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Effect of cavity disinfectants on adhesion to primary teeth – A systematic review

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Resumo

O tratamento das lesões de cárie está, frequentemente, associado à remoção de tecido cariado e posterior restauração da estrutura dentária remanescente. Alguns autores têm vindo a propor o uso de desinfetantes cavitários para reduzir, ou mesmo eliminar, o efeito dos microrganismos presentes nas cavidades dentárias antes da sua restauração.

O presente estudo teve como objetivo avaliar o efeito da aplicação de diferentes desinfetantes cavitários na força de adesão e no sucesso clínico de restaurações em dentes temporários, quer em resina composta, quer em ionómero de vidro.

A pesquisa foi realizada com recurso às bases de dados *Cochrane Library*, *PubMed/MEDLINE*, *SCOPUS* e *Web of Science*, para artigos publicados até 14 de fevereiro de 2021. Nenhuma restrição de região, língua ou data de publicação foi aplicada. A pesquisa seguiu a metodologia PICO. A avaliação da qualidade de cada estudo *in vitro* incluído foi realizada de acordo com a lista CONSORT para estudos *in vitro* sobre materiais dentários.

Foram incluídos, por preencherem os critérios de inclusão, dezasseis estudos *in vitro* e um estudo *in situ.*

A clorohexidina foi o desinfetante cavitário mais estudado e, de acordo com os resultados, a sua utilização não compromete a adesão à dentina. O hipoclorito de sódio é também uma alternativa. No entanto é necessária a realização de um maior número de estudos, para que este possa ser aplicado de forma segura em dentes temporários. Apesar de terem sido estudados outros desinfetantes cavitários, não há ainda evidência suficiente que suporte a sua escolha, devendo por isso ser evitado o seu uso.

Palavras-chave: cárie dentária; dentes primários; desinfetantes cavitários; força de adesão; ionómero de vidro; resina composta

Abstract

Dental caries' treatment is often associated with the removal of the decayed tissue and the restoration of the remaining dental structure. Some authors have been proposing the use of cavity disinfectants in order to reduce, or even to eliminate, the effect of the microorganisms present in dental cavities prior to its restoration.

The aim of this study was to evaluate the effect of the application of different cavity disinfectants on bond strength and clinical success of composite and glass-ionomer restorations on primary teeth.

The research was conducted using Cochrane Library, PubMed/MEDLINE, SCOPUS and Web of Science, for articles published up to 14th February 2021, with no restrictions on region, language or year of publication. The search was performed according to the PICO strategy. The evaluation of the methodological quality of each *in vitro* study was assessed using the CONSORT checklist for reporting *in vitro* studies on dental materials.

Sixteen *in vitro* studies and one *in situ* study fulfilled the inclusion criteria and were analysed.

Chlorhexidine was the most studied cavity disinfectant, and according to the results, its use does not compromise dentin bonding. Sodium hypochlorite is a promising alternative but more research on its use is required to clearly state that it can safely be used as a cavity disinfectant for primary teeth. Although other disinfectants were studied, there is a low-level evidence attesting its effects on adhesion and so its use should be avoided.

Keywords: bond strength; cavity disinfectants; composite resin; dental caries; glass-ionomer; primary teeth

Introduction

Dental caries has a high prevalence worldwide, affecting more than 2.4 thousand million adults and 621 million children with primary teeth.[1] It can be defined as a multifactorial pathology arising from the interaction between dental structure and microbial biofilm, due to an imbalance between remineralization and demineralization, with the last one prevailing.[2,3]

Although complete removal of the decayed and necrotic tissue is directly related to restorations' clinical success, cariogenic bacteria can be pushed deep inside the dentinal tubules while removing the carious tissue and remain viable for a long time. In fact, the remaining of cariogenic bacteria in the cavity can be associated with the development of secondary caries.[4–6]

