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**RESISTÊNCIA DE UNIÃO DE SISTEMAS ADESIVOS UNIVERSAIS E
CONTEMPORÂNEOS EM DENTES DECÍDUOS: REVISÃO SISTEMÁTICA E
META-ANÁLISE EM REDE**

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia da Universidade Federal do Rio Grande do Sul como requisito parcial para a obtenção do título de Mestre em Odontologia, Área de Concentração em Clínica Odontológica/Odontopediatria.

Linha de Pesquisa: Biomateriais e Técnicas Terapêuticas em Odontologia

Orientadora: Prof^a. Dr^a. Tathiane Larissa Lenzi.

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RESUMO

O objetivo do presente estudo foi revisar sistematicamente a literatura para comparar a resistência de união de sistemas adesivos universais, em ambas as estratégias de aplicação, com sistemas adesivos convencionais (*etch-and-rinse*) e autocondicionantes (*self-etch*) em dentes decíduos. Uma ampla busca foi realizada nas bases de dados PubMed/MEDLINE, Scopus, LILACS, Embase e Web of Science, sem limite de ano de publicação ou idioma, a fim de identificar estudos *in vitro* relacionados com a questão de pesquisa. Dois revisores, de maneira independente, selecionaram os estudos, extraíram os dados e avaliaram o risco de viés. Comparações diretas entre adesivo universal nos modos convencional e autocondicionante e sistemas adesivos convencionais e autocondicionantes foram realizadas considerando diferentes substratos (esmalte e dentina hígidos e dentina cariada) por meio de meta-análises de efeitos aleatórios. Meta-análise em rede também foi realizada para comparar os valores de resistência de união de todas as estratégias adesivas em dentina hígida. Dos 3,276 estudos potencialmente elegíveis, 18 foram selecionados para leitura completa e 8 foram incluídos na revisão sistemática. Todos os estudos incluídos nas meta-análises avaliaram um sistema adesivo universal suave contendo 10-MDP (Single Bond Universal, 3M ESPE). Nas comparações diretas, não houve diferença entre o sistema adesivo universal no modo autocondicionante e adesivos autocondicionantes ao esmalte hígido (Diferença média (DM) = 5,22 95% Intervalo de Confiança (IC) -9,09; 19,52). Em dentina hígida, os valores de resistência de união do sistema adesivo universal no modo convencional foram superiores aos dos sistemas convencionais (DM = 5,50 95% IC 4,03; 6,96). Em dentina cariada, os resultados favoreceram os adesivos convencionais em relação ao sistema adesivo universal no modo autocondicionante (DM = -3,88 95% IC -7,40; -0,37). A probabilidade de ranqueamento mostrou que a melhor estratégia adesiva em dentina hígida foi sistema adesivo universal no modo convencional. A maioria dos estudos foi classificada como risco de viés médio. Os achados laboratoriais sugerem que sistema adesivo universal suave contendo 10-MDP pode substituir os adesivos convencionais e autocondicionantes para restaurar dentes decíduos.

Palavras-chave: Adesivos Dentinários; Dente Decíduo; Resistência à Tração; Metanálise em Rede

ABSTRACT

The purpose of the present study was to systematically review the literature to compare the bond strength of universal adhesives, in both application strategies, with etch-and-rinse and self-etch adhesive systems to primary teeth. A broad search was carried out in PubMed/MEDLINE, Scopus, LILACS, Embase, and Web of Science databases with no restrictions of publication year and language. Two reviewers independently selected the studies, extracted the data, and assessed the risk of bias. Direct comparisons among universal adhesive in etch-and-rinse and self-etch modes and etch-and-rinse and self-etch adhesive systems were performed considering different substrates (sound enamel and dentin, and carious dentin) through meta-analyses of random effects. A network meta-analysis was also performed to compare the bond strength of all adhesive approaches in sound dentin. From 3,276 potentially eligible studies, 18 were selected for full-text analysis, and 8 were included in the systematic review. All studies included in the meta-analyses evaluated a mild universal adhesive containing 10-MDP (Scotchbond Universal, 3M ESPE). In the direct comparisons, there was no difference between universal adhesive in the self-etch mode and self-etch adhesives to sound enamel (Mean difference (MD) = 5.22 95% Confidence Interval (CI) 9.09;19.52). In sound dentin, the bond strength values of the universal adhesive in the etch-and-rinse mode were higher than etch-and-rinse systems (MD 5.50 95% CI 4.03; 6.96). In carious dentin, the results favored the etch-and-rinse adhesive over universal adhesive in the self-etch mode (MD -3.88 95% CI -7.40;-0.37). The ranking probability showed that the best adhesive strategy in sound dentin was the universal adhesive system in the etch-and-rinse mode. Most studies were classified as medium risk of bias. Laboratory findings suggest that that a mild universal adhesive system containing 10-MDP can substitute the etch-and-rinse and self-etch adhesives for restoring primary teeth.

Keywords: Dentin-Bonding Agents; Tooth, Deciduous; Tensile Strength; Network Meta-Analysis

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1 INTRODUÇÃO

A adesão em Odontologia foi inicialmente vislumbrada por Michael Buonocore com a introdução do condicionamento ácido (VAN MEERBEEK *et al.*, 2003), o que impulsionou o desenvolvimento de materiais e técnicas capazes de favorecer a íntima interação com os substratos dentários. Com isso, preparamos cavitários tradicionais, com formas de retenção, contorno e conveniência, foram substituídos por “preparos adesivos”, mais biológicos por priorizar a realização de remoção seletiva de tecido cariado (SCHWENDICKE *et al.*, 2016), possibilitando a preservação do tecido dentário e manutenção da vitalidade pulpar.

Os sistemas adesivos disponíveis comercialmente tem sido classificados em gerações, número de passos operatórios ou de acordo com a estratégia adesiva. Esta última, de forma simplista, permite agrupar os materiais em duas categorias: *etch-and-rinse* (condicione e lave) ou convencionais e *self-etch* ou autocondicionantes. Na primeira, o ácido fosfórico é aplicado sobre esmalte e dentina, seguido de abundante lavagem e remoção da umidade excessiva antes da aplicação de primer e adesivo, que podem estar apresentados em dois frascos ou em apenas um. Na estratégia autocondicionante, a aplicação prévia do ácido fosfórico não é necessária, sendo os sistemas apresentados em dois frascos (um primer/ácido mais um adesivo) ou em único frasco (uma só solução com as funções de ácido, primer e adesivo) (VAN LANDUYT *et al.*, 2007). Existem ainda aqueles, mais recentes, que permitem serem empregados em qualquer uma das formas explicitadas anteriormente e que recebem a denominação de sistemas universais ou multi-modo (NAGARKAR *et al.*, 2019).

