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Review Article

Current Aspects of Dental Adhesives

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Abstract

Background: Adhesive systems have advanced by leaps and bounds, either the ingredients or the mechanism of action. As a result, the overall operative time reduced greatly. The adhesive systems, as tested, provided acceptable improvements and predictable results. In dental practice, only the most effective measurement is used to ensure acquiring the best outcome. So, variety of the adhesives have not used completely in all dental clinics.

Objectives: The aim of this article is to review the most used adhesive systems from important aspects; As the main components and the detailed process allowing the dentist to choose the best course of actions regarding the case provided.

Methodology: Data Collection was achieved by collecting the related articles between the years 2004 to 2019 that have been published in PubMed indexed journals.

Conclusion: Improved adhesive materials have made resin-based composite restorations more reliable and long lasting.

Keywords: *Adhesive Dentistry; Tooth Substrates; Hybrid Layer; Nanpleakage; Resin Tags*

Introduction

It is clear that the first trials of Buonocore's to achieve bonding to enamel in 1955 [1] and to dentin in 1956 [2] had a great revolutionary effect in adhesive dentistry. The enamel bonding was easier than that of the dentin because of its nature and stable composition. Controversy, dentin is a dynamic and regenerative tissue. Bonding to dentin is more challenging and requires precise and careful techniques. Dentin bonding is a form of tissue engineering, in which mineral is replaced with resin monomers to form a biocomposite comprising dentin collagen and cured resin. The adhesive-dentin interface is expected to form a tight and permanent connection between dentin and composite resins. Dentin bonding can be accomplished with etch-and- rinse (ER) or self-etch (SE) adhesives. The common issue for both is to create a route for adhesive resin infiltration into collagenous matrix. In ER bonding systems this pathway is created with acid, which dissolves the minerals to the depth of 5- 10 μ and leaves the highly porous dentin collagen network suspended in water. Then the collagen network is infiltrated with resin monomers [3]. SE systems contain acidic resin monomers that simultaneously etch and prime the dental substrate [4]. Adhesives contain solvents (water, ethanol, or acetone) to dissolve the monomers, maintain the expanded state of the collagen network, and allow the monomers to fill the spaces within and around the collagen fibrils. Chemical polymerization of

these monomers, activated by the curing light, results in a polymer-collagen biocomposite, commonly called the hybrid layer [3,4]. They give many benefits like reducing chair time, inexpensive application, the required bonding with enamel and dentin. Most importantly, they assure minimum postoperative effects and as much patient comfort as possible [5]. According to dentine bonding systems (DBS), the material containing glutaraldehyde or has an acidic attribute gives an antibacterial effect. However, the antibacterial properties shown by these products appear to be unreliable [6,7]. Inclusion of antibacterial components into DBS has also been attempted using several methods, and the results of *in vitro* tests indicate that some of the trials seem promising [8]. Knowledge about hydrolytic degradation and nano-leakage phenomena is an important contribute to the reduction in the bond strength resulted by overtime-dentine-adhesives.

Obstacles in dentin bonding

To know the problems involved in dentin bonding, we need to provide a brief overview of the dentin structure and composition to understand the complexity of the tissue in relation to the adhesion and adhesive performance. Approximately 50 % by volume of dentin is minerals, the rest being type I collagen and non-collagenous proteins (30 % by vol.) and water (approximately 20 % by vol.) [9]. Inter-tubular dentin contains well-organized mineralized collagenous organic matrix. Dentinal tubules have an inverted-cone shape, narrowing from the dentin-pulp border toward the dentin-enamel junction (DEJ). Each tubule contains highly mineralized peritubular dentin, the amount of which increases toward the DEJ. Therefore, in cavities, the relative tubular and intertubular dentin areas vary depending on the depth and location of the cavity. Since dentin permeability depends on the size and patency of dentinal tubules, regional variations in dentin permeability and intrinsic wetness (due to dentinal fluid) depend strongly on the depth and location of the cavity [10]. These variations in dentin structure and permeability directly affect bonding strength. It is true that higher surface moisture results in lower bond strengths that occurred in deep cavities [3,11-13]. Mineral content, structure and composition of dentin in both caries-affected dentin (CAD) and caries-infected dentin (CID) are different from sound intact dentin. These variation depending on the depth and location of cavity and play a role in bond strength between dentin and adhesive system. Dentinal tubules (DTs) are wide at the dentin-pulp border and gradually narrow toward the dentin-enamel junction, with the increasing amounts of highly mineralized peritubular dentin. As the tubule diameter decreases, the intrinsic wetness and dentinal fluid flow into the bonded surface decrease. Carvalho., *et al*. and Perdigao in their studies revealed that the following variables: EL, enamel lesion; CID, caries-infected dentin; CAD, caries-affected dentin; DT, dentinal tubules play an important role in bond strength. Regarding measuring immediate bond strengths, Comparison among previous variables in superficial and deep dentin clarified that generally 30 - 50% measuring values of deep dentin lower than that occurred in superficial dentin [11,12]. The relationship between morphology and permeability and how they affect adhesion has been thoroughly discussed in some reviews [11,12]. There are lacking studies that compare the bond strength durability between deep and shallow cavities. However, it may be safe to speculate that lower immediate bond strength and increased risk for hydrolytic degradation of hybrid layer increased with time.