According to Dalkilic *et al*[7], fermenting microorganisms can remain viable for 139 days in a restored cavity. Moreover, bacteria present in smear layer may remain viable and proliferate, allowing their metabolism products to reach and to cause inflammatory changes in the dental pulp. Bacteria penetration through restoration and teeth interface (microinfiltration) can also explain restorations' failure.[8–10]

As so, some authors have been proposing the use of cavity disinfectants in order to reduce, or even to eliminate, the effect of the microorganisms present in a dental cavity before a restoration is placed.[9–11]

Considering the available disinfectants, chlorhexidine, sodium hypochlorite and fluoridated solutions are the most used. Despite their benefits, their effect on adhesion to dentin, especially that of primary teeth, is still unknown.[8,12,13]

Among the paediatric population, dental caries treatment is the most common procedure to be performed in a dental appointment.[13] Restorations' success rate is associated to dentist's experience and patient's collaboration. However, one of the most common causes of failure is the development of secondary caries.[14–16]

Thereby, the aim of this systematic review was to evaluate the effect of the application of different cavity disinfectants on bond strength and clinical success of composite and glass-ionomer restorations on primary teeth.

Materials and Methods

The present systematic review was registered on the International Prospective Register of Systematic Reviews (PROSPERO) platform (ID CRD42020199614), and followed the PRISMA protocol (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols)[17] – Attachment I.

The research questions were developed according to the PICO (Population, Intervention, Comparison, Outcome) methodology, as described in Table 1.

Table 1 – Problem, Intervention, Comparison, Outcome (PICO) strategy.

Parameter	*In vitro* studies	Clinical / *in situ* studies
P (Population)	Primary teeth / dentin discs	Children in need of a restoration
I (Intervention)	Restoration with prior application of a cavity disinfectant	
C (Comparison)	Restoration without the application of a cavity disinfectant	
O (Outcome)	Effect of cavity disinfection on dentin bond strength	Effect of cavity disinfection on clinical success

The inclusion and exclusion criteria are presented in Table 2.

Table 2 – Inclusion and exclusion criteria.

Inclusion Criteria	Primary teeth evaluation
	Bond strength / clinical success evaluation
	Existence of a control group
	Evaluation of commercially available adhesive systems and composite resins or glass-ionomer
	Application of only one cavity disinfectant per experimental group
	Report of results as mean and standard deviation
Exclusion Criteria	Permanent teeth evaluation
	Evaluation of teeth with endodontic treatment
	Evaluation of adhesion of cements, posts, sealants or brackets

	Use of experimental adhesive systems or of mixtures of adhesives with disinfectants
	Revisions, animal or cell studies, letters, abstracts, comments and clinical cases

An electronic research was conducted in Cochrane Library (www.cochranelibrary.com), PubMed/MEDLINE (pubmed.ncbi.nlm.nih.gov), SCOPUS (www.scopus.com) and Web of Science (webofknowledge.com). The research keys used in each database can be found in Table 3.

Table 3 – Search keys used in the different databases.

Database		Search keys
Cochrane Library	#1	MeSH descriptor: [Dentin] explode all trees
	#2	dentin
	#3	cavity
	#4	MeSH descriptor: [Disinfection] explode all trees
	#5	disinfect*
	#6	antibacteria*
	#7	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
	#8	chlorhexidine
	#9	MeSH descriptor: [Chlorhexidine] explode all trees
	#10	“sodium hypochlorite”
	#11	MeSH descriptor: [Sodium Hypochlorite] explode all trees
	#12	laser
	#13	MeSH descriptor: [Lasers] explode all trees
	#14	ozone
	#15	MeSH descriptor: [Ozone] explode all trees
	#16	“aloe vera”
	#17	MeSH descriptor: [Aloe] explode all trees
	#18	ethanol
	#19	MeSH descriptor: [Ethanol] explode all trees
	#20	EDTA
	#21	MeSH descriptor: [Edetic Acid] explode all trees
	#22	“green tea”
	#23	EGCG
	#24	“bond strength”
	#25	adhesion

