UNIVERSIDADE FEDERAL DE SANTA MARIA
CENTRO DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS GRADUAÇÃO EM CIÊNCIAS ODONTOLÓGICAS

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RESISTÊNCIA DE UNIÃO DE SISTEMAS ADESIVOS EM DENTINA PREVIAMENTE EXPOSTA A MATERIAIS CONTENDO EUGENOL

Santa Maria, RS
2020

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Dissertação apresentada ao Curso de Mestrado do Programa de Pós-Graduação em Ciências Odontológicas da Universidade Federal de Santa Maria (UFSM), como requisito para a obtenção do título de **Mestre em Ciências Odontológicas com ênfase em Materiais Dentários.**

Orientador: Prof. Dr. Fabio Zovico Maxnuck Soares

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This study was financied in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) – Finance Code 001

da Rosa, Lucas Saldanha

Resistência de união de sistemas adesivos em dentina previamente exposta a materiais contendo eugenol / Lucas Saldanha da Rosa.- 2020.

90 p.; 30 cm

Orientador: Fabio Zovico Maxnuck Soares

Dissertação (mestrado) - Universidade Federal de Santa Maria, Centro de Ciências da Saúde, Programa de Pós Graduação em Ciências Odontológicas, RS, 2020

1. Eugenol 2. Sistemas adesivos 3. Dentina I. Zovico Maxnuck Soares, Fabio II. Título.

Sistema de geração automática de ficha catalográfica da UFSM. Dados fornecidos pelo

autor(a). Sob supervisão da Direção da Divisão de Processos Técnicos da Biblioteca Central. Bibliotecária responsável Paula Schoenfeldt Patta CRB 10/1728.

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Santa Maria, RS
2020

AGRADECIMENTOS

Este trabalho só está acontecendo graças ao apoio, comprometimento e compreensão de muitas pessoas, dentre as quais agradeço especialmente:

- a minha família, pois sem ela nada disso seria possível;

- ao meu orientador, professor, mentor e amigo Fabio Zovico Maxnuck Soares, pela oportunidade e por todo esse tempo de valor imensurável o qual, com muita dedicação, confiou e não desistiu de mim. Espero sempre continuar ao seu lado;

- à prof. Rachel de Oliveira Rocha, por todos os ensinamentos e apoio. Sem você, nada seria o mesmo;

- à Andressa Cargnelutti Follak e à Bruna Dias Ilha, por todo o apoio, parceria e aos ótimos momentos que compartilhamos;

- a todos integrantes do Laboratório de Biomateriais por toda a convivência e troca de experiências;

- aos meus amigos, que têm gostos muito duvidosos para escolherem companhias;

- aos colegas, por seguirem firmes juntos até o final nessa jornada;

- aos professores e servidores do Curso de Odontologia e, em especial, aos da pós-graduação, pelo trabalho impecável que executam. Tudo só é possível graças a vocês;

- à UFSM e a CAPES por proporcionarem ensino gratuito e de qualidade, assim como incentivarem o desenvolvimento da pesquisa e da ciência no país;

A todos aqueles que de alguma forma contribuíram para a minha evolução como ser humano.

RESUMO

RESISTÊNCIA DE UNIÃO DE SISTEMAS ADESIVOS EM DENTINA PREVIAMENTE EXPOSTA A MATERIAIS CONTENDO EUGENOL

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O cimento de óxido de zinco e eugenol (OZE) ainda é uma realidade no cotidiano clínico. O eugenol presente no cimento afeta a polimerização de monômeros, como os presentes em sistemas adesivos. Estudos anteriores têm mostrado divergência em relação a influência do efeito do eugenol ao longo do tempo na resistência de união (RU) de sistemas adesivos, sendo que nenhum avaliou tempos maiores do que 45 dias. São apresentadas duas pesquisas avaliando os efeitos de cimentos com OZE na RU de sistemas adesivos. A primeira é uma revisão sistemática e metanálise sobre a influência de materiais temporários à base de eugenol na RU de sistemas adesivos em dentina. Buscas foram realizadas nas bases de dados PubMed, Web of Science e Scopus sem limitação de ano ou língua, resultando em 603 estudos em potencial, que passaram por critérios de inclusão e exclusão. Dos 35 trabalhos lidos na íntegra, 27 foram eleitos para a revisão sistemática e 26 para a metanálise. Após a seleção, extração dos dados e definição dos riscos de viés, a metanálise foi feita utilizando variância invertida e modelo de efeitos aleatórios ($p<0,05$). Heterogeneidade foi verificada com o teste Q de Cochran e I2. Materiais temporários à base de eugenol foram associados estatisticamente a menores valores de RU. Análises de subgrupos também mostraram os mesmos efeitos após 24 horas e 7 dias, assim como quando divididos em cimentos resinosos, sistemas adesivos de condicionamento ácido total e sistemas adesivos autocondicionantes. Tempos entre 14 e 45 dias não apresentaram diferenças. Evidências laboratoriais sugerem que há decréscimo na RU de adesivos em dentina para dentes expostos a cimentos de OZE em até uma semana, independente da estratégia utilizada. A segunda pesquisa tem por objetivo avaliar a RU em microcisalhamento (µSBS) de um sistema adesivo à dentina previamente restaurada provisoriamente com cimento de OZE durante diferentes tempos. Sessenta e quatro incisivos bovinos hígidos tiveram suas superfícies dentinárias expostas e foram divididos em 8 grupos (n=8), sendo os grupos 24 horas, 7, 15, 30, 60, 120 e 180 dias restaurados provisoriamente com cimento OZE pelos tempos correspondentes, mais um grupo controle sem restaurações provisórias. Após a remoção mecânica do cimento de OZE e limpeza das superfícies, um sistema adesivo de condicionamento total foi aplicado e cilindros de resina composta foram confeccionados para teste de µSBS. Análise de falha foi feita utilizando um estereomicroscópio e a análise dos dados foi feita utilizando Kruskal Wallis e teste post hoc de Dunn (significância de 5%). Menores valores de µSBS foram encontrados nos grupos experimentais 24h, 7, 15 e 30d. quando comparados ao controle ($p<0,05$). Valores similares de µSBS foram encontrados entre os grupos 60, 120, 180d e controle. Cimentos de OZE prejudicam a resistência de união de sistemas adesivos de condicionamento ácido total até 30 dias. Em 60 dias já é seguro realizar restaurações com materiais resinosos. Conclui-se que cimentos de OZE reduzem a RU de sistemas adesivos em dentina em até 30 dias, sendo o período até 7 dias crítico.

Palavras-chave: Eugenol. Sistemas adesivos. Dentina.

ABSTRACT

BOND STRENGTH OF ADHESIVE SYSTEMS TO DENTIN PREVIOUSLY EXPOSED TO EUGENOL-CONTAINING MATERIALS

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Zinc oxide-eugenol cement (ZOE) is still a reality in clinical practice. Eugenol present in cement affects the polymerization of monomers, such as those found in adhesive systems. Previous studies have shown divergence regarding the influence of the effect of eugenol over time on the bond strength (BS) of adhesive systems, with none evaluating times longer than 45 days. Two studies are presented evaluating the effects of cement with ZOE in the BS of adhesive systems. The first of them is a systematic review and meta-analysis on the influence of temporary eugenol-based materials on adhesive systems bond strength to dentin. Searches were performed in the PubMed, Web of Science and Scopus databases without limitation of year or language, resulting in 603 potential studies, which met inclusion and exclusion criteria. Of the 35 full-text read, 27 were elected for systematic review and 26 for meta-analysis. After selection, data extraction and definition of risk of bias, the meta-analysis was performed using inverted variance and a random effects model ($p < 0.05$). Heterogeneity was verified with Cochran Q and I2 tests. Temporary eugenol-based materials were statistically associated with lower BS values. Subgroup analyzes also showed the same effects after 24 hours and 7 days, as well as when divided into resin cements, total-etching adhesive systems and self-etching adhesive systems. Times between 14 and 45 days showed no differences. Laboratory evidence suggests that there is a decrease in the BS to dentin of adhesives systems exposed to ZOE cements up to one week, regardless of the strategy used. The second research have the objective of evaluating the micro shear bond strength(μSBS) of an adhesive system to dentin previously provisionally restored with ZOE cement during different times. Sixty-four healthy bovine incisors had their dentin surfaces exposed and were divided into 8 groups (n = 8), with the groups 24 hours, 7, 15, 30, 60, 120 and 180 days provisionally restored with ZOE cement for the corresponding times, another control group without provisional restorations. After the mechanical removal of the ZOE cement and cleaning of the surfaces, an adhesive system of total conditioning was applied and cylinders of composite resin were made for μSBS test. Failure analysis was performed using a stereomicroscope and data analysis was performed using Kruskal Wallis and Dunn's post hoc test (5% significance). Lower RU values were found in the experimental groups 24h, 7, 15 and 30d. when compared to the control ($p < 0.05$). Similar μSBS values were found between groups 60, 120, 180d and control. ZOE cements impair the bond strength of total acid conditioning adhesive systems for up to 30 days. In 60 days, it is already safe to perform restorations with resinous materials. It was concluded that ZOE cements reduce the BS of adhesive systems to up to 30 days, with a critical period up to 7 days.

Keywords: Eugenol. Adhesive systems. Dentin.

SUMÁRIO

1 INTRODUÇÃO

Cimento de óxido de zinco e eugenol (OZE) é um material amplamente utilizado em tratamentos odontológicos, como cimento endodôntico, cimento provisório para restaurações indiretas, assim como cimento restaurador provisório (SARAC et al., 2005). Apresenta baixa solubilidade (0,1 e 3,5%), bom escoamento, radiopacidade, além de ter baixo custo (ALEXANDRE; ROSA; CHAIN, 2013). É um excelente material para lesões profundas, uma vez que possui propriedades sedativas, reduzindo inflamações pulpares, em casos de pulpites reversíveis (HE; PURTON; SWAIN, 2010).

Materiais resinosos são indiscutivelmente uma realidade no meio odontológico e desde a sua introdução, sistemas como resinas compostas, cimentos resinosos e sistemas adesivos, têm sido usados com cautela quando empregados após a utilização de materiais restauradores provisórios contendo eugenol na composição, os quais exercem influência negativa na polimerização desses materiais (ITSKOVICH; LEWINSTEIN; ZILBERMAN, 2014). Essa influência acaba refletindo em menores valores de dureza e resistência de união, principalmente à dentina (KOCH et al., 2013; MARSHALL; MARSHALL; HARCOURT, 1982).

A reação de presa do OZE é uma reação ácido base em que, na presença de água, óxido de zinco e eugenol formam uma matriz de eugenolato de zinco que cercam partículas de óxido de zinco não reagidas. A questão crítica nessa reação está na sua reversibilidade, pois mesmo após a presa do cimento, na presença de água, ocorre a hidrólise do eugenolato, voltando a haver eugenol disponível no meio (HUME, 1984; KOCH et al., 2013).