Procedimentos restauradores com técnica simplificada e rapidez sempre foram objeto de interesse da Odontopediatria e não seria diferente com os sistemas adesivos autocondicionantes, que permitem de forma simultânea a desmineralização e a infiltração e impregnação do substrato (VAN MEERBEEK *et al.*, 2011). Das primeiras gerações de sistemas adesivos autocondicionantes para as de hoje, houveram mudanças significativas no que se refere a sua composição, sendo que duas se destacam. O pH dos adesivos autocondicionantes ficou em geral mais ameno/suave (acima de 2,0-2,5) fazendo com que a interação com a dentina fosse menos agressiva. Com isso, não há remoção de toda lama dentinária (*smear layer*) da embocadura dos túbulos dentinários e remove-se menos mineral da dentina, expondo, assim, menos fibras colágenas. Monômeros funcionais capazes de se unir quimicamente ao cálcio (como o monômero

10-MDP) foram incorporados ao adesivo, o que se acredita que possam promover uma maior estabilidade da união à dentina com o passar do tempo (VAN MEERBEEK *et al.*, 2011).

A adesão em dentes decíduos, no entanto, é influenciada de forma intensa pelas características que os diferem dos dentes permanentes. Dentes decíduos apresentam o esmalte em menor espessura (DE MENEZES *et al.*, 2010), com camada aprismática mais espessa e uniforme (FAVA *et al.*, 1997) e maior densidade dos prismas (DE MENEZES *et al.*, 2010) que dentes permanentes. Além disso, apresentam menor conteúdo mineral, com concentrações inferiores de cálcio e fosfato (DE MENEZES *et al.*, 2010) quando comparados aos dentes permanentes. Estas características podem influenciar as propriedades mecânicas do esmalte de dentes decíduos, mas ainda assim não interferem de maneira significativa no seu comportamento como um substrato distinto para a adesão.

A dentina de dentes decíduos apresenta menor conteúdo mineral (ANGKER *et al.*, 2004) e maior concentração de carbonato (SØNNU CLASEN *et al.*, 1997) quando comparada à dentina de dentes permanentes. A maior densidade tubular da dentina de dentes decíduos (LENZI *et al.*, 2013) resulta em menor área de dentina intertubular disponível para adesão, além de promover vias de difusão mais rápidas e fáceis para o agente condicionador (SELVIG, 1968).

Todas essas características conferem a esse substrato maior solubilidade e menor capacidade de tamponamento e, como consequência, maior reatividade a soluções acídicas, resultando em zonas de desmineralização mais profundas quando a dentina decídua é condicionada pelo tempo recomendado para dentes permanentes (NOR *et al.*, 1996). Quanto maior a profundidade de desmineralização da dentina, menor a capacidade de difusão e impregnação dos monômeros, resultando em camadas híbridas mais espessas (LENZI *et al.*, 2013) e com fibrilas colágenas expostas total ou parcialmente (LENZI *et al.*, 2013). Com isso, a degradação da união tende a ser percebida, em avaliações laboratoriais, mais precocemente em dentes decíduos (LENZI *et al.*, 2012).

Uma revisão sistemática de estudos laboratoriais verificou similar desempenho, em termos de resistência de união, entre sistemas adesivos convencionais e autocondicionantes em dentina hígida e cariada de dentes decíduos (LENZI *et al.*, 2016). Por outro lado, os sistemas adesivos convencionais apresentaram desempenho superior em esmalte decíduo.

Sistemas adesivos universais com pH suave e com monômeros funcionais como o 10-MDP tem apresentado bons resultados na adesão à dentina de dentes permanentes (CUEVAS-SUÁREZ *et al.*, 2019). A ausência do passo de condicionamento com ácido fosfórico parece simplificar a técnica, prover mineral na superfície dentinária para reagir com o 10-MDP e levar a menor exposição de colágeno. Porém, o pH suave leva a um padrão menos favorável de interação com o esmalte, sendo sugerido o condicionamento seletivo do esmalte para restaurações em dentes permanentes (CUEVAS-SUÁREZ *et al.*, 2019).

Uma recente revisão sistemática de estudos laboratoriais mostrou que os sistemas adesivos universais também podem ser usados em ambas as estratégias de aplicação em dentina de dentes decíduos. No entanto, ainda há dúvidas quanto à necessidade de condicionamento seletivo de esmalte decíduo (FRÖHLICH *et al.*, 2021). Além disso, nenhuma revisão sistemática comparou o desempenho de sistemas adesivos universais, em ambas as estratégias de aplicação, com os sistemas adesivos convencionais e autocondicionantes. A compilação dos dados laboratoriais pode fornecer conclusões mais sólidas e elucidar se os adesivos universais podem substituir os sistemas adesivos contemporâneos para restaurar dentes decíduos.

Sendo assim, a presente dissertação tem como objetivo comparar os valores de resistência de união de sistemas adesivos universais, em ambas estratégias de aplicação, com sistemas convencionais e autocondicionantes em dentes decíduos.

2 ARTIGO CIENTÍFICO

Bonding Performance of Universal and Contemporary Adhesives in Primary Teeth: A Systematic Review and Network Meta-Analysis of In Vitro Studies

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Abstract

Purpose: To systematically review the literature to compare the bond strength of universal adhesives with etch-and-rinse and self-etch systems to primary teeth.

Methods: The search was carried out in PubMed/MEDLINE, Scopus, LILACS, Embase, and Web Of Science databases with no restrictions. Two reviewers independently selected the studies, extracted the data, and assessed the risk of bias. Direct comparisons among universal adhesive in etch-and-rinse (UER) and self-etch (USE) modes and etch-and-rinse (ER) and self-etch (SE) systems were performed considering different substrates (sound enamel and dentin, and carious dentin) through meta-analyses of random effects. A mixed treatment comparisons meta-analysis was also performed comparing the bond strength of all adhesive approaches on sound dentin. **Results:** From 3,276 potentially eligible studies, 18 were selected for full-text analysis, and eight were included in the systematic review. All studies included in the meta-analyses evaluated the same universal adhesive (Scotchbond Universal). In direct comparisons, there was no difference between USE and SE to sound enamel (DM equals 5.22; 95 percent confidence interval [95% CI] equals -9.09 to 19.52). In carious dentin, the results favored only ER over USE (DM equals -3.88; 95% CI equals -7.40 to -0.37). In sound dentin, the bond strength values of UER were higher than ER (DM equals 5.50; 95% CI equals 4.03 to 6.96). The rank probability showed that the best treatment on sound dentin was UER. **Conclusion:** Pooled in vitro data suggest that a mild 10-MDP-based universal adhesive system can substitute the etch-and-rinse and self-etch adhesives for restoring primary teeth.