	#26 adhesive #27 MeSH descriptor: [Dental Cements] explode all trees #28 primary #29 deciduous #30 MeSH descriptor: [Tooth, Deciduous] explode all trees #31 temporary #32 #1 OR #2 OR #3 #33 #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 #34 #24 OR #25 OR #26 OR #27 #35 #28 OR #29 OR #30 OR #31 #36 #32 AND #33 AND #34 AND #35
PubMed	(dentin[MeSH Terms] OR dentin OR cavity) AND (disinfection[MeSH Terms] OR disinfect* OR antibacteria* OR agents, antibacterial[MeSH Terms] OR chlorhexidine[MeSH Terms] OR chlorhexidine OR "sodium hypochlorite" OR sodium hypochlorite[MeSH Terms] OR laser OR lasers[MeSH Terms] OR ozone OR ozone[MeSH Terms] OR "aloe vera" OR aloe[MeSH Terms] OR ethanol OR ethanol[MeSH Terms] OR EDTA OR Edetic acid[MeSH Terms] OR "green tea" OR EGCG) AND ("bond strength" OR adhesion OR adhesive OR adhesives[MeSH Terms]) AND (deciduous tooth[MeSH Terms] OR deciduous OR primary OR temporary)
SCOPUS	TITLE-ABS-KEY (dentin OR cavity) AND TITLE-ABS-KEY (disinfect* OR antibacterial* OR chlorhexidine OR "sodium hypochlorite" OR laser OR ozone OR "aloe vera" OR ethanol OR EDTA OR "green tea" OR EGCG) AND TITLE-ABS-KEY ("bond strength" OR adhesion OR adhesive) AND TITLE-ABS-KEY (primary OR deciduous OR temporary)
Web of Science	TS= ((dentin[MeSH Terms] OR dentin OR cavity) AND (disinfect* OR antibacteria* OR chlorhexidine OR "sodium hypochlorite" OR laser OR ozone OR "aloe vera" OR ethanol OR EDTA OR "green tea" OR EGCG) AND ("bond strength" OR adhesion or adhesive) AND (primary OR deciduous OR temporary))

The search was limited to articles published until February the 14th of 2021, with no restrictions on region, language, or year of publication. A manual search for other references in reviews and in the included articles was performed.

Duplicate articles were removed with Endnote 20 (Clarivate™, Boston, USA). Two independent reviewers analysed titles, abstracts and full texts and a third one's opinion was obtained when necessary.

Selected articles were read by the same two independent authors, who collected the following data on the *in vitro* studies: authors and year of publication, number of elements per group (n), materials used (cavity disinfectant, type of adhesive system and restorative material), storage and bond strength results.

Regarding the clinical / *in situ* studies, the following data was acquired: authors and year of publication, type of teeth, number and ages of children per group (n), materials used (cavity disinfectant, type of adhesive system and restorative material) and results (pigmentation, marginal gaps or existence of carious lesions).

Quality assessment

The evaluation of the methodological quality of each *in vitro* study was assessed using the modified Consolidated Standards of Reporting Trials (CONSORT) checklist[18] for reporting *in vitro* studies on dental materials. When applying this checklist, items 5 to 9 could not be evaluated since these are designed to evaluate sample standardization. Two authors assessed the risk of bias independently, and any disagreement was solved by consensus.

Results

Initial research on electronic databases resulted in 585 articles. After evaluating titles and abstracts, 41 articles were selected for full text analysis and of those 17 studies fulfilled the inclusion and exclusion criteria. The flowchart of the data selection process is detailed in Figure 1.