Em materiais resinosos, a reação de polimerização ocorre dentro das fases de ativação, iniciação, propagação e terminação. Na fase de propagação, onde radicais livres fazem a quebra de duplas ligações gerando união das partes em uma reação em cadeia, o eugenol pode interagir com esses radicais livres, os aprisionando. Dessa forma há uma diminuição na quebra de ligações, prejudicando toda a conclusão do processo. Isso resulta em produtos subpolimerizados, em que as características e propriedades desejadas se tornam deficientes (CARVALHO et al., 2007; FUJISAWA, KADOMA, 1997; GANSS; JUNG, 1998; HE; PURTON; SWAIN, 2010).

O fato desse material ser usado de forma provisória na maioria dos casos, implica a sua remoção para posterior aplicação de um material definitivo, seja em uma restauração direta ou indireta. Para tal, usam-se diversas técnicas para a limpeza do substrato, em especial da dentina, que por possuir uma estrutura mais complexa, contendo matéria orgânica, água, túbulos e uma rede de fibras colágenas, acaba sendo mais complexa e mais crítica que o esmalte dentário em questões de adesão (AROLA et al., 2017).

A concentração de eugenol liberada pelo cimento tende a ser maior na superfície dentária e vai diminuindo conforme vai em direção a polpa. A difusão do eugenol também tende a ser maior nas primeiras horas, diminuindo ao longo do tempo. Além da hidrólise do cimento, o eugenol liberado tende a ser disperso pela água do ambiente ao longo do tempo, o que torna esse efeito potencialmente tempo-dependente (HUME, 1984).

A presença de resíduos de OZE no interior dos túbulos dentinários após a remoção do cimento sempre foi uma questão crítica, uma vez que uma superfície visualmente livre de contaminantes pode ainda possuir resíduos (TERATA, 1993). Estudos apresentaram diferentes métodos de limpeza do substrato, mostrando que poderiam fazer diferença na resistência de união de sistemas adesivos à dentina (FONSECA et al., 2005; FRANKENBERGER et al., 2007; SARAC et al., 2005). Há quem associe menores valores de resistência de união de dentes previamente restaurados com OZE pelo simples fato de as partículas do cimento obstruírem os túbulos dentinários, e não pelo efeito do eugenol em si (PEUTZFELDT; ASMUSSEN, 2006).

Apesar de estudados há vários anos, os efeitos deletérios do cimento de óxido de zinco e eugenol ainda são controversos nos trabalhos (AL WAZZAN; HARBI; HAMMAD, 1997; BAYINDIR; AKYIL; BAYINDIR, 2003; CARVALHO et al., 2007; ERKUT et al., 2007; PAUL; SCHÄRER, 1997; PIRES et al., 2018; ROSALES-LEAL et al., 2003; YAP et al., 2001), que apresentam grande variação de materiais empregados, assim como períodos de tempo de envelhecimento. Ainda que haja alguns estudos com maiores tempos de envelhecimento, e mesmo assim discordantes (KOCH et al., 2013; PINTO et al., 2014), não há trabalhos avaliando os efeitos do OZE em sistemas adesivos por períodos mais longos de tempo.

Dessa forma, o intuito dessa dissertação é avaliar, em dois trabalhos, o efeito de cimentos contendo eugenol na resistência de união de sistemas adesivos.

2 ARTIGO 1 - DO EUGENOL-BASED MATERIALS AFFECT THE BOND STRENGTH OF ADHESIVE SYSTEMS? A SYSTEMATIC-REVIEW AND META-ANALYSIS OF IN VITRO STUDIES

Este artigo será submetido ao periódico Dental Materials, Elsevier, ISSN: 0109-5641, Fator de impacto = 4.495; Qualis A1. As normas para publicação estão descritas no Anexo B.

Do eugenol-based materials affect the bond strength of adhesive systems? A systematic-review and meta-analysis of in vitro studies

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ABSTRACT

Objective. To evaluate through a systematic review and meta-analysis the influence of temporary eugenol-based materials on the bonding of adhesive systems to dentin.

Data and source. A literature search was conducted in PubMed, Web of Science, and Scopus databases. Laboratory studies evaluating the influence of temporary eugenol-based materials on the bond strength of adhesive systems were searched with no year or language restriction.

Study selection: From 603 potentially eligible studies, 35 were selected for full-text analysis, 27 were included in the systematic review and 26 in the meta-analysis. Two reviewers independently selected the studies, extracted the data, and assessed the risk of bias. Meta-analysis was performed using the inverse variance and a random-effects model ($p \leq 0.05$). Heterogeneity was assessed with the Cochran Q test and I2 statistics.

Results. Temporary eugenol-based materials were statistically associated with lower bond strength values (p<0.00001). Subgroup analysis considering the exposure time of temporary eugenol-based materials also showed a significant reduction of bond strength after 24h (p=0.003) and after seven days (p<0.00001) but no significant differences were observed after 14 to 45 days (p=0.92). Subgroup analysis considering luting cement (p=0.02), total-etch systems (p=0.0003), and self-etch systems (p=0.0001) separately also showed a significant reduction of bond strength.

Conclusions. The mate-analysis based on laboratory evidence suggests a decrease in adhesive systems bond strength to dentin previously exposed to eugenol-based temporary materials regardless of the bonding approach. After maintained for 14 days, the adverse effect of eugenol-based temporary restorations stop being noted.

KEY WORDS: Adhesive systems; Bond strength; Dentin-bonding agents; Zinc oxide-eugenol cement.

1. Introduction

Several factors may impair the bonding of adhesive systems to enamel and dentin, including those related to the substrate itself [1] and the adhesive systems, such as composition and bonding strategy [2]. Moreover, the interaction between the adhesive components and dentin can also be compromised by previous substrate contamination with saliva, blood, or any other material.

Zinc oxide-eugenol cement is widely used in prosthodontics, endodontics, and restorative dentistry as liners, temporary restorations, and luting materials. Despite the advantages related to low-cost, easily-handling and sedative effect [3, 4], eugenol-containing temporary cement may have a detrimental effect on the bonding of adhesives systems to dentin [5]. Eugenol (2-methoxy-4-allylphenol) is a phenolic compound that reacts with free radicals and may inhibit the polymerization of resin monomers [6], including adhesive systems, reducing their bond strength values. The reaction between zinc oxide and eugenol in the presence of water results in zinc eugenolate but this reaction is reversible when exposed to water, with the consequent release of eugenol and zinc hydroxide [7]. The released eugenol in contact with dentin's surface can modify its characteristics [8]. Also, eugenol can be trapped into dentin tubules and contribute to impair the polymerization of adhesive systems [9, 10]. Therefore, it is expected that factors such as the removal technique and the exposure time to eugenol based-materials could be important when considering its influence on adhesive restorations.

Despite the possible detrimental effect of eugenol, contradictory findings exist concerning bond strength to dentin previously exposed to eugenol based-materials. A significant decrease in bond strength of adhesives to dentin was noticed, regardless of the bonding strategy - total-etch [11-15] or self-etch [5, 11, 14, 16], suggesting that using eugenol based-materials before adhesive restorations placement should be avoided. However, a more pronounced reduction seems to be related to the use of self-etch systems [11].

Thus, this study aimed to systematically review the literature for laboratory studies that evaluated the influence of temporary eugenol-based materials on the dentin bond strength of adhesive systems. The following research question was answered: Do temporary eugenol-based materials reduce the bond strength values of adhesive systems to dentin?

2. Materials and methods

This systematic review was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [17].

2.1. Search strategy

A literature search conducted in MEDLINE via PubMed, Web of Science (ISI – Web of Knowledge) and Scopus databases to identify studies that evaluated the effect of eugenol-based restorations on the bond strength of adhesive systems. The search was conducted with no publication year or language limits. The subject search used a combination of controlled vocabulary and free text terms based on the search strategy available for the PubMed/MEDLINE database, as follow: (((((((((((((((((Dentin-Bonding

Agents[MeSH Terms]) OR Dentin-Bonding Agents) OR Agents, Dentin-Bonding) OR Dentin*[MeSH Terms]) OR Dentin*) OR Bonding Agents) OR Agents, Dentin Bonding) OR Dentin Bonding Agents) OR Adhesive*) OR Adhesive systems) OR Total-etch adhesive*) OR Conventional adhesive*) OR Etch-and-rinse adhesive) OR All-in-one adhesive*) OR All-in-one) OR Self-etch*)) AND ((((((((((((Zinc Oxide-Eugenol Cement[MeSH Terms]) OR Zinc Oxide-Eugenol Cement) OR Cement, Zinc Oxide-Eugenol) OR Oxide-Eugenol Cement, Zinc) OR Zinc Oxide Eugenol Cement) OR ZOE) OR ZOE cement) OR zinc oxide cement) OR temporary restoration) OR temporary cement) OR eugenol-based restoration*) OR oxide-eugenol) OR eugenol)) AND (((((((((((((Tensile strength[MeSH Terms]) OR Tensile strength) OR Bond*) OR Bond strength) OR Degradation bond strength) OR Longevity) OR Microtensile) OR Micro tensile) OR Microshear) OR Micro shear) OR Shear) OR Shear strength[MeSH Terms]) OR Shear strength) OR Dentin Bond*). This strategy was adapted to Web of Science and Scopus platforms. To retrieve all relevant papers, reference lists of included papers and related reviews also were checked. The search results were cross-checked to find and remove duplicates. The last search was executed on march, 2020.

2.2. Selection, inclusion and exclusion criteria

The titles and abstracts of studies were reviewed independently by two review authors (L.S.R. and F.Z.M.S) and were selected according to the inclusion criteria: (1) studies that evaluated the influence of eugenol-based materials on the performance of adhesive systems, and (2) in vitro studies that assessed the bond strength to coronal enamel and/or dentin. The full texts of all studies that full-filled the inclusion criteria for eligible papers were then reviewed independently considering the exclusion criteria: (1) did not evaluate immediate or aged bond strength data, and (2) lack of control group (without the use of eugenol-based material). Papers that did not provide mean values of bond strength, in megapascals (MPa) and respective standard deviation, even after e-mail requests to authors (at least twice), were excluded.

The independent reviewers were calibrated in accordance with inclusion/exclusion criteria and agreement between reviewers was found to be good (Kappa = 0.89), any disagreement was resolved by consensus with a third reviewer (R.O.R.).

2.3. Data extraction

The following data were extracted from the included articles: demographic information (authors and publication year, first author's country) and research methodology (mean values and standard deviations (SD) of the bond strength, the type of mechanical test, the number of teeth, number of specimens, substrate, days of storage, cleansing method, temporary agent, adhesive system, and composite resin). For those articles that provided insufficient data to be included, the first or corresponding author was contacted whether they could provide additional data. One reviewer collected the data of the included studies using a predefined data extraction sheet.

2.4. Risk of bias assessment

Two authors (L.S.R. and F.Z.M.S) independently evaluated the risk of bias of each included study based on previous systematic reviews of in vitro studies [18, 19]. The description of the following parameters was checked in each study: randomization of the teeth for experimental groups, sample size calculation, use of sound teeth, similar cross-section area for specimens for both control and experimental groups, failure mode description, restorative procedures by a single operator, blinding the operator of the testing machine, materials used according to the manufacturer's instructions, and the same and informed cleansing method to remove the temporary cement. If the parameter was described in the text, the study received a “yes”, otherwise it had a “no”. The risk of bias was classified according to the sum of “yes” received as follows: 1 to 3 = high; 4 to 6 = medium; 7 to 9 = low risk of bias.