Carious and sclerotic dentin and their effect in bonding

Bonding to sclerotic and caries-affected dentin is still a challenge. In general, for both caries-affected and sclerotic dentin, researches have shown that etch-and-rinse adhesives were more effective than self-etch adhesives [14-16]. To increase bond strength of sclerotic and carries-affected dentin, etching time has to be increased as well as the concentration of phosphoric acid in etch-and-rinse technique. Which only possible if over-etching of sound dentin was avoided [12].

Adhesive layer thickness

Through the acid etching technique, enamel and dentin pores are prepared to adhere to the adhesive liquid. Specifically, the inter-prismatic enamel, the dentinal tubules, inter-tubular dentin as well as the peri-tubular dentin. Complete penetration of adhesive liquid into enamel micro-channels and dentinal tubules gives high bond strength values. As fluids are present in dentinal tubules, it is advisable that the hydrophilic interface of the adhesive bond to the dentin to form a thick hybrid layer. There are few strategies should be followed to ensure the achievement of strong bonding. One of them is to use air pressure to forcefully push the liquid of adhesive into the pores for

a few seconds. Another strategy is to make multi-coating of cavity wall to prevent the tearing of adhesive due to viscosity. Some manufacturers recommended using a micro-brush to vigorous rubbing of the adhesive to the cavity. Having a thick adhesive layer is better than a thin one for many reasons. It penetrates all the pores and creates a thick resin layer which limit water permeability and fluids movements. As a result, adhesives with high acetone concentration are susceptible to produce thin bonding layer and more sensitive than water based or ethanol based adhesives [17]. The problem turns out complex with hydrophilic adhesives, e.g. Seventh generation one-step adhesives and universal bond where they produce too thin film [18]. Multi-coats technique is useful in case of self-etch adhesives as the etching efficacy increases with the help of fresh acidic monomers [19]. A few researchers found that the adhesive performance can be improved by adding a hydrophobic resin layer on the top layer but it wasn't appealing as it is more technique sensitive and time consuming [20,21].

Self-etching adhesives and incorporating antibacterial properties

According to *in vitro* researches, microleakge and bacterial penetration have not prevented by the seal of tooth-restoration interface made during the use of self-etching adhesive systems. This will be resulted in secondary caries [22,23]. Hence, the antibacterial effect is essential for adhesives. Studies revealed that the antibacterial effects are related to low pH nature or specific antibacterial molecules like glutaraldehyde or 12- methacryloyloxydodecyl pyridinium bromide (MDPB) [24]. As copolymerization of the adhesive immobilize MDPB, MDPB containing adhesives might be effective against microleakage invading bacteria. "Most of the materials lost their antibacterial properties within 14 days or less: Adper Prompt l- Pop after 24 hours, AdheSe and Xeno III within 48 hours and Clearfil Protect Bond after 14 days". As a chemical reaction, decomposition of the components into the surroundings can occur at varying rates [25,26]. Hypothesizes say that the majority of MDPB molecules copolemerize and a miniscule amount remain unchanged. Those unchanged one are able to manifest antimicrobial properties. Self-etching adhesive material could play a major role in eliminating bacteria or minimizing it at least during tooth preparation. As none of the self-etching adhesive systems that was tested had a long-lasting antibacterial properties, the main cause for the secondary caries which is the bacterial invasion into the microleakage is still not solved [27,28]. However, as the DBS (Dentin bonding system) could inhibit the invading bacteria after placement of restoration and the residual bacteria in the cavity, it is worthwhile the attempts to developing it.