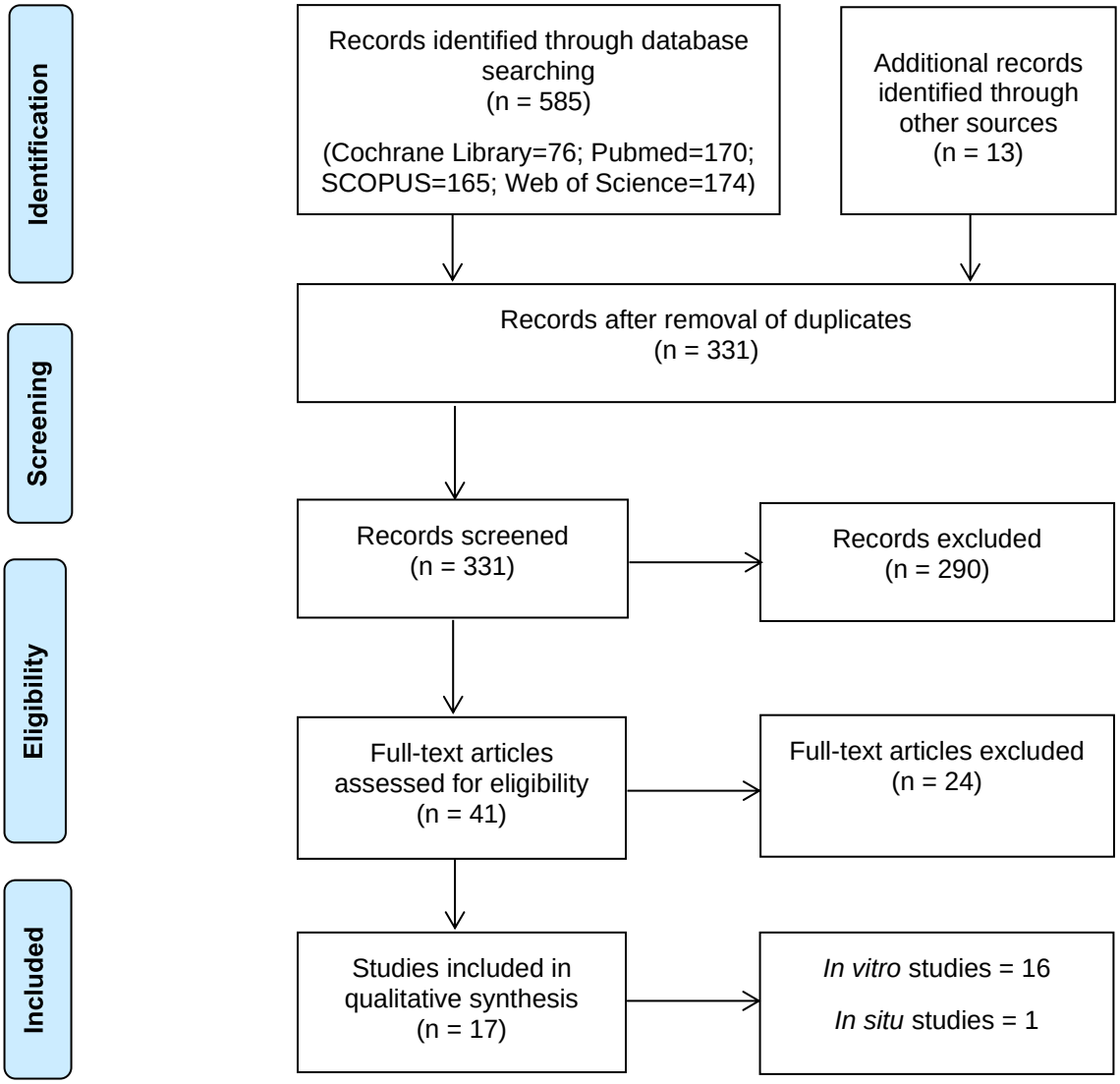

Figure 1 – Flowchart of the data selection process.

Sixteen *in vitro* studies[13,19–33] were included in this systematic review. Relevant information on each study is summarized in Table 4.

The earliest study was published in 2003[13] and the most recent one in 2020[23].

Most authors used primary molars[13,20–22,24–33], but Monghini *et al*[19] evaluated canines and Mohammadi *et al*[23] used anterior teeth. Sample size varied from 2[33] to 20[22,34] teeth per group.