2.5. Data analysis

Meta-analyses were performed using the inverse variance method and the random-effect model comparing experimental (temporary eugenol-based materials exposed substrate) and control (no temporary eugenol-based materials exposed substrate) groups; $p \leq 0.05$ (Z test) was considered significant. For studies that evaluated more than one adhesive system, cleaning method, or exposure time to temporary material, means were combined into one mean and standard deviation of bond strength for each group (experimental and control) using a formula suggested by Cochrane Statistical Guidelines.

The analyses were performed in Review Manager (RevMan) [computer program] version 5.4, The Cochrane Collaboration, 2020 and forest plots were created to illustrate the meta-analyses. Statistical heterogeneity among studies was assessed by the Cochran Q test, and inconsistency test (I^2), with $I^2 > 75\%$ considered considerable heterogeneity, and the chi-squared test with a p value <0.10 to define significant heterogeneity [20].

3. Results

3.1. Study Selection

Figure 1 shows the flowchart summarizing the study selection process. The search strategy identified 601 potentially relevant records of PubMed (MEDLINE), 57 of ISI Web of Science, and 64 of Scopus databases. The first screening resulted in 35 studies remained for full-text reading, and after, 27 papers were included in the systematic review. One paper presented insufficient data and was not included in the meta-analyses; thus, 26 studies were considered in the meta-analyses.

3.2. Descriptive analysis

Table 1 describes a detailed summary of the included studies. Most studies were conducted by Brazilians (7 studies), in English (two studies were in Chinese), and were published between 1992 and 2018.

All included researches conducted a mechanical test, mostly (18) 'macro' tests (shear and tensile bond strength tests) [5, 10, 12-14, 21-33] and 9 conducted 'micro' tests (microshear and microtensile tests) [11, 34-41].

The majority of papers (26) considered the bond strength to dentin, and none of them evaluated enamel as bonding substrate. The exposure time to temporary eugenol-based materials ranged from one to forty-five days of storage. It was verified that in the greater part of works (16) the specimens were submitted to 7 days of temporary eugenol-based materials exposure. From the 26 studies included in the meta-analysis, 15 evaluated luting cements, 23 total-etch systems and 11 self-etch systems. The most noted temporary agent brand was Temp Bond, whereas related to adhesive systems the most observed were Adper Single Bond (8 studies), Gluma, and Clearfill SE Bond, totalizing 23 total-etch systems and 11 self-etch systems. Luting cement was used in 15 studies (7 brands), and 15 commercial brand names of resin composite were used in 12 studies. Regarding the cleaning method for temporary eugenol-based materials, scaler was the most adopted, combined or not with pumice.

3.3. Meta-analysis

The meta-analyses were performed considering the influence of temporary eugenol-based materials on the bond strength of adhesive systems to dentin (global analysis – figure 2). The exposure time to temporary eugenol-based materials was considered in the subgroups analyses, including 24 hours (figure 3), 7 days (figure 4), and 14 to 45 days (figure 5), as the luting cement (figure 6), and the adhesive systems by etching strategy were also considered in a separate analysis (figures 7 and 8).

The global meta-analysis favored the bond strength to dentin unexposed to temporary eugenol-based materials (control group), i.e., temporary eugenol-based materials impair the bond strength of adhesive systems to dentin, with an effect size of Z=4.3 ($p<0.00001$) with heterogeneity of 78%. Figure 1 presents the forest plot of the analysis between temporary eugenol-based materials exposed and unexposed dentin. The negative effect of temporary eugenol-based materials on bond strength was also verified for the subgroup meta-analysis, considering the exposure times, lower bond strength was observed for temporary eugenol-based materials groups at 24 hours (effect size of Z=2.93; p=0.003) and 7 days subgroups (effect size of Z=5.22; $p<0.00001$). However, after 14 to 45 days of temporary eugenol-based materials exposure subgroup, no significant difference was observed between control and experimental groups (effect size of Z=0.1; p=0.92). Considerable heterogeneity was found for the 24 hours of exposure time subgroups meta-analyses (I^2 = 92%; $p<0.00001$). For 7 days and 14 to 45 days subgroups meta-analysis, the heterogeneity was respectively, $I^{2=}$ 43% (p=0.04) and I^2 = 0% (p=0.90).

The adverse effect of temporary eugenol-based materials on bond strength was also observed for subgroups analysis considering luting cement (effect size of 2.39, $p<0.00001$); total-etch adhesive systems (effect size of 3.59, $p<0.00001$) and self-etch adhesive systems (effect size of 3.83, p=0.0001). Heterogeneity was observed for subgroups, luting cement (I^2 = 75%, p<0.00001), total-etch adhesive systems (I^2 = 76%, p<0.00001), and self-etch adhesive systems subgroup (I^2 = 69%, p=0.0004).

3.4. Assessment of risk of bias

In this systematic review, of the total of 27 papers included, none were classified as low risk of bias, whereas 92,6% of included studies scored medium risk of bias, and only two studies were classified as having a high risk of bias (Table 2).

The parameters that most frequently received "No" (not clearly described in the text) were the sample size calculation, presence of a blinded operator of the testing machine, and failure mode analysis description. Randomization of specimens for experimental groups was not informed by 9 studies [10-12, 23, 28, 29, 35, 37, 39]

4. Discussion

Temporary restorations are frequently necessary for direct and indirect procedures until the placement of final restorations. Zinc oxide-eugenol based temporary cement is the most used material for this purpose, given its adequate sealing ability, sedative effect, being easy to handle, and removal [3]. The eugenol, however, supposedly interfere in resin polymerization, as on the bonding performance. The present systematic review and meta-analysis was the first to summarize the data from laboratory studies regarding the influence of temporary eugenol-based materials on the bond strength of adhesive systems to dentin. The pooled bond strength data showed statistically lower bond strength values for dentin exposed to temporary eugenol-based materials (experimental group) compared to non-exposed dentin (control group). The adverse effect of the temporary eugenol-based materials persists even when the restoration is maintained for up to 7 days, and it only ceased to influence the bond strength values when the temporary eugenol-based restorations were maintained for longer periods (14 to 45 days).

The low bond strength values obtained from dentin previously exposed to temporary eugenol-based materials may be a consequence of the impaired degree of conversion of a resin-based material. Eugenol is a recognized radical scavenger that can protonize the free radicals of polymeric materials during the polymerization, imparting their degree of conversion [42], and ultimately, the bond strength. Moreover, alterations on the dentin substrate have also been observed as eugenol released can chelate calcium from dentin causing a softening effect [8]. In a previous systematic review, Altman et al. (2015) [42] found that the eugenol-based sealer reduces the bond strength of fiber posts luted to root canal with resin cement, regardless of the type of adhesive. Nevertheless, the present systematic review considered the eugenol influence on the bonding of adhesive systems to coronal dentin, and also pointed out the negative eugenol on bond strength values.

The stratification of our meta-analysis by the exposure time of temporary eugenol-based restoration showed, however, that the negative influence of eugenol was not perceived when the restorations were maintained for 14 to 45 days, indicating no detrimental effect of temporary eugenol-based material on the bond strength of adhesive systems after at least 14 days. It should be noted, however, that only 3 studies evaluated eugenol exposition longer than 7 days; two studies considered 14 days[5, 40], and one study included an evaluation after 45 days [37].This result confirms the primary studies in which the effect of eugenol was not seen after at least 14 days, probably by the reduced eugenol concentration in dentin [9], incapable of exerting an inhibitory effect on resin polymerization [40].

The subgroup meta-analysis also demonstrates that temporary eugenol-based material produces an adverse effect on the bond strength of luting cement to coronal dentin, as pointed out by previous systematic review, considering the bond strength of fiber posts luted to root canal with resin cement. In our systematic review, adhesive systems were also adversely affected by temporary eugenol-based material, regardless of the etching strategy. Although it is attributed to acid etching to the possible elimination of residual eugenol and consequently the adverse effect on etch-and-rinse adhesives [9], this has not been confirmed in this systematic review, as the subgroup meta-analysis by adhesive system strategy pointed out higher bond strength values for control groups, regardless of whether it is an etch-and-rinse or self-etch system.

In the present study, the meta-analysis could not be stratified by substrate, because none of the 27 studies included in the systematic review evaluated the bond strength to the enamel. This may be associated with a presumed minor or even non-existent effect of eugenol on enamel bonding, because of its histological characteristics, and less diffusion of eugenol inside it. Regarding the adhesive systems, several trademarks were evaluated in primary studies, with representatives of the etch-and-rinse and self-etching categories, as well as the temporary cement. Also, four mechanical tests (shear and microshear, tensile, and microtensile) were used to evaluate the bond strength, as well as the dentin of bovine and human teeth were considered as bonding substrate. This variability contributes to the heterogeneity, which is consistent with previous systematic reviews of in vitro studies [19, 44]. Furthermore, undescribed parameters, such as sample size calculation, presence of a blinded operator of the testing machine, and failure mode analysis description., contributed to the classification of most studies as having a medium risk of bias, highlighting the need for more accuracy in the description of the methodology, even in laboratory studies [45].

Even if the present systematic review considered only laboratory studies, the obtained results reveal that the use of the eugenol-containing temporary material affects the bond strength of adhesive systems, at least up to one week. Further studies should be conducted considering longer exposure time to determine until when eugenol based material compromises the bond strength of the adhesive system, enabling to outline a protocol for temporary restorations.

5. Conclusions

Based on this meta-analysis of in vitro studies, temporary eugenol-based materials reduced the bond strength values of adhesive systems to dentin, regardless of the bonding approach. The adverse effect disappears if the temporary eugenol-based restoration is maintained for at least 14 days.