KEYWORDS: PRIMARY TOOTH; DECIDUOUS; ADHESIVES; SYSTEMATIC REVIEW

Introduction

Adhesive systems can be classified according to their bonding strategy to dental substrates into etch-and-rinse or self-etch adhesives.^{1,2} The etch-and-rinse strategy involves the prior application of phosphoric acid, being available for use in three steps (acid etching, primer, and adhesive) or two steps (primer and adhesive joined into one single material).² Self-etch systems contain monomers with acidic functional groups that simultaneously etch and prime tooth substrate.¹ Self-etch adhesives can involve two steps or a single step, depending on how the acidic primer and adhesive resin are provided by the manufacturers.¹ A previous systematic review³ showed that an adequate bonding to dentin of primary teeth could be achieved with either etch-and-rinse or self-etch adhesives. Etch- and-rinse adhesive systems, however, performed better in enamel, being the preferred choice for restoring primary teeth. The main challenge for current dental adhesives is to provide similar bonding effectiveness to dental substrates of different natures (i.e., sound, carious dentin and enamel).¹

Considering the differences in professional judgment regarding the selection of the adhesive strategy and the number of steps, “universal” or “multi-mode” adhesive systems have been introduced for use in any bonding strategy: etch-and-rinse; self-etch; or selective enamel-etch⁴. They are essentially one-step self-etch adhesives that may be associated with phosphoric acid etching, depending on the specific clinical situation and the operators’ preferences.⁴ The in vitro evidence suggests that the bonding performance of universal adhesives depends on their pH. Mild universal adhesives provide better resin-dentin bond stability in both etch-and-rinse and self-etch strategies. On the other hand, the bond strength of mild universal adhesives to enamel can be improved by using acid etching.⁵ These findings; however, are focused on permanent teeth and cannot be directly extrapolated to primary teeth. Primary and permanent teeth present differences in microstructure⁶ and composition,⁷ which may interfere in the adhesive performance. Furthermore, a systematic quantitative evaluation comparing the bonding effectiveness of universal, etch-and-rinse, and self-etch adhesive systems has never been undertaken. Pooled in vitro data could provide more solid conclusions on which adhesive strategy to use for restoring primary teeth.

Therefore, the purpose of this systematic review and mixed treatment comparison meta-analysis was to address if universal adhesives are the best option to restoring primary teeth by comparing the bond strength of universal adhesive systems to dental substrates, in both strategies, with etch-and-rinse and self-etch adhesives.

Methods

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Statement for Network Meta-analysis (PRISMA-NMA).⁸

Search strategy and selection criteria

A comprehensive literature search was undertaken using PubMed/MEDLINE, Scopus, LILACS, Embase, and Web Of Science databases to identify studies related to the research question and published up to November 2020. The search was conducted with no publication year or language restrictions. The subject search used a combination of controlled vocabulary and free text terms based on the search strategy for the PubMed/MEDLINE database as follows:

(((((((((Universal adhesive*) OR Multi-mode adhesive*) OR Multimode adhesive*) OR One-step adhesive*) OR Multi-mode bond*) OR Multimode bond*) OR Universal bond*)) AND (((((((Adhesives[MeSH Terms]) OR Adhesive*) OR Total-etch*) OR Etch-and-rinse adhesive*) OR Conventional adhesive*) OR Self-etch*) OR One-bottle adhesive*) OR All-in-one adhesive*)) AND (((((((((Bond strength) OR Degradation bond strength) OR Bond*) OR Longevity) OR Durability) OR Tensile strength[MeSH Terms]) OR Tensile) OR Microtensile) OR Microshear) OR Shear).

The search strategy was adapted for the Scopus, LILACS, Embase, and Web Of Science databases (see Supplemental Electronic Data-sTable 1). Also, the references of all identified articles were manually searched for further relevant studies. The results of searches of various databases were cross-checked in order to locate and eliminate duplicates.

The reviewers were previously trained and calibrated for study selection with lectures about systematic review steps and features of the databases. Initially, two reviewers screened titles and abstracts independently and selected articles based on the inclusion criterion: in vitro studies that evaluated the bonding of any universal adhesive system in primary teeth. The interexaminer agreement calculation (Kappa equals 1.00) indicated excellent agreement.

Full-text articles of studies selected in the previous step were retrieved and independently reviewed by two authors following the exclusion criteria: Articles that, (1) did not compare the performance of the universal adhesive with etch-and-rinse

and/or self-etch adhesive system; (2) did not evaluate the bond strength to dentin and/or enamel; (3) did not use human primary teeth; (4) did not evaluate immediate or aged bond strength data; and (5) used any etch-and-rinse or self-etch system outside the strategy proposed by the manufacturers. The calculation of interexaminer agreement (Kappa equals 0.95) indicated excellent agreement.

Any disagreement in either step was solved by a discussion between the reviewers. If discrepancies remained, a third author was consulted. When the same bond strength data were reported in different studies, the study with more complete data was considered.

Data extraction

Two authors independently collected the data of the eligible studies. For each study, the following data were systematically extracted: publication details (title, authors, and year), methodology (sample size, dental substrate type [enamel/dentin] and nature [sound/carious], adhesive area, commercial brands and manufacturers of the adhesives, water storage time, and type of bond strength test) and outcome information (bond strength means [MPa] and standard deviations).

Assessment of risk of bias

The reviewers also independently assessed the risk of bias based on the following criteria: teeth randomization; sample size calculation; materials used according to manufacturers' instructions; adhesive procedures performed by a single operator; and blinding of the operator of the testing machine. If the authors reported the parameter, the publication had a yes on that specific parameter; if it was not possible to find the information, the study received a no. Studies that reported one or two items were classified as high risk of bias, studies that reported three or four items were classified as medium risk, and studies with five items were considered low risk. For the final classification of risk of bias, disagreements between the reviewers were resolved by consensus.

Data synthesis

Direct comparisons among universal adhesives in the etch-and-rinse and self-etch modes and for etch-and-rinse and self-etch systems were computed considering different substrates (sound enamel and dentin and carious dentin) through meta-analyses of random effects. In addition, network meta-analyses were conducted when more than two treatments were evaluated, thus allowing direct and indirect comparisons between treatments. To simultaneously consider both direct and indirect evidence, a Bayesian

analysis of mixed treatment comparisons (MTC) was conducted. All treatment alternatives were performed on similar groups of specimens, meeting the assumption of transitivity of this network analysis.

First, MTC analyses using both fixed and random models were computed, and the goodness of fit of the models was measured using the residual deviation and the residue information criterion (DIC). The random-effects model with homogeneous variability between studies was chosen for final MTC analysis. A node split analysis for inconsistency was performed for the pairs with both direct and indirect evidence. Meta-analyses and network meta-analyses were conducted using the R packages “GeMTC” and “meta” 3.6.1 software (R Core Team, Vienna, Austria). For each included study, the mean difference (MD) and 95 percent confidence intervals (CI) were calculated.