Even though all authors studied healthy dentin, Ersin *et al*[26] additionally evaluated carious dentin and Lenzi *et al*[30,31] also evaluated demineralized dentin (artificially induced lesions).

After extraction, teeth were stored in thymol[13,22,26], chloramine[21,24,25,30,31], distilled water[21,24,25,28,30–33], saline solution[19,20] or sodium azide[19,29]. Ricci *et al*[27] and Mohammadi *et al*[23] didn't report data on the storage medium used after teeth extraction.

All authors used water to store the specimens after adhesive experiments and before bond strength evaluation.

All authors reported results on adhesion to composite resin. Only Ersin *et al*[26] also reported results on adhesion to glass-ionomer materials.

Most of the authors reported the use of 2% chlorhexidine[13,22–24,26–28,30,31,33] as a cavity disinfectant. A few studies reported results on the application of sodium hypochlorite[21,25,32], Er:YAG laser[19,20,29], KTP laser[33], ozone[33], doxycycline[23], ethylenediaminetetraacetic acid (EDTA)[23], propolis[33] and Aqua-prep™ (Bisco, USA)[20].

Except for Vieira *et al*[13], all of the authors studying the effect of 2% chlorhexidine as a cavity disinfectant[22–24,26–28,30,31,33] reported positive results allowing for maintenance or an increase in bond strength values. Vieira *et al*[13] were the only authors applying chlorhexidine before etching the specimens with phosphoric acid.

The authors evaluating the effect of the application of sodium hypochlorite tested different concentrations, ranging from 2.5[21] to 10%[25]. Regardless of the concentration, all authors[21,25,32] reported positive results allowing for maintenance or even an increase in bond strength values.

The Er:YAG laser was evaluated by three studies[19,20,29]. Monghini *et al*[19] reported negative results when testing the laser with three different working parameters. However, Scatena *et al*[29] didn't find statistically significant differences regarding bond strength results for different focal distances (mm) and Yildiz *et al*[20] even reported an increase in bond strength values.

Oznurhan *et al*[33] assessed the use of a KTP laser as a cavity disinfectant and reported positive results.

Ozonated water[33] and gaseous ozone[33] were also tested as cavity disinfectants and the authors reported a maintenance of the bond strength values.

Aqua-prep™ [20], an aqueous solution of fluoride and hydroxyethyl methacrylate (HEMA), 2% Doxycycline[23], 17% EDTA[23], and 30% propolis[33] were all evaluated in only one study each and all of the products were associated with a maintenance of the bond strength values.

No clinical studies were identified and only one *in situ* study regarding the use of a cavity disinfectant in primary teeth was evaluated. Ricci *et al*[34] developed a split-mouth experimental protocol that included children aged between 8 and 11 years old with at least two contralateral primary molars with small carious lesions. Chlorhexidine was used as a cavity disinfectant after enamel and dentin were etched with 35% phosphoric acid. The solution was removed with absorbent papers and the cavities were restored with Prime & Bond NT® (Dentsply, USA) and Filtek™ Z250 (3M, USA). All the procedures were done under rubber dam and the teeth were collected later, after exfoliation. The teeth were grouped according to the time of oral function after restoration: up to 30 days, 1 to 5 months, 10 to 12 months, and 18 to 20 months. A progressive decrease in bond strength values was reported for control and experimental groups as the time in oral function increased. However, a statistically significant decrease was reported sooner for the control group (it started in the 1 to 5-month period while for the experimental group it started in the 10 to 12-month period). Also, significantly higher bond strength values were reported for the experimental group at 1 to 5 and 18 to 20-month periods.

Quality assessment

Methodological quality assessment outcomes are presented in Table 5. All studies presented accurate information regarding each item from 1-10. However, none of them provided results with confidence intervals. In addition, only two studies[20,23] reported study limitations and sources of potential bias (item 12).

Table 4 – Characteristics of the *in vitro* studies included in the systematic review.