Acknowledgements

This work was partially supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

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Tables and illustrations

Paper	Country	Substrate	Teeth origin	Teeth per group	Exposure time	Temporary Cement	Cleansing Method	Adhesive System	Composite/ Cement	Test
Al-Wazan et al. 1997	Saudi Arabia	Dentin	Human	10	7 days	Temp Bond Temp Bond NE	Excavator Pumice	Gluma	FluoroCore Ti-Core	SBS
Bagis et al., 2011	Turkey	Dentin	Human	5	7 days	Temp Bond Temp Bond NE	Scaler	Single Bond Clearfil Liner Bond 2V	RelyX ARC Panavia F Rely X Unicem	μTBS
Boushell et al., 2011	United States	Dentin	Human	10	10 days	IRM	Hand instument	LS System Adhesive Self-Etch Primer and Bond Adper Scotchbond SE	Filtek LS Filtek Z250	SBS
Carvalho et al., 2007	Brazil	Dentin	Human	6	24 hours	IRM	Scaler Pumice	Single Bond Clearfil SE Bond iBond	Filtek Z250	μSBS
Erkut et al., 2007	Turkey	Dentin	Human	10	7 days	Rely X Temp NE Rely X Temp E	Scaler Pumice	Single Bond One-Step	RelyX ARC Duo Link	SBS
Fiori-Júnior et al., 2010	Brazil	Dentin	Human	10	24 hours	Hydro C RelyX Temp NE	Excavator	Single Bond	RelyX ARC	SBS

						Temp Bond			RelyX Unicem	
Fonseca et al., 2005	Brazil	Dentin	Bovine	5	7 days	Dycal Provy TempBond NE	Scaler Pumice Sandblasting	Single Bond	RelyX ARC Filtek Z250	μTBS
Frankenberger et al., 2007	Germany	Dentin	Human	20	7 days	TempBond TempBond NE	Scaler Prophypearls Clinpro powder	XP Bond/SCA Syntac Optibond FL	Calibra	μTBS
Han et al., 2008	China	Dentin	Human	10	24 hours	ZOE cement Zinc phosphate cement	75% alcohol	Super-Bond C&B adhesive	Super-Bond C&B	SBS
Leirskar et al., 2000	Norway	Dentin	Human	17 16 16	6 days	ZOE	Hand instrument Ethanol 96%	Scotchbond Multi-Purpose	Z100	SBS
Macch et al., 1992	Argentina	Dentin	Human	7 19 19 15 15 12	15 min 48 hours	IRM Grossman Maistro Dycal Lumicon Cavit	Scaler Dry cotton pallet	Prisma Universal Bond	Fulfil	TBS
Martin et al., 1997	Switzerland	Dentin	Human	8	24 hours	Freegenol Temp Bond	Scaler Cotton pallet Pumice	Prime & Bond 2.0	Dyract Cem	SBS
Mayer et al., 1997	Germany	Dentin	Human	20	24 hours	Temp Bond	Spatula	Ecusit Optibond	Exp luting resin composite Herculite	TBS

Munirathinam et al., 2012	India	Dentin	Human	5	24 hours	ZOE Temp NE	Water and air Pumice Ultrasonic scaler + 0,2 chlorhexidine Cotton pallet + EDTA	Excite DSC	Variolink II + Esthet X Micromatrix	SBS
Nasreen et al., 2014	India	Dentin	Human	10	24 hours 7 days 14 days	Orafil-G IRM	Scaler + pumice	Adper SE Plus Adper Easy One	Filtek Z-350	SBS
Paul et al., 1997	Switzerland	Dentin	Human	8	24 hours	Temp Bond Freegenol Fermit Kerr Life	Cotton pallet + pumice	ART Bond AllBond2 Syntac P-Bond	Porcelite U Dual Cement	SBS
Peutzfeld et al., 1999	Denmark	Dentin	Human	8	7 days	Cavit IRM	Carving instrument + water	Scotchbond Multi-Purpose Plus Gluma CPS	Z100	SBS
Peutzfeld et al., 2006	Denmark	Dentin	Human	8	7 days	IRM	Spatula	Gluma Classic OptiBond FL AdheSE AdperPrompt L-Pop Clearfil SE Bond iBond OptiBond Solo Plus Xeno III	Herculite XRV	SBS

Pinto et al., 2014	Brazil	Dentin	Human	5	24 hours 7 days 45 days	IRM	Spatula	Adper Sigle Bond 2 Clearfil S3 Bond System	Opalis	μTBS
Ribeiro et al., 2011	Brazil	Dentin	Human	5	7 days	Temp Bond Freegenol	Dental instrument, cotton pallet and pumice	Adper Single Bond 2 Adper Prompt	RelyX ARC	μTBS
Salama et al., 2005	United States	Dentin	Human primary	8	7 days	ZOE 10:1 ZOE 10:2	Ultrasonic scaler	Prime & Bond NT Opti Bond Solo Plus	Herculite XRV	SBS
Sanabe et al., 2009	Brazil	Dentin	Human	4	7 days	IRM Cavit	Dental instrument and pumice	Adper Single Bond Clearfil SE Bond	Z250	μTBS
Silva et al., 2011	Brazil	Dentin	Human	10	24 hours 7 days 14 days	IRM	Scaler and pumice	Adper SE Plus	Filtek Z-350	μSBS
Terata et al., 1994	Japan	Dentin	Bovine	10	7 days	Eugedain Propac Nogenol Freegenol HY Bond	Dental probe	Super-Bond C&B	Super-Bond C&B	TBS
Wongsorachai et al., 2018	Thailand	Dentin	Human	5	24 hours	IRM	Ultrassonic scaler and pumice	OptiBond FL Clearfil SE Bond	Filtex Z350 XT	μTBS
Yap et al., 2001	Singapore	Dentin	Human	8	7 days	IRM Hy-Bond	Ultrassonic scaler and pumice	Scotchbond Multi-Purpouse Plus	Z100	SBS

Zhang et al., 2004	China	Dentin	Bovine	8	7 days	ZOE	Mechanically removed and rinsed with water	Gluma Prime & Bond NT	Charisma	SBS

μSBS: microshear bond strength; μTBS: microtensile bond strength; SBS: shear bond strength; TBS: tensile bond strength

Table 1 – Descriptive data from included studies in systematic review.

Paper	Randomization	Sample size	Teeth free of caries	Similar cross section	Failure mode	Manufacturer´s instructions	Single operator	Operator blinded	Cleansing method	Risk of bias
Al Wazan	Y	N	N	Y	N	Y	N	N	Y	medium
Bagis	Y	N	Y	Y	Y	Y	N	N	Y	medium
Boushell	Y	N	Y	Y	Y	Y	N	N	Y	medium
Carvalho	N	N	Y	Y	Y	Y	N	N	Y	medium
Erkut	N	N	Y	Y	N	Y	N	N	Y	medium
Fiori-Junior	Y	N	N	Y	N	Y	N	N	Y	medium
Fonseca	N	N	Y	Y	N	Y	N	N	Y	medium
Frankenberger	Y	N	Y	Y	N	N	N	N	Y	medium
Han	Y	N	Y	Y	N	Y	N	N	Y	medium
Leirskar	N	N	Y	Y	Y	Y	N	N	Y	medium
Macchi	Y	N	Y	Y	N	N	N	N	Y	medium
Martin	Y	N	N	N	N	N	N	N	Y	high
Mayer	N	Y	Y	Y	N	Y	N	N	Y	medium
Munirathinam	N	N	Y	Y	Y	Y	N	N	Y	medium
Nasreen	Y	N	Y	Y	N	Y	N	N	Y	medium
Paul	Y	N	N	Y	N	Y	N	N	Y	medium
Peutzfeld	Y	N	Y	Y	N	Y	N	N	Y	medium
Peutzfeld	Y	N	Y	Y	N	Y	N	N	Y	medium
Pinto	N	N	Y	Y	Y	Y	N	N	Y	medium
Ribeiro	Y	N	Y	Y	Y	Y	N	N	Y	medium
Salama	Y	N	Y	Y	N	Y	N	N	Y	medium
Sanabe	N	N	Y	Y	Y	Y	N	N	Y	medium
Silva	Y	N	Y	Y	N	Y	N	N	Y	medium
Terata	N	N	N	Y	N	Y	N	N	Y	high
Wongsorachai	Y	N	Y	Y	Y	Y	N	N	Y	medium
Yap	Y	N	Y	Y	Y	Y	N	N	Y	medium
Zhang	Y	N	N	Y	Y	Y	N	N	Y	medium

Table 2 – Risk of bias assessment.

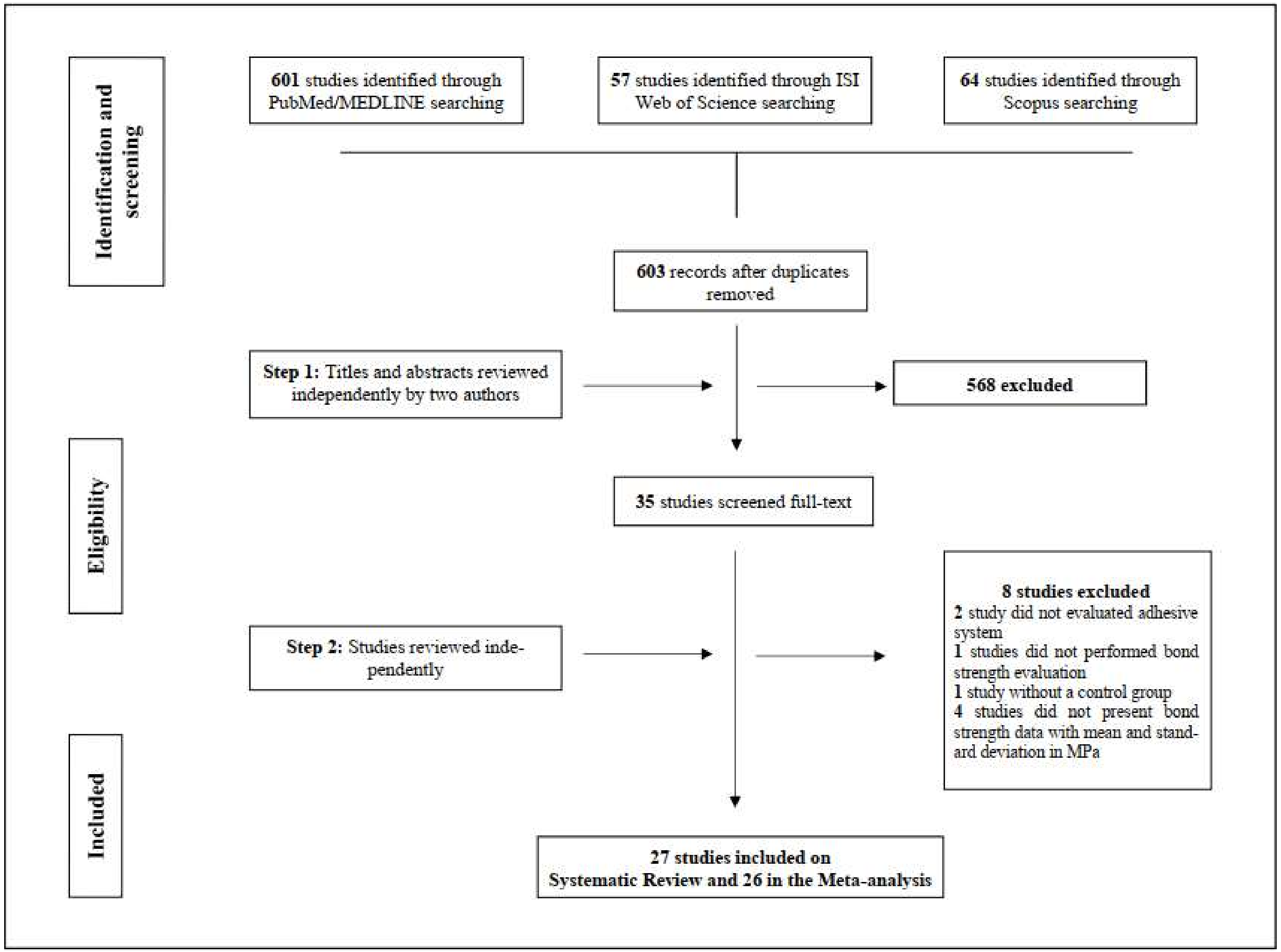

Figure 1 – Flowchart diagram of study selection according to PRISMA statement.

