen fibers; T = tubule; ND = normal dentin (14)

-Figure 4. Prisma flow chart

- 8.3 Tables

Table 1. Table of results