Authors, year	Groups (n)	Teeth	Storage	Materials	Results (MPa)
Vieira *et al*, 2003[13]	G_1 – 37% phosphoric acid + adhesive (10) + resin G_2 – 2% CHX + 37% phosphoric acid + adhesive (10) + resin	Molars	0.1% Thymol	Adhesive: 3M Single Bond (3M, USA) Resin: Filtek ™ Z250 (3M, USA)	G_1: 19.88±1.04 G_2: 17.99±1.15 G_1*/G_2
Correr *et al*, 2004[25]	G_1 – 35% phosphoric acid + adhesive 1 (15) G_2 – 35% phosphoric acid + 10% NaOCl + adhesive 1 (15) G_3 – 37% phosphoric acid + adhesive 2 (15) G_4 – 37% phosphoric acid + 10% NaOCl + adhesive 2 (15) G_5 – Adhesive 3 (15) G_6 – 10% NaOCl + adhesive 3 (15) + resin	Molars	0.5% Chloramine	Adhesive: 1 – 3M Single Bond; 2 – Prime & Bond 2.1® (Dentsply, Brazil); 3 – Clearfill™ SE Bond (Kuraray, USA) Resin: Filtek ™ Z250	G_1: 15.8±1.9 G_2: 14.6±1.3 G_3: 10.2±0.7 G_4: 9.9±0.2 G_5: 13.3±1.2 G_6: 10.7±1.0 G_1*/G_3
Monghini *et al*, 2004[19]	G_1 – None (12) G_2 – Laser Er;YAG 60 mJ/2 Hz (12) G_3 – Laser Er;YAG 80 mJ/2 Hz (12) G_4 – Laser Er;YAG 100 mJ/2 Hz (12) + 35% phosphoric acid + adhesive + resin	Canines	0.9% Saline solution with 0.4% sodium azide	Adhesive: 3M Single Bond Laser: Kavo Key Laser 2 (Kavo Dental, Germany) Resin: Filtek™ Z250	G_1:17.89±4.75 G_2:12.34±4.85 G_3:10.30±3.67 G_4:10.41±4.20 G_1*/G_2;G_3;G_4
Ersin *et al*, 2009[26]	G_1 – 25% polyacrlylic acid + 2% CHX + GIC 1 (sound dentin) (3) G_2 – 25% polyacrlylic acid + 2% CHX + GIC 1 (carious dentin) (3) G_3 – 25% polyacrlylic acid + GIC 1 (sound dentin) (3)	Molars	0.1% Thymol	Adhesive: Prime & Bond® (Dentsply, Brazil); GIC: 1 – Ketac™ Molar (3M, Germany); 2 – Vitremer™ (3M, USA) Resin: Surefil™ (Dentsply, USA)	G_1: 8.7±4.3 G_2: 7.1±5.2 G_3: 9.2±5.2 G_4: 10.3±6.6 G_5: 12.4±5.7 G_6: 14.4±6.6