Study or Subgroup	Eugenol Mean	Eugenol SD	Eugenol Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Al Wazan 1997	4.02	2.83	20	6.77	3.42	40	4.1%	-0.84 [-1.40, -0.28]
Bagis 2011	15.74	5.7	15	21	8.35	30	3.8%	-0.68 [-1.32, -0.04]
Boushell 2011	16.6	7.77	20	28	7.08	20	3.6%	-1.50 [-2.21, -0.79]
Carvalho 2007	23.9	6.28	18	29.3	4.51	18	3.6%	-0.97 [-1.66, -0.27]
Erkut 2007	17	5.4	40	18.27	6.83	60	4.5%	-0.20 [-0.60, 0.20]
Fiori-Junior 2010	4.51	2.72	20	5.33	2.24	60	4.2%	-0.34 [-0.85, 0.17]
Fonseca 2005	25.05	5.37	15	23.63	5.37	30	3.9%	0.26 [-0.36, 0.88]
Han 2008	15.51	3.15	10	16.95	1.94	10	3.0%	-0.53 [-1.42, 0.37]
Leirskar 2000	25.87	8.72	33	19	6	16	3.9%	0.85 [0.23, 1.47]
Macchi 1992	1.41	1.02	19	1.59	1.25	68	4.2%	-0.15 [-0.66, 0.36]
Martin 1997	0.27	0.42	8	2.54	2.71	16	3.0%	-0.97 [-1.87, -0.07]
Mayer 1997	11.4	8.55	40	12.4	8.01	40	4.4%	-0.12 [-0.56, 0.32]
Munirathinam 2012	2.65	0.59	20	4.67	0.48	20	2.6%	-3.68 [-4.73, -2.63]
Nasreen 2014	19.5	5.1	60	22.23	2.62	20	4.2%	-0.59 [-1.10, -0.07]
Paul 1997	4.18	6.72	32	6.75	6.29	128	4.6%	-0.40 [-0.79, -0.01]
Peutzfeld 1999	16.5	7.26	16	17.5	6.01	32	3.9%	-0.15 [-0.75, 0.45]
Peutzfeld 2006	13.93	6.87	64	14.44	6.27	64	4.7%	-0.08 [-0.42, 0.27]
Pinto 2014	40.47	17.98	30	49.75	12.08	10	3.5%	-0.54 [-1.27, 0.18]
Ribeiro 2011	33.4	14.68	10	38.95	15.49	20	3.4%	-0.35 [-1.12, 0.41]
Salama 2005	9.94	2.07	32	12.22	1.02	16	3.8%	-1.25 [-1.90, -0.59]
Sanabe 2009	35.9	14.76	8	40.92	12.24	16	3.1%	-0.37 [-1.23, 0.49]
Silva 2011	23.36	5.83	90	24.8	6.11	30	4.5%	-0.24 [-0.66, 0.17]
Terata 1994	9.7	2.39	20	10.62	2.54	40	4.1%	-0.36 [-0.91, 0.18]
Wongsorachai 2018	37.13	9.68	30	51.49	4.99	30	3.9%	-1.84 [-2.45, -1.23]
Yap 2001	17.08	4.95	16	18.97	7.2	16	3.6%	-0.30 [-1.00, 0.40]
Zhang 2004	13.75	4.52	16	13.23	4.57	16	3.6%	0.11 [-0.58, 0.81]
Total (95% CI)			**702**			**866**	**100.0%**	**-0.53 [-0.77, -0.29]**

Heterogeneity: $Tau^2 = 0.29$; $Chi^2 = 112.45$, df = 25 ($P < 0.00001$); $I^2 = 78\%$
Test for overall effect: $Z = 4.30$ ($P < 0.0001$)

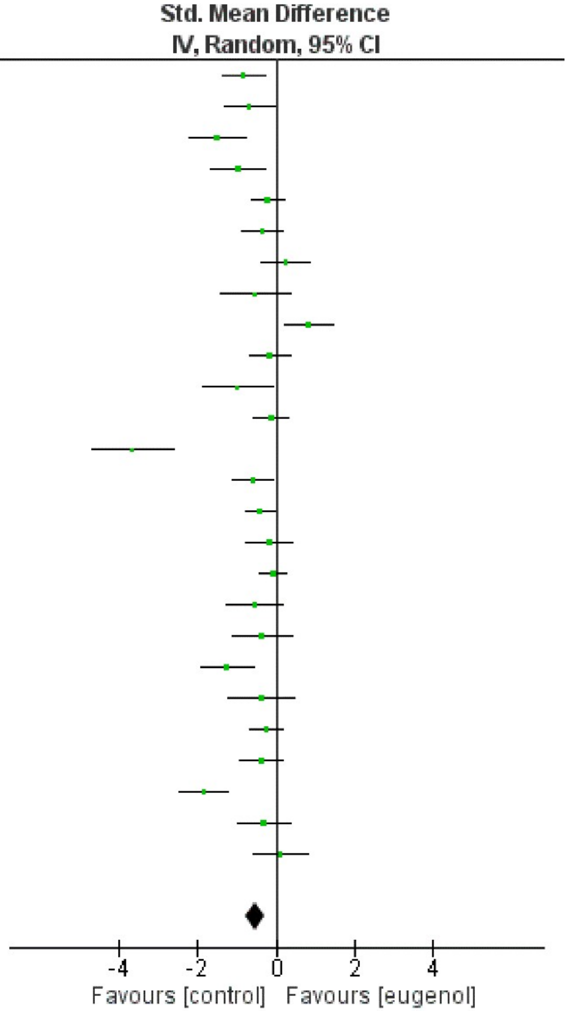

Figure 2 – Global meta-analysis of bond strength, in MPa. Substrates previously exposed to eugenol-based materials versus control.

	Eugenol for 24h			Control				Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Carvalho 2007	23.9	6.28	18	13.9	4.51	18	9.2%	1.79 [1.00, 2.57]
Fiori-Junior 2010	4.51	2.72	20	5.33	2.24	60	9.7%	-0.34 [-0.85, 0.17]
Han 2008	15.51	3.15	10	16.95	1.94	10	8.9%	-0.53 [-1.42, 0.37]
Martin 1997	0.27	0.42	8	2.54	2.71	16	8.9%	-0.97 [-1.87, -0.07]
Mayer 1997	11.4	8.55	40	12.4	8.01	40	9.8%	-0.12 [-0.56, 0.32]
Munirathinam 2012	2.65	0.59	20	4.67	0.48	20	8.5%	-3.68 [-4.73, -2.63]
Nasreen 2014	13.18	1.44	20	22.23	2.62	20	8.2%	-4.20 [-5.35, -3.05]
Paul 1997	4.18	6.72	32	6.75	6.29	128	9.9%	-0.40 [-0.79, -0.01]
Pinto 2014	33.6	14.17	10	49.75	12.08	10	8.7%	-1.17 [-2.14, -0.21]
Silva 2011	13.9	3.4	10	24.3	8.4	10	8.6%	-1.55 [-2.58, -0.53]
Wongsorachai 2018	37.13	9.68	30	51.49	4.99	30	9.5%	-1.84 [-2.45, -1.23]
Total (95% CI)			**218**			**362**	**100.0%**	**-1.12 [-1.88, -0.37]**

Heterogeneity: $Tau^2 = 1.44$; $Chi^2 = 133.18$, df = 10 (P < 0.00001); $I^2 = 92\%$
Test for overall effect: Z = 2.93 (P = 0.003)

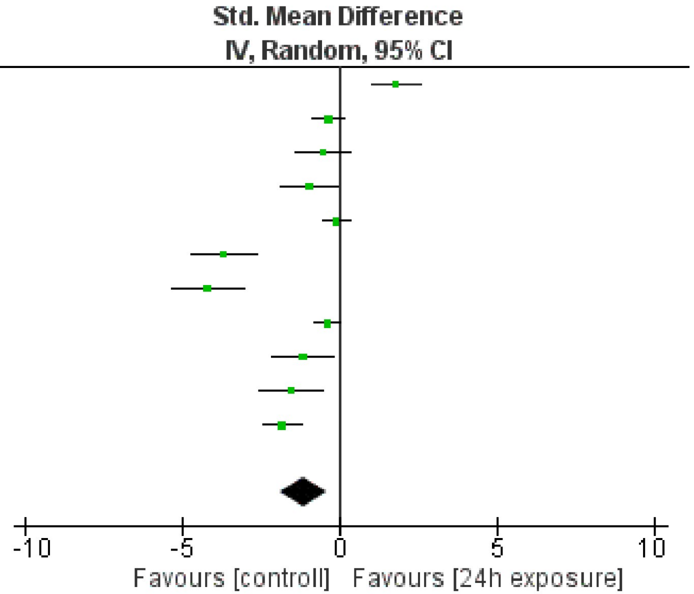

Figure 3 – Subgroup meta-analysis of bond strength, in MPa. Substrates previously exposed to eugenol-based materials for 24 hours versus control.

Study or Subgroup	Eugenol Mean	Eugenol SD	Eugenol Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Fixed, 95% CI
Al Wazan 1997	4.02	2.83	20	6.77	3.42	40	10.9%	-2.75 [-4.38, -1.12]
Bagis 2011	15.74	5.7	15	21	8.35	30	1.7%	-5.26 [-9.41, -1.11]
Erkut 2007	17	5.4	40	18.27	6.83	60	5.0%	-1.27 [-3.68, 1.14]
Fonseca 2005	25.05	5.37	15	23.63	5.37	30	2.6%	1.42 [-1.91, 4.75]
Nasreen 2014	22.93	2.51	20	22.23	2.62	20	11.5%	0.70 [-0.89, 2.29]
Peutzfeld 1999	16.5	7.26	16	17.5	6.01	32	1.7%	-1.00 [-5.12, 3.12]
Peutzfeld 2006	13.93	6.87	64	14.44	6.27	64	5.6%	-0.51 [-2.79, 1.77]
Pinto 2014	40.55	23.8	10	49.75	12.08	10	0.1%	-9.20 [-25.74, 7.34]
Ribeiro 2011	33.4	14.68	10	38.95	15.49	20	0.2%	-5.55 [-16.90, 5.80]
Salama 2005	9.94	2.07	32	12.22	1.02	16	38.0%	-2.28 [-3.15, -1.41]
Sanabe 2009	35.9	14.76	8	40.92	12.24	16	0.2%	-5.02 [-16.88, 6.84]
Silva 2011	26	3.8	10	24.3	8.4	10	0.9%	1.70 [-4.01, 7.41]
Terata 1994	9.7	2.39	20	10.62	2.54	40	16.9%	-0.92 [-2.23, 0.39]
Yap 2001	17.08	4.95	16	18.97	7.2	16	1.6%	-1.89 [-6.17, 2.39]
Zhang 2004	13.75	4.52	16	13.23	4.57	16	2.9%	0.52 [-2.63, 3.67]
Total (95% CI)			**312**			**420**	**100.0%**	**-1.44 [-1.98, -0.90]**

Heterogeneity: $Chi^2 = 24.76$, $df = 14$ ($P = 0.04$); $I^2 = 43\%$

Test for overall effect: $Z = 5.22$ ($P < 0.00001$)

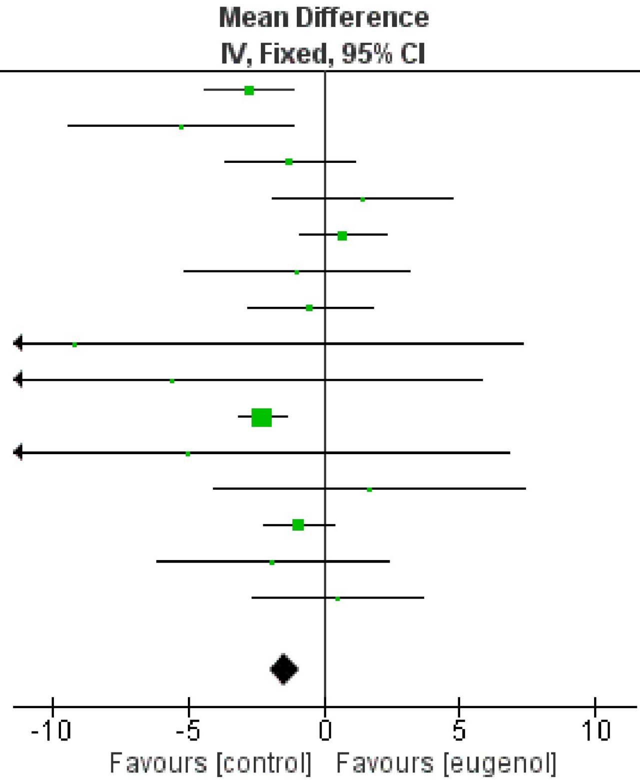

Figure 4 – Subgroup meta-analysis of bond strength, in MPa. Substrates previously exposed to eugenol-based materials for 7 days versus control.