Results

Study selection

The search strategy identified 3,276 potentially relevant studies, removing duplicates. After screening the titles and abstracts, 18 studies were assessed for more detailed information and 10 studies were excluded after review of the full-text articles. Finally, eight laboratory studies met the eligibility criteria and were included in the systematic review. Figure 1 presents a flowchart of the study selection process and the reasons for exclusions.

Study characteristics

Table 1 shows descriptive extracted data from the included studies in the systematic review that were published in English and reported between 2016 and 2020. Publications were conducted in Brazil,⁹⁻¹² Iran,¹³ Portugal,¹⁴ Republic of Korea,¹⁵ and Thailand.¹⁶ Most studies evaluated the adhesive effectiveness on sound dental substrates. Six^{10,12-16} studies evaluated the bond strength to sound dentin, while two^{9,12} studies tested the adhesive performance to the enamel of primary teeth. Only three⁹⁻¹¹ used carious dental substrates. All included studies reported immediate bond strength data. Microshear,^{9,12,16} microtensile,^{10,11,14,15} and shear¹³ tests were used. Regarding sample size, the number ranged from six to 12 teeth per group.

Scotchbond Universal (3M ESPE, St. Paul, Minn., USA) was the universal adhesive most tested, except in only one study¹⁴ that evaluated the performance of the Futurabond (VOCO GmbH, Cuxhaven, Germany). Adper Single Bond 2 (3M ESPE) and Clearfil SE Bond (Kuraray Noritake, Osaka, Japan) were the etch-and-rinse and

self-etch adhesives, respectively, commonly tested. The main components and manufacturers' instructions of the adhesive systems included were summarized in the Supplemental Electronic Data-s Table 2.

Risk of bias of the included studies

Of the eight included studies, four^{10,11,14,16} were classified with medium risk, two^{14,16} were classified as high risk, and the other two^{9,12} were classified as having a low risk of bias (Table 2). The items that most frequently received "no" were sample size calculation and blinding of the operator of the testing machine. All studies performed teeth randomization and the materials were used according to manufacturers' instructions.

Meta-analyses results

Sound enamel

For the direct comparison between universal adhesive in the self-etch mode (USE) and self-etch adhesive systems (SE), two^{9,12} selected articles were grouped and showed no difference in the bond strength values. The heterogeneity was considered high (I^2 equals 96 percent; Figure 2).

Carious dentin

For the direct comparisons between USE and universal adhesive in the etch-and-rinse mode (UER), USE and SE, UER and etch-and-rinse adhesive systems (ER), UER and SE, and ER and SE, two^{10,11} included articles were grouped and showed no difference in the bond strength values. There was no heterogeneity (I^2 equals zero percent). Regarding the direct comparison between USE and ER, a favorable difference in the use of ER was found (MD equals -3.88; 95 percent confidence interval equals -7.40 to -0.37 percent), also without heterogeneity (I^2 equals zero percent; Figure 3).

Sound dentin

Almost all direct comparisons (USE and UER, USE and SE, UER and SE, SE and ER, USE and ER) showed similar bond strength values. Heterogeneity ranged from I^2 equals 69 percent to I^2 equals 96 percent. Only in the direct comparison between ER and UER, a favorable difference in the use of UER (MD equals 5.50; 95 percent confidence interval equals 4.03 to 6.96) was found (I^2 equals zero percent).

Six^{10,12-16} studies presented more than two arms; thus, they were included in the network meta-analysis. The rank probability showed that the best treatment was UER (Figure 4). Node split analysis showed no inconsistency of the network model. Table 3

shows the contribution of MTC analysis for the pairs of direct comparisons. It can be observed that the difference between bond strength of ER and UER found in the direct evidence lost significance in the MTC analysis (MD equals 5.20 95 percent confidence interval equals -3.90; 15.00).

Means of bond strength and standard deviations of the adhesive systems tested in the included studies are available in the Supplemental Electronic Data-sTable 3.

Discussion

Considering the great number of commercially available adhesive systems, the choice of bonding strategy and number of steps has been often a matter of personal preference. Based on that, manufacturers have released more versatile adhesive systems, so-called “universal” or “multi-mode” adhesives, that include etch-and-rinse and self-etch options, aiming to make the clinical procedures user-friendlier.

Although clinical trials provide greater scientific evidence and laboratory bond strength testing cannot predict the clinical effectiveness of dental materials,¹⁷ in vitro studies are essential to determine the potential for clinical applicability. This is the first systematic review and meta-analysis that analyzed the pooled effect of data from in vitro studies comparing the bond strength of universal adhesives with etch-and-rinse and self-etch systems to primary teeth.

It is important to highlight that a limited number of adhesive systems were tested in the included studies. Adper Single Bond 2 and Clearfil SE Bond were the etch-and-rinse and self-etch adhesives, respectively, frequently evaluated. Scotchbond Universal was the universal adhesive most tested, except in only one study¹⁴ that evaluated the performance of the Futurabond. Thus, this study was not included in the analyses.

Meta-analyses of direct comparisons among universal adhesive in the etch-and-rinse and self-etch modes and among etch-and-rinse and self-etch systems were performed considering different substrates. For enamel, only the comparison between universal adhesives in self-etch mode and self-etch adhesives could be made. There was no difference in the bond strength between them. After analyzing the single study⁹ included in this review that evaluated the influence of the etching strategy of universal adhesive to primary enamel, it was possible to note that etch-and-rinse mode improved bond strength. Similarly, a systematic review⁵ found that universal adhesives performed better in permanent enamel when applied after acid etching.

Since enamel bonding is mainly based on micromechanical interlocking of a

low-viscosity resin into microporosities, the extent and depth of the etching pattern depend on the acidity of the conditioner. Self-etch adhesives tested as well as Scotchbond Universal have a low acidity (mild pH; Supplemental Electronic Data-Table 2), and consequently, a reduced ability to demineralize even primary enamel that presents lower mineral content¹⁸ compared to permanent teeth.

For carious dentin, the bonding of the universal adhesive was not influenced by the etching strategy. There was only a significant difference in the bond strength values between universal adhesive in self-etch mode and etch-and-rinse adhesives, favoring the latter. However, only two studies^{10,11} were included in the analysis, and the results are focused on immediate bond strength evaluation. Only one study¹⁰ included in this review evaluated the influence of the etching strategy on the immediate and one-year bond strength of universal adhesive to sound and carious dentin of primary teeth. There was no difference between universal adhesive, in both etching strategies, with etch-and-rinse and self-etch adhesives on carious dentin. Moreover, the bond strength of universal adhesive remained stable over time, in both etching modes, showing better results than etch-and-rinse and self-etch systems.