Adhesive systems and their hydrolytic degradation

Dentin wet bonding requires primers or primer/ adhesives to contain hydrophilic and ionic monomers in order to ensure proper hybridization of exposed collagen matrix. 2-Hydroxyethyl methacrylate (HEMA) has many advantages that make it the most commonly used hydrophilic adhesive monomer. HEMA is a small monomer, well solvable in water, ethanol, and/or acetone. It acts as a solvent for hydrophobic monomers; and is relatively biocompatible in polymerized form. Van Landuyt., *et al.* in an extensive review listed 62 commercially available adhesives for investigation. About 48 of these adhesives (77%) were contained HEMA of hydrophilic nature. This study revealed that hydrophilicity is a double-sided sword, as, for example, HEMA absorbs water both in the cured and uncured states, which may inhibit polymerization, reduce mechanical properties, and lead to the hydrolytic degradation of polymerized adhesive [29].

Collagen network and their hydrolytic degradation

Loss of collagen in the hybrid layer has identified many years ago *in vitro* and *in vivo* studies of aged resin-dentin bonds and numerous studies have confirmed time-related loss of collagen in the hybrid layer [30-34]. Human dentin contains several enzymes that together can degrade dentin- collagen-matrix proteins, including type I collagen. These enzymes belong to matrix metalloproteinases (MMPs) or cysteine cathepsins [34]. To date, intact human dentin has been shown to contain MMP-8 (collagenase-2) [35,36], MMP-2 and -9 (gelatinases) [35-42], MMP-3 (stromelysin-1) [43,44], MMP-20 [45,46], cysteine cathepsin B [42,47] and cysteine cathepsin K [42]. Intense gelatinolytic activity is present in dentinal tubules [48,49] and MMP-20 is found in dentinal fluid [50]. The physiological roles of these enzymes in dentin still unknown, but they have been suggested to participate in peritubular and tertiary dentin formation. They also participate in the release of dentinal growth factors during caries which in turn would regulate pulp defensive reactions [34,51-55]. Both MMPs and cysteine cathepsins have also been indicated to participate in dentinal caries pathogenesis [42,56-62]. MMP-2, -9, and -8 are present in

carious dentin [39,46,53,57] and their activation in pH fluctuations relevant to caries lesions. The role of MMPs in the degradation of dentin collagen have been demonstrated [57,59]. The acidity of the ER [63] and SE [64] adhesives also activates dentinal enzymes. Cysteine cathepsins have also been identified in carious dentin [42,62]. It is important to note that cathepsin K and B, MMP-2 and -9 dramatically increased in caries-affected dentin compared to sound intact dentin [42]. Several MMPs are increasing in dentinal tubules of carious teeth [50,60,65]. As shown in studies, MMP inhibitors negate humane salivary MMP effects [59,66] as well as decreasing caries progression rate in dentin [59,64,66].

Effect of over-drying and over-wetting

Some dental practitioners preferred to over-dry the enamel surface until frosted enamel appearance would observed as that was believed to be a good etching. Studies showed that the adverse effects of over-drying on enamel was less than that occurred in dentine [17]. It is very difficult to make over-dry of enamel without over-dry the dentin substrate. Over-drying the dentin surface can result in collagen network collapse and the evaporation of fluids inside the dentinal tubules then bond strength is strong decreased. On the other hand, over-wetting may lead to over-wet phenomenon that give manifestation of water globule and blister formation that resulted in dilution of liquid of adhesives. It is highly noted to balance the draying and wetting of the tooth surface after the acid etch procedure and before applying the adhesive. In case of using etch and rinse technique, the dentist should choose the adhesive carefully according to the type of adhesive solvent and depending on the case provided; For water-ethanol type of adhesives, dentin surface should be prepared with gentle dry because the water of the solvent will re-wet the slightly dried dentin surface. Scotchbond Multipurpose and Optibond FL are instances of adhesive containing hydrophilic primer that are more tolerant to excessive drying and can re-hydrate the dried dentin collapsed collagen network [67]. On the other hand, if the adhesive solvent was acetone based, tooth surface should be prepared wet and moist. If the tooth was over-dried, the adhesive will lose 66% of its efficiency and give only 33% of the required results. the mechanism of action of acetone based adhesive is to infiltrate and take place of the water in the dentinal tubules then evaporate leaving the required space for the adhesive component to settle. If there is no water because of the excessive drying, there will be no infiltration to the full depth of dentinal tubules as well as the collapsed collagen network. The technique of acetone based adhesives is called "Wet Bonding Technique". As the self-etch require no separate etching, rinsing and drying steps, they are not affected by excessive drying or wetting [67,68].