Study or Subgroup	Eugenol Mean	Eugenol SD	Eugenol Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Nasreen 2014	22.41	3.01	20	22.23	2.62	20	50.1%	0.06 [-0.56, 0.68]
Pinto 2014	47.25	13.06	10	49.75	12.08	10	24.9%	-0.19 [-1.07, 0.69]
Silva 2011	24.1	4.2	10	24.3	8.4	10	25.0%	-0.03 [-0.91, 0.85]
Total (95% CI)			**40**			**40**	**100.0%**	**-0.02 [-0.46, 0.42]**

Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 2 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.10 (P = 0.92)

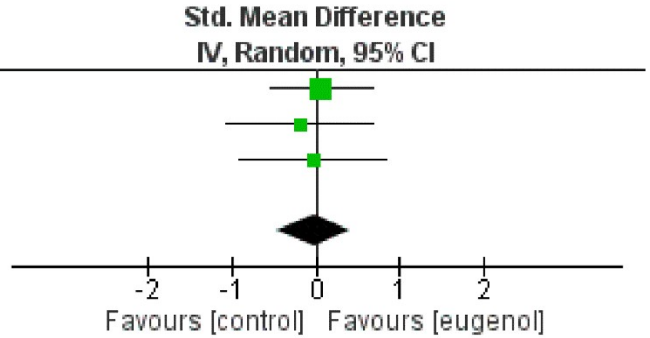

Figure 5 – Subgroup meta-analysis of bond strength, in MPa. Substrates previously exposed to eugenol-based materials for 14 to 45 days versus control.

Study or Subgroup	Eugenol Mean	Eugenol SD	Eugenol Total	No Eugenol Mean	No Eugenol SD	No Eugenol Total	Weight	Std. Mean Difference IV, Random, 95% CI
Al Wazan 1997	4.02	2.83	20	6.82	3.48	20	7.0%	-0.87 [-1.52, -0.21]
Bagis 2011	15.74	5.7	15	16.95	4.16	15	6.6%	-0.24 [-0.95, 0.48]
Erkut 2007	14.1	4.29	20	12.34	4.25	20	7.1%	0.40 [-0.22, 1.03]
Fiori-Junior 2010	4.51	2.72	20	5.75	2.2	40	7.5%	-0.51 [-1.06, 0.03]
Fonseca 2005	25.05	5.37	15	23.63	5.37	30	7.1%	0.26 [-0.36, 0.88]
Macchi 1992	1.41	1.02	19	1.43	1.09	61	7.7%	-0.02 [-0.53, 0.50]
Martin 1997	0.27	0.42	8	2.07	3.4	8	5.1%	-0.70 [-1.72, 0.32]
Munirathinam 2012	2.65	0.59	20	4.67	0.48	20	4.9%	-3.68 [-4.73, -2.63]
Nasreen 2014	19.5	5.1	60	22.23	2.62	20	7.7%	-0.59 [-1.10, -0.07]
Paul 1997	4.18	6.71	32	6.84	5.95	96	8.3%	-0.43 [-0.83, -0.03]
Peutzfeld 1999	16.5	7.26	16	18	6.02	16	6.7%	-0.22 [-0.91, 0.48]
Ribeiro 2011	33.4	14.68	10	39.25	17.43	10	5.7%	-0.35 [-1.23, 0.54]
Sanabe 2009	35.9	14.76	8	39.95	11.35	8	5.2%	-0.29 [-1.28, 0.70]
Terata 1994	9.7	2.39	20	10.33	2.31	30	7.4%	-0.26 [-0.83, 0.30]
Yap 2001	17.08	4.95	16	15.35	4.83	8	5.9%	0.34 [-0.52, 1.20]
Total (95% CI)			**299**			**402**	**100.0%**	**-0.42 [-0.76, -0.08]**

Heterogeneity: Tau² = 0.33; Chi² = 56.38, df = 14 (P < 0.00001); I² = 75%
Test for overall effect: Z = 2.39 (P = 0.02)

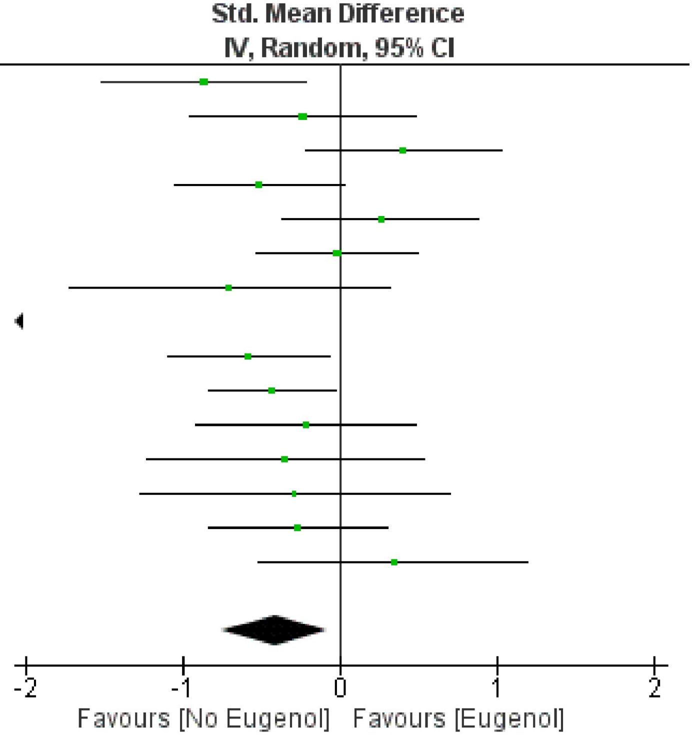

Figure 6 – Subgroup meta-analysis of bond strength, in MPa. Substrates previously exposed to eugenol-based materials versus control using luting cements.

Study or Subgroup	Eugenol Mean	Eugenol SD	Eugenol Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Al Wazan 1997	4.02	2.83	20	6.77	3.42	40	5.0%	-0.84 [-1.40, -0.28]
Bagis 2011	19.08	6.07	5	23.13	6.12	10	3.3%	-0.62 [-1.73, 0.48]
Carvalho 2007	28.3	3.8	6	31.3	2.7	6	3.0%	-0.84 [-2.04, 0.36]
Erkut 2007	17	5.4	40	18.27	6.83	60	5.5%	-0.20 [-0.60, 0.20]
Fiori-Junior 2010	4.51	2.72	20	5.33	2.24	60	5.2%	-0.34 [-0.85, 0.17]
Fonseca 2005	25.05	5.37	15	23.63	5.37	30	4.8%	0.26 [-0.36, 0.88]
Han 2008	15.51	3.15	10	16.95	1.94	10	3.9%	-0.53 [-1.42, 0.37]
Leirskar 2000	25.87	8.72	33	19	6	16	4.8%	0.85 [0.23, 1.47]
Macchi 1992	1.41	1.02	19	1.59	1.25	68	5.2%	-0.15 [-0.66, 0.36]
Martin 1997	0.27	0.42	8	2.54	2.71	16	3.9%	-0.97 [-1.87, -0.07]
Mayer 1997	5.9	4.9	20	7.5	4.5	20	4.8%	-0.33 [-0.96, 0.29]
Munirathinam 2012	2.65	0.59	20	4.67	0.48	20	3.4%	-3.68 [-4.73, -2.63]
Paul 1997	4.18	6.72	32	6.75	6.29	128	5.6%	-0.40 [-0.79, -0.01]
Peutzfeld 1999	16.5	7.26	16	17.5	6.01	32	4.9%	-0.15 [-0.75, 0.45]
Peutzfeld 2006	18.45	10.38	16	19.6	7.8	16	4.6%	-0.12 [-0.82, 0.57]
Pinto 2014	43.03	14.01	15	60.4	5.2	5	3.3%	-1.32 [-2.43, -0.21]
Ribeiro 2011	39.4	15.6	5	46.15	16.34	10	3.3%	-0.39 [-1.48, 0.69]
Salama 2005	9.94	2.07	32	12.22	1.02	16	4.7%	-1.25 [-1.90, -0.59]
Sanabe 2009	41.7	15.1	4	41.35	13.7	8	3.0%	0.02 [-1.18, 1.22]
Terata 1994	9.7	2.39	20	10.62	2.54	40	5.1%	-0.36 [-0.91, 0.18]
Wongsorachai 2018	40.87	6.98	15	54.18	3.82	15	3.7%	-2.30 [-3.25, -1.35]
Yap 2001	17.08	4.95	16	18.97	7.2	16	4.6%	-0.30 [-1.00, 0.40]
Zhang 2004	13.75	4.52	16	13.23	4.57	16	4.6%	0.11 [-0.58, 0.81]
Total (95% CI)			**403**			**658**	**100.0%**	**-0.53 [-0.82, -0.24]**

Heterogeneity: Tau² = 0.36; Chi² = 92.29, df = 22 (P < 0.00001); I² = 76%

Test for overall effect: Z = 3.59 (P = 0.0003)

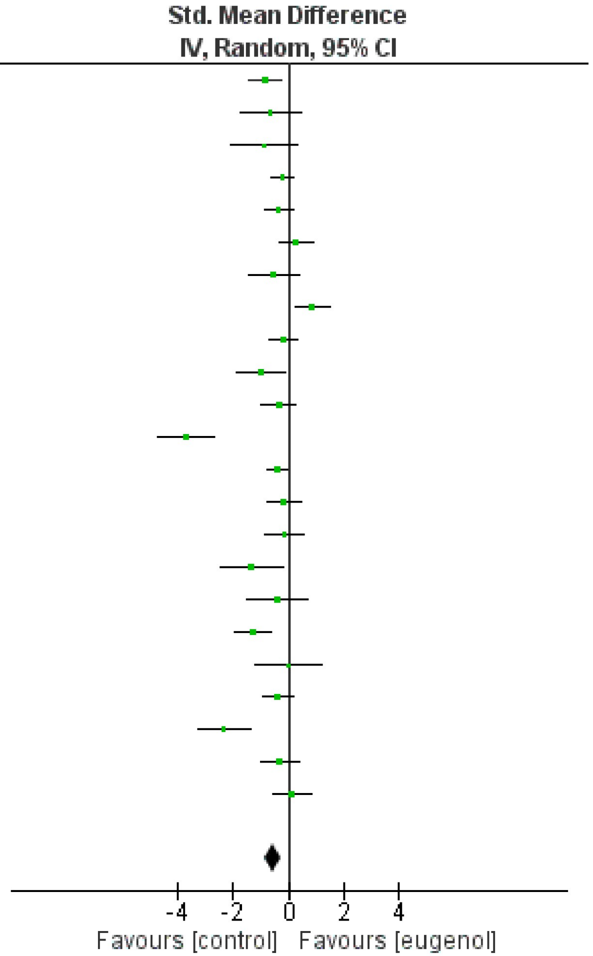

Figure 7 – Subgroup meta-analysis of bond strength, in MPa. Substrates previously exposed to eugenol-based materials versus control using total-etch adhesive.