For sound dentin, the etching strategy did not influence the bond strength of universal adhesive. Similar bond strength was found comparing universal adhesive in self-etch mode with self-etch and etch-and-rinse adhesives. Moreover, there was no difference in bonding between universal adhesive in etch-and-rinse mode and self-etch adhesive systems. Conversely, the bond strength of universal adhesive in etch-and-rinse mode was higher than for etch-and-rinse adhesive systems. This significance, however, was lost in MTC analysis. The rank probability, based on immediate bond strength data, showed that the universal adhesive in etch-and-rinse mode was the best approach on sound dentin.

A recent systematic review⁵ reported that the long-term bonding performance of universal adhesives on permanent teeth depends on their pH. Overall, mild universal adhesives are most stable compared to intermediately strong and ultra-mild universal adhesives,⁵ irrespective of the etching approach. The dentin is partially demineralized when mild-self-etch adhesives are used, leaving a substantial amount of hydroxyapatite crystals around the collagen fibrils.¹ Therefore, self-etch adhesives could interact with dentin in two ways: micromechanically and chemically.¹ The micromechanical interaction occurs due to polymerization of the monomers that infiltrate into the dentin, while the chemical interaction occurs due to ionic bonding between functional

monomers and calcium in the residual dentin hydroxyapatite.¹⁹

The 10-methacryloyloxydecyl dihydrogen phosphate (MDP) monomer, present in the composition of some adhesives such as Scotchbond Universal, promotes the protection of collagen fibers through the formation of MDP-calcium salts on the adhesive interface, thus increasing its mechanical strength and preventing its degradation over time.²⁰

A randomized clinical trial²¹ compared the performance of Scotchbond Universal, applied in both adhesion strategies, after selective carious tissue removal in primary molars. The etching strategy did not influence the restorations' longevity after an 18-month of follow-up, but there was a tendency for a better outcome in self-etch mode. Based on the findings of the present systematic review, clinicians may use the universal adhesive in self-etch or etch-and-rinse mode, with the latter preferable in clinical situations involving a considerable amount of enamel, such as fractures.

It is relevant to emphasize the limitations of the present systematic review. As already pointed out, only immediate bond strength data of a single mild 10-MDP-based universal adhesive system could be pooled. Few studies, and most with a small number of samples were selected. Among variables related to in vitro studies, the type of test may influence bond strength data. Nevertheless, only one study¹³ included in the analyses performed a macro-test and did not impact heterogeneity. Most studies were classified as having a medium risk of bias. Lack of information about sample size calculation and blinding of the operator of the test machine are the main reasons for this and should be carefully considered in further studies. In vitro studies should improve the conducting and reporting of laboratory testing using a research reporting guidelines checklist²² in order to minimize bias and optimize efficacy for subsequent randomized clinical trials. Additionally, further studies comparing the long-term bonding performance of different universal adhesives with contemporary adhesive systems in primary teeth are necessary.

Conclusions

Based on this study's results, the following conclusion can be made:

1. Pooled in vitro data suggest that a mild 10-MDP-based universal adhesive system can substitute the etch-and-rinse and self-etch systems for restoring primary teeth.
2. Clinical trials comparing the efficacy of universal and contemporary adhesive systems in resin composite restorations placed in primary teeth are necessary to improve the weak evidence for clinical decision-making.

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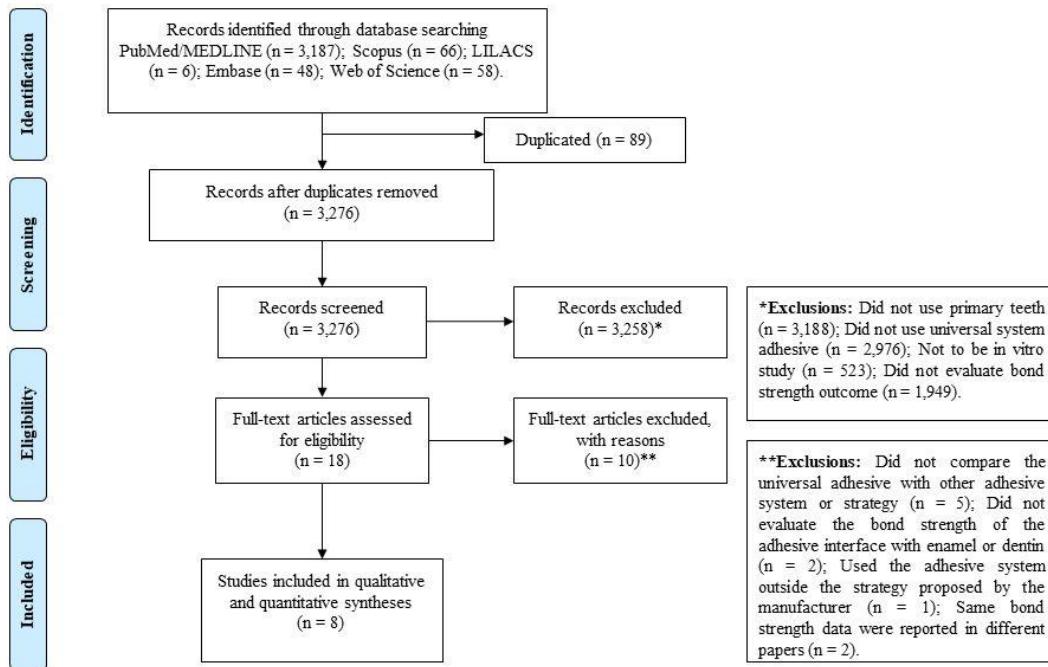


Figure 1. Flowchart diagram of study selection according to the PRISMA statement.

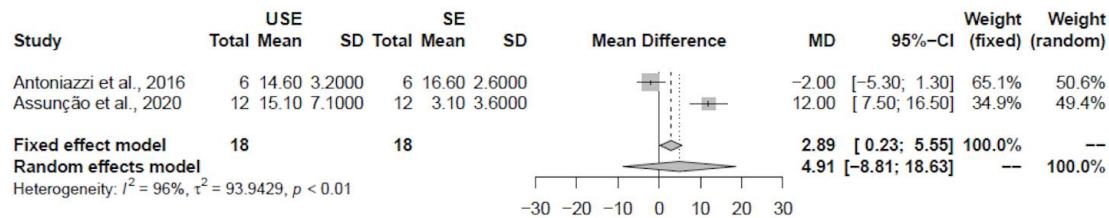


Figure 2. Summary of meta-analysis findings comparing the bond strength of universal adhesive in the self-etch mode and self-etch adhesives to sound enamel.