Adhesive types that working in moisture and contaminated field

Recently, manufacturers attempted to develop the bonding systems in the presence of moisture by using noble metals [69]. It is known that adhesives performance decreases greatly when exposed to excessive moisture and loses the bond strength [70]. The detrimental effect of moisture on bonding may relate to water adsorption and exertion of a plasticizing effect in the polymer network from the creation of hydrated zones at polar monomer sites, and oxidation of pendant C=C bonds attached to the network which release by-products such as formaldehyde, so producing a plasticizing effect [71]. Some researchers believed that moisture-insensitive products perform well in a wet condition whereas others introduced moisture-active adhesives (MAD). The former type of product, which may be termed a moisture resistant adhesive, is available in a primer formulation that replaces the conventional bonding agents applied to the enamel surface and consists of an aqueous solution of methacrylate functionalized polyalkenoic acid co-polymer and hydroxyethyl-methacrylate. In contrast to the moisture-insensitive primer (MIP), MAD require rather than tolerate the presence of moisture to induce polymerization initiation. The moisture active adhesive represents a distinct material available as a cyanoacrylate-based paste formulation, applied to intentionally-wetted etched enamel without the use of a primer [72]. "Transbond™ MIP is a hydrophilic or "moisture friendly" material that allows to bond in a moist environment without compromising bond strength". After etching the tooth surface, using a single coat of Transbond primer will still give an acceptable result. As for Transbond™ XT light cure adhesive, laboratory tests proved that it will give a similar bond strength whether the surface is dry or saliva-contaminated. On the other hand, Smartbond TM is an adhesive filled with particles based on cyanoacrylate chemistry. It is single-phase with two main steps. Firstly, the isocyanate group react with water, making unstable carbamic acid. It will decompose to carbon dioxide and amine quickly. Secondly, the amine with residual unreacted isocyanate groups, substituting urea groups and cross-linking the adhesive.

Bio-modification of dental adhesive system

Since the pulpal cells cannot remodel or repair lost dental tissue, current restorative therapy aims to replace decayed tissue to restore tooth morphology and function. However, development of biomodification strategies, such as increased collagen crosslinking and biomimetic remineralization, to improve the tissue properties and stability by chemically modifying the tissue offer an interesting approach for adhesive dentistry [73-76].