Study or Subgroup	Eugenol Mean	Eugenol SD	Eugenol Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Random, 95% CI
Bagis 2011	14.21	6.19	5	24.36	10.34	10	6.4%	-1.03 [-2.19, 0.13]
Boushell 2011	16.6	7.77	20	28	7.08	20	9.9%	-1.50 [-2.21, -0.79]
Carvalho 2007	21.7	6.21	12	27.9	4.89	12	8.5%	-1.07 [-1.94, -0.20]
Mayer 1997	16.9	7.9	20	17.3	7.8	20	10.8%	-0.05 [-0.67, 0.57]
Nasreen 2014	19.5	5.1	60	22.23	2.62	20	11.8%	-0.59 [-1.10, -0.07]
Peutzfeld 2006	12.42	4.43	48	12.72	4.6	48	12.8%	-0.07 [-0.47, 0.33]
Pinto 2014	24.57	8.28	15	39.1	4.2	5	6.1%	-1.84 [-3.03, -0.64]
Ribeiro 2011	27.4	12.3	5	31.75	11.19	10	6.8%	-0.35 [-1.44, 0.73]
Sanabe 2009	30.1	13.8	4	40.5	11.53	8	5.7%	-0.78 [-2.04, 0.48]
Silva 2011	23.36	5.83	90	24.8	6.11	30	12.7%	-0.24 [-0.66, 0.17]
Wongsorachai 2018	33.52	10.69	15	48.82	4.65	15	8.5%	-1.81 [-2.67, -0.94]
Total (95% CI)			**294**			**198**	**100.0%**	**-0.75 [-1.14, -0.37]**

Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 31.97$, df = 10 (P = 0.0004); $I^2 = 69\%$
Test for overall effect: Z = 3.83 (P = 0.0001)

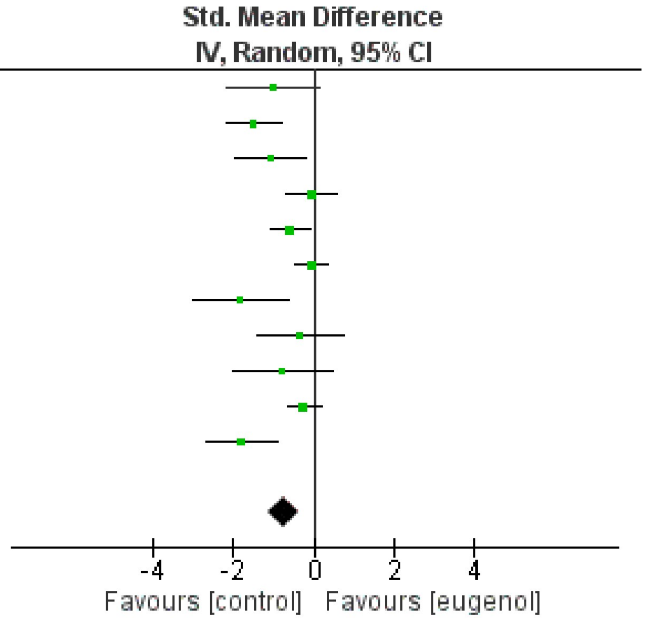

Figure 8 – Subgroup meta-analysis of bond strength, in MPa. Substrates previously exposed to eugenol-based materials versus control using self-etch adhesive.

Highlights

Temporary eugenol-based materials significantly reduce bond strength of adhesive systems from 24 hours to 7 days.

Temporary eugenol-based materials have no significant influence on bond strength values of adhesive systems after 14 to 45 days.

Temporary eugenol-based materials significantly reduce bond strength values of adhesive systems independently of the etching strategy.

3 ARTIGO 2 - EFFECT OF TIME OF EUGENOL-BASED TEMPORARY CEMENT RESTORATIONS ON DENTIN BOND STRENGTH

Este artigo será submetido ao periódico The Journal of Adhesive Dentistry, Quintessence, ISSN: 1461-5185, Fator de impacto = 2.379; Qualis A2. As normas para publicação estão descritas no Anexo A.

Effect of time of eugenol-based temporary cement restorations on dentin bond strength

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Keywords: Adhesion; Eugenol; Dentin; Dental Cements; Adhesives; Microshear Bond Strength.

Acknowledgments

This study was financed by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

Effect of time of eugenol-based temporary cement restorations on dentin bond strength

Abstract

Purpose: To evaluate the effect of zinc oxide-eugenol (ZOE) temporary restorative cement on the bond strength of a total-etch adhesive system.

Materials and methods: Microshear bond strength to bovine dentin previously exposed to a ZOE temporary restorative cement by different times were assessed. Flat dentin surfaces from sixty-four sound bovine incisors (n=8) were exposed to ZOE temporary restorative cement for 24 hours and 7, 15, 30, 60, 120, and 180 days before adhesive system (Adper Single Bond 2) application. Dentinal surfaces not exposed to ZOE temporary restorative cement were considered as a control group. Immediately after temporary cement mechanically removal, resin composite cylinders (0.72mm2) were built and submitted to the microshear bond strength test (μSBS) after 24h. Failure analysis was performed using a stereomicroscope (400X). Data analysis used Kruskal Wallis, and post hoc Dunn tests (significance of 5%).

Results: Lower bond strength values were found with 24 hours, 7, 15, and 30 days ZOE temporary restorative cement exposition compared to the control group ($p<0.05$). Similar bond strength was found between ZOE temporary restorative cement exposition times of 60, 120, and 180 days and control group.

Conclusion: ZOE temporary restorative cement jeopardizes the dentin bond strength of a total-etch adhesive system for up to 30 days. The negative influence of ZOE temporary restorative cement on bonding ceases after 60 days of restoration placement.

Introduction

Zinc oxide-eugenol (ZOE) cement is commonly used as a temporary restorative material in endodontics;[11,25] and restorative dentistry[4] because of its excellent analgesic and sealing properties, radiopacity, low cost, and easy removal. Possibly the main limitation of ZOE cement is its negative effect on polymeric materials, impairing their polymerization.[7] Eugenol, a phenolic component of ZOE cement molecule has radical-scavenging activity, inhibiting free radical polymerization in methacrylate systems.[3,10] Accordingly, adhesive systems based on bis-GMA and HEMA are affected. Besides that, the cement particles that remain on the smear layer and inside the dentin tubules may also contribute to the delaying of the polymerization reaction, reducing bond strength at the adhesive interface[2,5,12,18,24] and acting as a physical barrier to monomers diffusion.

The adverse effect of ZOE temporary restorative cement on adhesive systems, as lower bond strength values, has been described[2,5,18,22] for both total-etch and self-etch adhesive systems. However, no influence has also been observed in other studies.[1,3,8,19,23,30] It is fair to suppose that the eugenol released may interact with calcium ions from hydroxyapatite after acid-etching, minimizing its negative effect on resin polymerization. However, eugenol-free cement also reduced bond strength to previously exposed dentin,[28] also supporting the detrimental effect of cements particle, as the removal of temporary cement by mechanical means seems to not be totally effective, leaving remnants inside the substrate, especially in dentin, because its structure allows the accumulation of material inside the dentinal tubules. Substrates that appear clinically clean may contain remnants of cement particles when observed under microscopy.[27]

Besides that, few studies evaluated the effect of eugenol on dentin bond strength for periods longer than 15 days, and the results are also controversial.[14,21] Thus, this study aimed to evaluate the effect of zinc oxide-eugenol temporary restorative cement on the bond strength of a total-etch adhesive system. The null hypotheses tested were that: a) there would be no differences in the bond strength of the adhesive system to ZOE temporary restorative cement exposed and non-exposed dentin, b) the ZOE temporary restorative cement exposure time would not influence the bond strength values.

Material and Methods

Tooth selection and preparation

Sixty-four freshly extracted, bovine incisors were stored in 0.5% chloramine at 4 ºC for up to 30 days before being used in this study. The root portion was removed using a diamond saw under water-cooling in a low-speed handpiece. The buccal surfaces were ground under water cooling using a 100-grit SiC paper in a polishing machine (EcoMet250, Buehler, Lake Bluff, IL, USA) to expose and obtain flat dentin surfaces which were further ground manually on wet #600-grit SiC paper for 60 seconds to standardize the smear layer.

Experimental design

The teeth were randomly assigned into 7 experimental groups (n=8) according to the ZOE temporary restorative cement exposure time (24 hours, 7, 15, 30, 60, 120, and 180 days), and the control group, without ZOE temporary restorative cement exposure.

Temporary restoration

Dentinal surfaces were covered with a thick layer of a polymer reinforced zinc oxide-eugenol temporary restorative cement (IRM, Dentsply Sirona, Petrópolis, Brazil) mixed according to manufacturer´s instructions and pressed against the surface with a glass slide.[5] After setting, specimens covered with ZOE temporary restorative cement were stored in distilled water at 37 ºC for the corresponding evaluation times. After each exposure time, the ZOE temporary restorative cement was removed mechanically using a spatula. The dentin surfaces were rinsed with air-water spray for 15 seconds and dried with mild airflow for 5 seconds.[24] Teeth from the control group were not exposed to ZOE temporary restorative cement.

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Bonding procedures

All bonding procedures were performed immediately after the ZOE temporary restorative cement removal. The 2-steps total-etch adhesive system Adper Single Bond 2 (3M ESPE, St. Paul, MN, USA) was applied following manufacturers' instructions by a single trained operator. Before the light-curing of the adhesive, starch tubes (1 mm high x 0,96 mm internal diameter) were positioned over the dentin.[26] After light-curing the adhesive, the composite resin (Z250, 3M ESPE, St. Paul, MN, USA) was applied into the starch tubes and using a WHO periodontal probe (Golgran, São Caetano do Sul, SP, Brazil). After that each filled tube was individually light-cured for 20 seconds, with a curing light (EMITTER C, SCHUSTER, Santa Maria, RS, Brazil). In each dentinal surface, 5 composite resin cylinders were built. The teeth with cylinders specimens were stored at 37 ºC in deionized water for 24 hours before the microshear bond strength test.