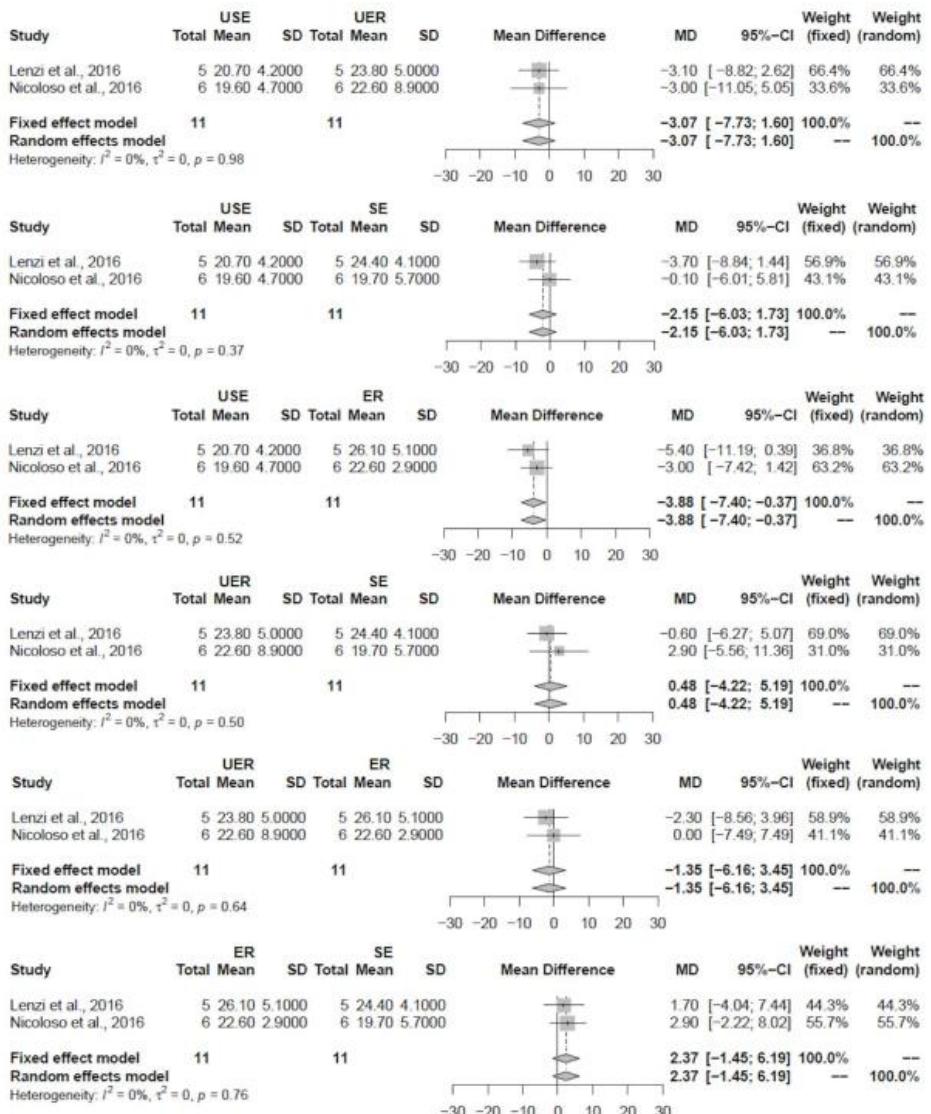


Figure 3. Summary of pairwise direct comparisons for carious dentin. Universal adhesive in the self-etch mode (USE) vs. universal adhesive in the etch-and-rinse mode (UER); universal adhesive in the self-etch mode (USE) vs. self-etch adhesive systems (SE); universal adhesive in the self-etch mode (USE) vs. etch-and-rinse adhesive systems (ER); universal adhesive in the etch-and-rinse mode (UER) vs. self-etch adhesive systems (SE); universal adhesive in the etch-and-rinse mode (UER) vs. etch-and-rinse adhesive systems (ER); etch-and-rinse adhesive systems (ER) vs. self-etch adhesive systems (SE).

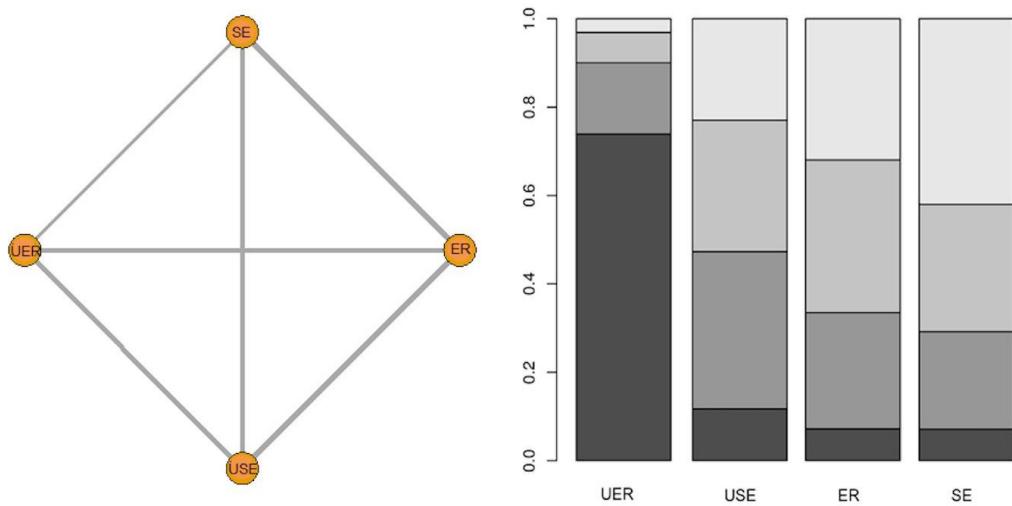


Figure 4. Geometry of the network and probability ranking of the best adhesive performance on sound dentin. The width of lines connecting each pair of adhesive strategies is proportional to the number of studies comparing the adhesive systems. SE: self-etch adhesive systems; ER: etch-and-rinse adhesive systems; USE: universal adhesive in the self-etch mode; UER: universal adhesive in the etch-and-rinse mode. The rank probability showed that the best bond strength result was for UER. After that, the final ranking was USE, ER and SE.