Use of Cross-linkers

The intermolecular and inter-micro-fibrillar crosslinking is the basis for the stability, strength, and viscoelasticity of dentin collagen matrix. The quantity and type of cross-linking also determines collagen thermal stability and ability to resist biodegradation. Increasing cross-linking of the exposed dentin collagen aims to improve hybrid layer matrix stability [75,76] and may also offer a means by which to increase the use of more hydrophobic adhesives without the risk of collagen matrix collapse during adhesive application. Studies of cross-linkers have primarily focused on their ability to enhance the mechanical properties of demineralized dentin [76]. In addition to stiffening, cross-linking can also affect enzymatic degradation by allosteric silencing of collagenolytic enzymes or by altering the enzyme-binding site in the collagen molecule [75-80]. The cross-linkers tested include synthetic cross-linkers such as carbodiimide and glutaraldehyde, physical (photo-oxidative) crosslinking with riboflavin, and naturally occurring compounds such as genipin and proanthocyanidins [76]. Glutaraldehyde is a widely known cross-linker that has been used in dental products, but its cytotoxicity seriously limits its clinical use [73,76]. Carbodiimide hydrochloride has very low cytotoxicity but may have limited cross-linking capacity [76]. It was demonstrated to eliminate collagen degradation and preserve bond strength *in vitro* even though the time needed for the effect may be still too long for clinical practice [6,73,81]. Dentin treatment with its effective in inhibiting dentinal MMP activity alone or mixed with HEMA, which indicates that it could be added to adhesive primers [80]. Proanthocyanidins are also effective [82,83]. An increase in immediate dentin bond strength may be achievable even with shorter treatment times [84,85], and improved durability of long-term bond strength has also been indicated [86,87]. Riboflavin has also been successfully tested, but the need for ultraviolet light or separate cross-linker light curing (88,89) reduces its clinical acceptability. Biomimetic Remineralization or Biological mineralization of all hard tissues is a progressive dehydration process; with the increasing mineral content, the water content of the collagen matrix decreases correspondingly to maintain a constant volume [74,75]. In dentin bonding, resin adhesive is incapable of dehydrating the collagen matrix sufficiently [3,90-92], leaving behind water that will allow hydrolysis of the hybrid layer components. Biomimetic remineralization mimics the progressive dehydration of natural bio-mineralization by replacing matrix water with apatite crystallites [74]. In the hybrid layer, replacing water with minerals would increase mechanical properties and inhibit water-related hydrolysis. In biomimetic remineralization of the hybrid layer, polyanions (e.g. polyacrylic acid or polyaspartic acid) bind to collagen and serve as analogs of dentin phosphor-proteins that regulate physiological mineralization, allowing calcium binding and promoting apatite nucleation. The hybrid layer is covered with a ''therapeutic'' composite containing amorphous calcium phosphate as a source for apatite. *In vitro* studies indicate that biomimetic remineralization has great potential for demineralizing hybrid layers or caries-like dentin [74]. These studies have also demonstrated the preservation of the mechanical properties of the hybrid layer [93] and bond strength [94] with time. Even if biomimetic remineralization strategy has great potential- and should perhaps be the ultimate goal of research-in preventing the loss of hybrid layer integrity, it must be realized that to date the strategy is still at the proof-of-concept stage. Development of clinically applicable materials that would contain and release the critical components of the process (at least calcium and phosphate source and biomimetic analogs) involves considerable challenges [73-75].

Hydrophilic adhesives reduction

In attempts to reduce the hydrolytic degradation of adhesive, less hydrophilic HEMA-free adhesives have been created [20]. However, the solvation effect of HEMA is also lost. When other solvents, such as acetone or ethanol, evaporate, water tends to separate adhesive components, making these adhesives prone to phase separation [95,96]. The resulting water blisters may lower the immediate bond strength. The studies examining the durability of bond strength with HEMA-free adhesives are limited and the results are conflicting, but

generally, loss of bond strength seems to occur [97-99]. Extended evaporation (air drying) of the adhesive layer may reduce the blister formation [97,98,100].

Limited shelf life and solvent evaporation effects

Many experiments were done to store monomers of different chemical build and nature, like being hydrophilic or hydrophobic, together in one bottle. The containments of the bottle can change through time. "Adhesive shelf life refers to the period in which adhesive remain performed effective optimum bond". The limited shelf life of the seventh generation adhesives (one-step self-etch) might be the result of the hydrolysis of its components [101]. The main cause for adhesives short shelf life is the evaporation of the volatile solvent after using the adhesive. It results in losing more than 50 % of its full bond strength. Continuous opening and repetitive use of the adhesive cause the extremely volatile acetone to evaporate which in turn increase the viscosity of the adhesive making it unable to penetrate the tooth tissues pores [102]. Pongprueksa., *et al.* reported a complete impairment of bond strength in which the ethanol solvent evaporation was more than 50%. That might be why it is preferable to use uni-dose package adhesive [103].

Conclusion

1. The techniques and materials that allow the use of hydrophobic adhesives offer another attractive alternative, but this approach may require new monomers with different chemistry. Combining cross-linkers with ethanol-wet bonding, DMSO, or a corresponding agent may offer an easier approach.
2. Dental adhesive systems which give good results even under unfavorable clinical conditions are more reliable. Comprehending each adhesive strong and weak points and employing meticulous techniques are fundamental for successful resin composite restoration.
3. The overall clinical success of composite restorations is multifactorial and therefore is unlikely to be predicted by even a battery of *in vitro* test methods. Only limited evidence exists to correlate marginal quality and bond strength in the laboratory with the clinical performance of bonded dental composites.
4. Improved adhesive materials have made resin composite restoration more preferable and durable.

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