	G_4 – 25% polyacrlylic acid + GIC 1 (carious dentin) (3) G_5 – 2% CHX + GIC 2 (sound dentin) (3) G_6 – 2% CHX + GIC 2 (carious dentin) (3) G_7 – GIC 2 (sound dentin) (3) G_8 – GIC 2 (carious dentin) (3) G_9 – 37% phosphoric acid + 2% CHX + adhesive + resin (sound dentin) (3) G_{10} – 37% phosphoric acid + 2% CHX + adhesive + resin (carious dentin) (3) G_{11} – 37% phosphoric acid + adhesive + resin (sound dentin) (3) G_{12} – 37% phosphoric acid + adhesive + resin (carious dentin) (3)				G_7: 11.2±4.8 G_8: 13.8±4.9 G_9: 22.9±6.9 G_{10}: 23.2±6.2 G_{11}: 20.2±5.8 G_{12}: 22.1±6.2 G_9*/G_1;G_2;G_3;G_4;G_5;G_6;G_7;G_8 G_{10}*/G_1;G_2;G_3;G_4;G_5;G_6;G_7;G_8 G_{11}*/G_1;G_2;G_3;G_4;G_5;G_6;G_7;G_8 G_{12}*/G_1;G_2;G_3;G_4;G_5;G_6;G_7;G_8
Ricci *et al*, 2010[27]	35% phosphoric acid + G_1 – 2% CHX + adhesive 1 (4) G_2 – deionized water + adhesive 1 (4) G_3 – 2% CHX + adhesive 2 (4) G_4 – deionized water + adhesive 2 (4) G_5 – 2% CHX + adhesive 3 (4) G_6 – deionized water + adhesive 3 (4) + resin	Molars	NA	Adhesive: 1 – Adper™ Single Bond (3M, USA); 2 – Prime & Bond NT® (Dentsply, USA); 3 – Excite® DSC (Ivoclar, Liechtenstein) Resin: Filtek™ Z250	G_1: 47.4±9.5 G_2: 41.4±11.9 G_3: 48.0±9.8 G_4: 40.8±13.4 G_5: 45.2±9.2 G_6: 43.4±12.0 G_1*/G_2 G_3*/G_4
Leitune *et al*, 2011[28]	37% phosphoric acid + G_1 – Adhesive (24h) (10)	Molars	Distilled water	Adhesive: Adper™ Scotchbond™ Multi Purpose (3M, USA) Resin: Filtek™ Z250	G_1: 22.37±3.69 G_2: 19.93±2.05 G_3: 22.30±3.66

	G_2 – Adhesive (6 months) (10) G_3 – 2% CHX + Adhesive (24h) (10) G_4 – 2% CHX + Adhesive (6 months) (10)				G_4: 24.48±2.24 G_2*/G_4
Scatena *et al*, 2011[29]	G_1 – None (10) G_2 – Laser Er:YAG (80mJ, 11mm) (10) G_3 – Laser Er:YAG (80mJ, 12mm) (10) G_4 – Laser Er:YAG (80mJ, 16mm) (10) G_5 – Laser Er:YAG (80mJ, 17mm) (10) G_6 – Laser Er:YAG (80mJ, 20mm) (10) + 37% phosphoric acid + adhesive + resin	Molars	0.4% Sodium azide	Laser: Kavo Key Laser 2 Adhesive: 3M Single Bond Resin: Filtek™ Z250	G_1: 7.32±3.83 G_2: 5.07±2.62 G_3: 6.49±1.64 G_4: 7.71±0.66 G_5: 7.33±0.02 G_6: 9.65±2.41 G_2*/G_4;G_6
Manfro *et al*, 2012[24]	37% phosphoric acid + G_1 – water + adhesive (7) G_2 – water + adhesive (12 months) (7) G_3 – 0.5% CHX + adhesive (7) G_4 – 0.5% CHX + adhesive (12 months) (7) G_5 – 2% CHX + adhesive (7) G_6 – 2% CHX + adhesive (12 months) (7) + resin	Molars	0.5% Chloramine	Adhesive: 3M Single Bond Resin: Filtek™ Z250	G_1: 50.8±12.8 G_2: 20.4±3.7 G_3: 49.3±2.6 G_4: 32.3±7.9 G_5: 44.0±8.7 G_6: 34.6±5.1 G_1*/G_2 G_2*/G_4;G_6 G_3*/G_4 G_5*/G_6
Lenzi *et al*, 2012[30]	35% phosphoric acid + G_1 – distilled water + adhesive (sound dentin) (5)	Molars	0.5% Chloramine	Adhesive: Adper™ Single Bond 2 Resin: Filtek™ Z250	G_1: 30.8±2.2 G_2: 32.8±3.8 G_3: 24.5±3.8 G_4: 25.6±3.6