Table 1. DESCRIPTIVE CHARACTERISTICS OF THE STUDIES INCLUDED IN THE SYSTEMATIC REVIEW AND META-ANALYSIS*

Author, year, country	Dental substrate	Substrate condition	N per group	Universal adhesive system	Adhesive strategy	Etch-and-rinse adhesive system(s)	Self-etch adhesive system	Storage time	Type of test
Antoniazzi <i>et al.</i> ⁹ (2016), Brazil	Enamel	Sound and artificial carious enamel	6	Scotchbond Universal†	SE and ER		Clearfil SE Bond 2 steps	Water at 37°C 24 hours	Microshear
Assunção <i>et al.</i> ¹² (2020), Brazil	Dentin and enamel	Sound	12	Scotchbond Universal	SE	Adper Single Bond 2‡ 2 steps	Bond Force 1 step	Water at 37°C 24 hours	Microshear
Kim <i>et al.</i> ¹⁵ (2017), Republic of Korea	Dentin	Sound	5	Scotchbond Universal	SE and ER	Prime & Bond NT 2 steps Scotchbond Multi-Purpose 3 steps	Clearfil S3 Bond 1 step	Water at 37°C 24 hours	Microtensile
Lenzi <i>et al.</i> ¹⁰ (2016), Brazil	Dentin	Sound and artificial carious dentin	5	Scotchbond Universal	SE and ER	Adper Single Bond 2 2 steps	Clearfil SE Bond 2 steps	Water at 37°C 24 hours	Microtensile
Memarpour <i>et al.</i> ¹³ (2018), Iran	Dentin	Sound	10	Scotchbond Universal	SE and ER	Adper Single Bond 2 2 steps		Water at 37°C 24 hours	Shear
Nicoloso <i>et al.</i> ¹¹ (2016), Brazil	Dentin	Artificial Carious Dentin	6	Scotchbond Universal	SE and ER	Adper Single Bond 2 2 steps	Clearfil SE Bond 2 steps	Water at 37°C 24 hours	Microtensile
Ramos <i>et al.</i> ¹⁴ (2016), Portugal	Dentin	Sound	4	Futurabond U	SE	Prime & Bond NT 2 steps	Clearfil Protect Bond 2 steps Clearfil S3 Bond Plus 1 step	1 week	Microtensile
Thanaratikul, Santiwong, Harnirattisai ¹⁶ (2016), Thailand	Dentin	Sound	10	Scotchbond Universal	SE and ER	Adper Single Bond 2 2 steps	Clearfil SE Bond 2 steps	Water at 37°C 24 hours	Microshear

*ER=etch-and-rinse; SE=self-etch

†Single Bond Universal (Brazil)

‡Adper Single Bond Plus (United States and Europe)

Table 2. RISK OF BIAS ASSESSMENT OF THE SELECTED STUDIES

Study	Teeth randomization	Sample size calculation	Materials used according to manufacturers' instructions	Adhesive procedures performed by a single operator	Blinding of the operator of the testing machine	Risk of bias
Antoniazzi et al.⁹ (2016)	Yes	Yes	Yes	Yes	Yes	Low
Assunção et al.¹² (2020)	Yes	Yes	Yes	Yes	Yes	Low
Kim et al.¹⁵ (2017)	Yes	No	Yes	No	No	High
Lenzi et al.¹⁰ (2016)	Yes	No	Yes	Yes	No	Medium
Memarpour et al.¹³ (2018)	Yes	No	No	No	Yes	High
Nicoloso et al.¹¹(2016)	Yes	Yes	Yes	Yes	No	Medium
Ramos et al.¹⁴ (2016)	Yes	No	Yes	Yes	No	Medium
Thanaratikul, Santiwong, Harmirattisai¹⁶ (2016)	Yes	Yes	Yes	Yes	No	Medium

Table 3. RESULTS FROM DIRECT AND MIXED TREATMENT COMPARISON (MTC) EVIDENCE*

Pairs	Direct evidence	MTC (Direct and indirect evidence)
	MD (95% CI)	MD (95% CI)
ER vs SE	1.01 (-7.41; 9.42)	-0.55 (-9.50; 8.40)
ER vs UER	5.50 (4.03; 6.96)	5.20 (-3.90; 15.00)
ER vs USE	1.36 (-3.56; 6.28)	-0.59 (-6.10; 7.20)
SE vs UER	3.35 (-3.04; 9.75)	5.70 (-4.10; 16.00)
SE vs USE	0.65 (-10.78; 2.07)	1.40 (-8.00; 10.00)
UER vs USE	-5.31 (-11.10; 0.48)	-4.40 (-14.00; 4.80)

*MD=mean difference; CI=confidence interval; ER=etch-and-rinse adhesive systems; SE=self-etch adhesive systems; USE=universal adhesive in the self-etch mode; UER=universal adhesive in the etch-and-rinse mode. Confidence intervals that included zero indicate absence of statistically significant differences on bond strength for pairwise comparisons.

Supplementary Electronic Data

sTable 1. Search strategy for each database

Database	Search strategy used	Hits
Pubmed/MEDLINE (https://www.ncbi.nlm.nih.gov/pubmed)	((((((Universal adhesive*) OR Multi-mode adhesive*) OR Multimode adhesive*) OR One-step adhesive*) OR Multi-mode bond*) OR Multimode bond*) OR Universal bond*)) AND (((((Adhesives[MeSH Terms]) OR Adhesive*) OR Total-etch*) OR Etch-and-rinse adhesive*) OR Conventional adhesive*) OR Self-etch*) OR One-bottle adhesive*) OR All-in-one adhesive*)) AND ((((((Bond strength) OR Degradation bond strength) OR Bond*) OR Longevity) OR Durability) OR Tensile strength[MeSH Terms]) OR Tensile) OR Microtensile) OR Microshear) OR Shear)	3,187
Scopus (https://www.scopus.com)	(universal AND adhesive OR multi-mode AND adhesive AND bond AND strength AND primary AND teeth OR deciduous AND tooth) universal adhesive OR multi-mode adhesive AND bond strength AND primary teeth OR deciduous tooth universal AND adhesive AND bond AND strength AND primary AND teeth	66
Lilacs (http://bases.bireme.br/)		
Embase (https://www-embase.ez45.periodicos.capes.gov.br/#search)	TS=(universal adhesive AND bond strength AND primary teeth)	48
Web of Science (https://login.webofknowledge.com)		58
Total		3,365