Microshear bond strength (μSBS) test

After storage the starch tubes were removed with water spray and Each specimen was examined under a stereomicroscope at 40X magnification (Stereo Discovery V20, Carl Zeiss; Rio de Janeiro, RJ, Brazil), and those with interfacial gaps, bubble inclusion, or other defects were excluded and replaced. The teeth were attached to a universal machine (Emic DL 1000, Equipment and Systems; São Jose dos Pinhais, PR, Brazil) using a stainless-steel wire loop (0.2 mm in diameter) placed as close as possible to resin/dentin interface. Shear force was applied at a crosshead speed of 1 mm/min until failure. All tests were performed by a single blinded operator.

Failure mode analysis

Specimens were examined under a stereomicroscope at 400X magnification by a blinded examiner. Failures were classified as mixed/adhesive (failure at the resin/dentin interface or mixed with cohesive failure of the adjacent substrate) or cohesive (resin composite or dentin).

Statistical Analysis

The experimental unit in the study was the tooth. Thus, the failure stress value for each tooth was calculated by averaging the values of the composite resin cylinders. The sample size had been determined that, considering a mean difference of 20% among groups and expecting a variation coefficient of 20%, a minimum of seven teeth per group was required to achieve a power of 0.8 and an error probability of 5%.

The bond strength values were calculated in MPa as means and standard deviations. Normal distribution of the data was not confirmed with the Kolmogorov-Smirnov test. The data were submitted to Kruskall-Wallis test, and post hoc Dunn test, at a significance level of 0.05. Statistical analyses were performed using Minitab software (Minitab; State College, PA, USA).

Results

The quantitative data are summarized in Table 2. The previous exposition to ZOE temporary restorative cement jeopardized the bond strength of the adhesive system to dentin even after 30 days. A statistically significant difference was found between the control group and the groups 24 hours ($p=0.006$), 7 days (0.028), 15 days ($p=0.013$) and 30 days ($p = 0.029$). No significant difference in µSBS was found between the control group and the groups 60 days ($p=0.91$); 120 days ($p=0.59$) and 180 days ($p=0.24$). No pre-testing failures were observed in any experimental group and all specimens showed adhesive mixed failure pattern.

Discussion

In the present study, ZOE restorative temporary cement significantly reduced the bond strength values at 30 days of exposition, leading us to partially reject the first null hypothesis. However, as the negative effect of ZOE temporary restorative cement on bonding was not detected after the exposure time of 60 days, leading us to reject the second null hypothesis. Two key factors attempt to explain the effect of eugenol-based materials on the reduced bonding properties of the adhesives to previously exposed dentin, as the influence on monomers' polymerization and mechanical obstruction of dentinal tubules by cement particles.

The setting reaction of the zinc oxide-eugenol cement is an acid-base chelation reaction to form a zinc eugenolate matrix surrounding by unreacted zinc oxide powder particles. This reaction is reversible on exposure to water, the matrix undergoes hydrolysis, with release eugenol to the environment.[20] Eugenol is a phenylpropanoid, a well-known free radical scavenger, that reacts with free radicals, inhibiting the polymerization of methacrylate monomers,[2] and compromising the bond strength. Thus, the eugenol incompatibility with the resin polymerization may explain the lower bond strength values obtained in this study in the first ZOE temporary restorative cement exposure times. Previous studies also found the negative effect of ZOE cement on the bond strength values, after the exposition time of 24 hours,[2,5,18,22] 7 days,[2,9,14] and even after 28 days of eugenol exposure.[14]

However, there are few data on the ZOE cement influence on the bond strength to dentin after longer exposure times, that could point out if eugenol negative effect would continue over time. ZOE temporary restorative cement did not affect the bond strength after exposition of 60 to 180 days comparing to control group. The authors speculate that the eugenol release cease after these times, as its interference on resin monomers' polymerization. A previous study already showed similar bond strength values between unexposed dentin and dentin exposed up to 45 days to ZOE temporary restorative cement.[21] Additionally, bond strength values remained stable up to 180 days, probably indicating that the eugenol released from the cement by hydrolysis was not able to reduce the adhesive polymerization after 60 days.[12] Furthermore, the replacement of the storage media (distilled water) every 7 days, avoiding eugenol saturation and simulating clinical situations[6] may also explain it.

Some authors attribute impaired bond strength to dentin previously exposed to ZOE temporary restorative cement to cement particles remaining on the smear layer and inside the dentin tubules, acting as a physical barrier that may compromise resin monomers infiltration and resin tags formation.[28,29] The cement removal is usually done mechanically with hand scaler or alongside with prophylaxis with pumice-water slurry,[16,27] even so, cement particles remain within the dentin tubules even though the dentin surface appears visually free of cement particles.[27] It remains to be seen, however, whether these particles are capable of damaging adhesion by eugenol releasing or acting as impurities on hybrid layer formation. According to Mayer et al. (1997)[15] the cement residues do not impair the bond strengths, even if ZOE particles interfere with the morphology of the resin-dentin hybrid layer as viewed under confocal laser scanning microscopy. In this study, after 60 days of ZOE temporary restorative cement, the bond strength of total-etch to dentin achieved similar values to non-exposed dentin (control group), supporting the idea that neither ZOE particles nor residual eugenol are able to interfere with bonding after longer times.

Probably the use of a total-etch adhesive system favored these results, likely reducing the amount of ZOE cement particles, as the pretreatment with phosphoric acid results in smear layer removal and intertubular dentin demineralization to a depth up to 10 μm,[17] being able to reduce the deleterious effect of prior ZOE temporary restorative cement dentin exposition.[1] Besides that, water rinsing after acid-etching also may contribute to remove the ZOE cement particles. Is worthy to mention that the adhesive used in this study has ethanol as one of the solvents and eugenol's high susceptibility to solvation in this media may have contributed to the presented results.[2] In this sense, further studies are required to explore more adhesive systems, mainly self-etch materials.

According to the present results, it may be hypothesized that longer delay times (at least 60 days) seems to be sufficient for eliminate the negative influence of ZOE temporary restorative cement on bonding, whereas freshly made ZOE temporary restorations compromised the bond strength to dentin.

Conclusion

Within the limitations of the current study, it is possible to conclude that the freshly ZOE temporary restorations jeopardize the dentin bond strength of a total-etch adhesive system to dentin. ZOE temporary restorations made after two months no longer have this negative effect.

Clinical relevance

The findings of this study suggest that restorative temporary cements containing eugenol may be safe to use prior resin restorations after two months of use.

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Tables

Table 1. Composition and manufacturer´s instructions of the materials used*

Material (Batch)	Composition	Application mode
IRM (Dentsply, Petrópolis, RJ, Brazil) (361346L)	1. Powder - zinc oxide, PMMA powder 2. Liquid - eugenol, acetic acid	1. Mixed at powder:liquid ratio 6:1 for 60 seconds
Fusion Duralink (Angelus, Londrina, PR, Brazil) 37% phosphoric acid (45347)	Phosphoric acid, filler, water, pigments	
Adper Single Bond 2 (3M-ESPE, St. Paul, MN, USA) (N868091)	Dimethacrylate resins, HEMA, Vitrebond™ Copolymer, Filler, Ethanol, Water, Initiators	1. Apply etchant for 15 seconds. Rinse for 10 seconds. Blot excess water using a cotton pellet or mini-sponge. The surface should appear glistening without pooling of water. 2. Immediately after blotting, apply 2-3 consecutive coats of adhesive for 15 seconds with gentle agitation using a fully saturated applicator. Gently air thin for five seconds to evaporate solvents. 3. Light cure for 10 seconds.
Filtek Z250 (3M-ESPE, St. Paul, MN, USA) (1924800555)	Bis-GMA, Bis-EMA, UDMA, zirconia, silica	1.Light-activation (40 seconds—600mW/cm^2)

*According information provided by manufacturers PMMA: polymethyl methacrylate; HEMA: 2-hydroxyethyl methacrylate; bis-EMA: ethoxylated bisphenol A dimethacrylate; bis-GMA: bisphenol A diglycidyl methacrylate; UDMA: urethane dimethacrylate

Table 2. µSBS (MPa) of the adhesive system to dentin of the experimental groups

Group according eugenol exposure and the time elapsed	Mean (standard deviation) [tested cylinders]	Median	Q1	Q3
Control	17.0 (2.7) [40]	16.4	15.5	17.9
24 hours	13.2 (1.4) [40]	12.7*	12.3	14.3
7 days	13.8 (2.5) [40]	13.1*	12.4	15.1
15 days	13.6 (2.4) [40]	12.7*	12.1	15.3
30 days	14.2 (3.4) [40]	13.1*	11.8	14.9
60 days	17.0 (2.3) [40]	17.4	15.4	18.2
120 days	15.8 (2.0) [40]	15.2	14.5	17.4
180 days	15.9 (4.1) [40]	14.1	13.4	17.9

Medians marked with * are significantly lower than the control group.

4 CONCLUSÃO

Com base nos achados do presente trabalho foi verificado que cimentos contendo eugenol na composição são capazes de influenciar de forma negativa a resistência de união de sistemas adesivos.

No primeiro trabalho, 27 estudos que avaliaram materiais contendo óxido de zinco e eugenol e sistemas adesivos foram selecionados dentre os 603 trabalhos iniciais encontrados nas principais bases de dados. Dos 27 estudos, 26 entraram na metanálise e foi realizada uma análise global, favorecendo o grupo controle. Nas análises por subgrupos, quando divididos em trabalhos que avaliaram 24 horas, 7 dias, cimentos resinosos, sistemas adesivos de condicionamento ácido total e sistemas adesivos autocondicionantes, todos independentemente, o grupo controle foi favorecido. Apenas a análise dos tempos entre 14 e 45 dias não apresentaram diferenças entre os grupos, possuindo um número muito pequeno de trabalhos com longos tempos de envelhecimento, indicando a necessidade de estudos que avaliem esses tempos ou tempos ainda maiores; o que levou a realização da segunda pesquisa.

No segundo trabalho, restaurações provisórias de OZE foram realizadas em dentina, mantidas por 24 horas, 7, 15, 30, 60, 120 e 180 dias e comparadas a um grupo controle, que não recebeu restaurações provisórias. Menores valores de resistência de união foram registrados nos grupos experimentais entre 24 horas e 30 dias. A partir de 60 dias, até 180 dias, OZE não teve influência estatisticamente significante nos valores de resistência de união com dentina.

Assim, conclui-se que os efeitos deletérios do eugenol na resistência de união de sistemas adesivos é dependente do tempo em que as restaurações provisórias com cimentos contendo eugenol na composição ficam em contato com o substrato até o momento da restauração final. Períodos de 24 horas até 7 dias são críticos, enquanto a partir de 14 dias os efeitos deletérios tendem a não serem mais percebidos.

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ANEXO A – NORMAS PARA PUBLICAÇÃO NO PERIÓDICO *THE JOURNAL OF ADHESIVE DENTISTRY*

GUIDELINES FOR AUTHORS

The Journal of Adhesive Dentistry is a bi-monthly journal that publishes scientifically sound articles of interest to practitioners and researchers in the field of adhesion to hard and soft dental tissues. The Journal publishes several types of peer-reviewed original articles:

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ANEXO B - NORMAS PARA PUBLICAÇÃO NO PERIÓDICO *DENTAL MATERIALS*

GUIDE FOR AUTHORS

INTRODUCTION

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• report statistical findings.

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