Table 2. Means of bond strength and standard deviations

Study	Universal adhesive as self-etch mode	Universal adhesive as etch-and-rinse mode	Self-etch adhesives	Etch-and-rinse adhesives
Antoniazzi <i>et al.</i> ⁹ (2016)	14.6 (3.2) sound enamel	21.1 (5.5) sound enamel	16.6 (2.6) sound enamel	
Assunção <i>et al.</i> ¹² (2020)	22.8 (4.8) sound dentin 15.7 (7.1) sound enamel		7.0 (4.7) sound dentin 3.1 (3.6) sound enamel	15.9 (4.1) sound dentin 12.8 (4.4) sound enamel
Kim <i>et al.</i> ¹⁵ (2017)	19.0 (6.8) sound dentin	25.2 (6.2) sound dentin	17.2 (6.7) sound dentin	22.8 (7.5) sound dentin
Lenzi <i>et al.</i> ¹⁰ (2016)	28.3 (5.5) sound dentin 20.7 (4.2) carious dentin	50.1 (7.4) sound dentin 23.8 (5.0) carious dentin	44.1 (6.0) sound dentin 24.4 (4.1) carious dentin	43.8 (6.4) sound dentin 26.1 (5.1) carious dentin
Memarpour <i>et al.</i> ¹³ (2018)	16.9 (2.6) sound dentin	17.6 (2.2) sound dentin		11.4 (1.9) sound dentin
Nicoloso <i>et al.</i> ¹¹ (2016)	19.6 (4.7) carious dentin	22.6 (8.9) carious dentin	19.7 (5.7) carious dentin	22.6 (2.9) carious dentin
Thanaratikul, Santiwong, Harnirattisai ¹⁶ (2016)	25.1 (2.4) sound dentin	24.3 (2.7) sound dentin	25.3 (2.7) sound dentin	19.1 (3.4) sound dentin

Table 3. Main components and manufacturer's instructions of adhesive systems tested

Material	Main Components	pH	Application Mode	
			Etch-and-rinse mode	Self-etch mode
Scotchbond Universal* (3M ESPE, St. Paul, MN, USA)	MDP phosphate monomer, HEMA, dimethacrylate resins, Vitrebond copolymer, filler, ethanol, water, initiators, silane	2.7	1. Apply etchant for 15 s 2. Rinse for 15 s 3. Air dry to remove excess of water 4. Apply the adhesive using the self-etch mode	1. Apply the adhesive for 20 s 2. Gentle air for 5 s 3. Light-cure for 10 s
Adper Single Bond 2** (3M ESPE, St. Paul, MN, USA)	Etchant: 35% phosphoric acid Adhesive: HEMA, water, ethanol, Bis-GMA, dimethacrylates, amines, metacrylate-functional copolymer of polyacrylic and polyitaconic acids, 10% by weight of 5 nanometer-diameter spherical silica particles	0.6 4.7	1. Apply etchant for 15 s 2. Rinse for 10 s 3. Blot excess water 4. Apply 2 consecutive coats of adhesive for 15 s with gentle agitation 5. Gently air dry for 5 s 6. Light-cure for 10 s	N.A.
Bond Force (Tokuyama Dental Corporation, Tokyo, Japan)	TEDGMA, phosphate monomer, camphorquinone, Adhesive SR (self-reinforcing) monomer, polymerizing monomer (HEMA, Bis-GMA, 3G), water, alcohol, glass filler, photopolymerization catalyst	2.3	N.A.	1. Apply the adhesive for 20 s 2. Gently air dry for 5 s 3. Light-cure for 10 s
Clearfil Protect Bond (Kuraray Noritake, Osaka, Japan)	Primer: MDPB, MDP, HEMA, Hydrophilic dimethacrylate, PI, Water Adhesive: MDP, BIS-GMA, HEMA, Hydrophobic dimethacrylate, PI (dl-camphorquinone), N,N-diethanol-p-toluidine, silanated colloidal silica, NaF	2.5 Not determined	N.A.	1. Apply primer and leave for 20 s 2. Dry with gentle air flow 3. Apply the adhesive 4. Gently air dry 5. Light-cure for 10 s
Clearfil S3 Bond Plus (Kuraray Noritake, Osaka, Japan)	MDP, BIS-GMA, HEMA, hydrophilic aliphatic dimethacrylate, hydrophobic aliphatic methacrylate,	2.3	N.A.	1. Apply the adhesive for 10 s 2. Dry with mild pressure air flow for

	colloidal silica, PI, accelerators, initiators, NaF, ethanol		5 s	3. Light-cure for 10 s
Clearfil SE Bond*** (Kuraray Noritake, Osaka, Japan)	Primer: MDP, HEMA, hydrophilic dimethacrylate, dl-camphorquinone, N,N-diethanol- <i>p</i> -toluidine, water Adhesive: MDP, Bis-GMA, HEMA, hydrophobic dimethacrylate, dl-camphorquinone, N,N-diethanol- <i>p</i> -toluidine, silanated colloidal silica	2.5 2.0	N.A.	1. Apply primer on dry dentin surface and left undisturbed for 20 s 2. Dry with air stream for 5 s 3. Apply the adhesive 4. Gently air dry 5. Light-cure for 10 s
Prime & Bond NT (Dentsply Sirona, Konstanz, Germany)	Etchant: 35% phosphoric acid Adhesive: Di- and trimethacrylate resins, Dipentaerythritol pentaacrylatemonophosphate (PENTA), nanofillers (amorphous silicon dioxide), photoinitiators, stabilizers, cetylamine hydrofluoride, acetone	0.6 1.7	1. Apply etching for 15 s 2. Rinse for at least 10 s 3. Air dry to remove excess of water 4. Apply generous amounts of adhesive for 20 s 5. Gently air dry 6. Light cure for 10 s	N.A.
Scotchbond Multi-Purpose (3M ESPE, St. Paul, MN, USA)	Etchant: 35% phosphoric acid Primer: Polyalkenoic acid, copolymer HEMA, water Adhesive: BIS-GMA, HEMA, benzoyl peroxide, triphenylphosphine, triphenylantimony, hydroquinone	0.6 3.9	1. Apply etchant for 15 s 2. Rinse and air dry to remove excess of water 3. Apply primer and dry for 5 s 4. Apply adhesive and light cure for 10 s	N.A.

Abbreviations: MDP: 10-methacryloyloxydecyl-dihydrogen-phosphate; Bis-GMA: bisphenyl-glycidyl methacrylate; HEMA: 2-hydroxyethyl methacrylate; TEGDMA: triethylene glycol dimethacrylate; MDPB: 12-methacryloyloxydodecylpyridinium bromide; PI: photoinitiator; NaF: sodium fluoride; N.A.: not applicable.

Single Bond Universal (**Adper Single Bond Plus (United States and Europe)

3 CONCLUSÃO

Uma adesão consistente e estável entre o material restaurador e o substrato dental não é apenas desejável sob o ponto de vista mecânico, mas também por razões biológicas e estéticas. Os achados laboratoriais sugerem que sistema adesivo universal com pH suave contendo 10-MDP pode substituir os sistemas adesivos convencionais e autocondicionantes para restaurar dentes decíduos. Cabe ressaltar, no entanto, que poucos estudos foram incluídos na revisão sistemática. Além disso, apenas valores de resistência de união imediatos de um único sistema adesivo universal puderam ser compilados.

Assim, estudos futuros comparando o desempenho clínico de sistemas adesivos universais e contemporâneos em restaurações de resina composta em dentes decíduos são necessários a fim de auxiliar os clínicos no processo de tomada de decisão.

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