	G_2 – 2% CHX + adhesive (sound dentin) (5) G_3 – distilled water + adhesive (artificial caries) (5) G_4 – 2% CHX + adhesive (artificial caries) (5)				G_1*/G_3;G_4 G_2*/G_3;G_4
Aras *et al*, 2013[32]	G_1 – 37% phosphoric acid (10) G_2 – 37% phosphoric acid + 5% NaOCl (10) G_3 – 5% NaOCl + 37% phosphoric acid (10) + adhesive + resin	Molars	Distilled water	Adhesive: Gluma® Confort Bond (Herause-Kulzer, Germany) Resin: Charisma® (Herause-Kulzer, Germany)	G_1: 14.51±2.89 G_2: 18.45±2.30 G_3: 17.06±2.99 G_1*/G_2
Lenzi *et al*, 2014[31]	35% phosphoric acid + G_1 – distilled water + adhesive (sound dentin) (5) G_2 – distilled water + adhesive (sound dentin) (6months) (5) G_3 – 2% CHX (without rinsing) + adhesive (sound dentin) (5) G_4 – 2% CHX (without rinsing) + adhesive (sound dentin) (6 months) (5) G_5 – distilled water + adhesive (artificial lesion) (5) G_6 – distilled water + adhesive (artificial lesion) (6 months) (5) G_7 – 2% CHX (without rinsing) + adhesive (artificial lesion) (5) G_8 – 2% CHX (without rinsing) + adhesive (artificial lesion) (6 months) (5)	Molars	Distilled water	Adhesive: Adper™ Single Bond Resin: Filtek™ Z250	G_1: 30.7±2.2 G_2: 25.9±5.7 G_3: 32.8±3.8 G_4: 31.3±2.6 G_5: 26.2±5.4 G_6: 20.0±3.9 G_7: 28.3±3.4 G_8: 26.9±5.9 G_1*/G_5;G_7 G_2*/G_6;G_8 G_3*/G_5;G_7 G_4*/G_6;G_8
Oznurhan *et al*, 2015[33]	G_1 – 2% CHX (2) G_2 – 30% propolis (2) G_3 – Gaseous ozone (2)	Molars	Distilled water	Adhesive: Adper™ Prime & Bond NT®	G_1: 7.58±3.18 G_2: 7.42±2.28 G_3: 5.84±2.62

	G_4 – Ozonated water (2) G_5 – Laser KTP (2) G_6 – None (2) + adhesive + resin			Resin: Tetric® N-Ceram (Ivoclar Vivadent, Liechenstein) Laser: Smartlite D (Deka, Italy)	G_4: 11.12±2.41 G_5: 9.58±2.92 G_6: 6.38±2.47 G_3*/G_5 G_4*/G_1;G_2;G_3;G_6
Yildiz *et al*, 2015[20]	G_1 – 37% phosphoric acid (3) G_2 – 37% phosphoric acid + Aqua-Prep™ (without rinsing) (3) G_3 – Laser Er:YAG (10Hz, 8mm) (3) + adhesive + resin	Molars	Saline solution	Adhesive: Adper™ Single Bond 2 Resin: Filtek™ Z250 Laser: Fidelis Plus III (Fotona, Slovenia) Aqua-Prep™ (Bisco, USA)	G_1: 14.28±5.22 G_2: 18.35±7.94 G_3: 20.57±9.02 G_1*/G_3
Bahrololoomi *et al*, 2017[21]	35% phosphoric acid + G_1 – none (14) G_2 – 2.5% NaOCl (14) G_3 – 5.25% NaOCl (14) + adhesive + resin	Molars	0.5% Chloramine	Adhesive: One-Step® Plus (Bisco, USA) Resin: AELITE (Bisco, USA)	G_1: 13.56±3.36 G_2: 13.53±3.64 G_3: 14.36±3.64
Ebrahimi *et al*, 2018[22]	G_1 – 37% phosphoric acid + adhesive 1 (20) G_2 – 37% phosphoric acid + adhesive 1 (3 months) (20) G_3 – 37% phosphoric acid + adhesive 1 + 2% CHX (without rinsing) (20) G_4 – 37% phosphoric acid + adhesive 1 + 2% CHX (without rinsing) (3 months) (20) G_5 – Adhesive 2 (20) G_6 – Adhesive 2 (3 months) (20) G_7 – Adhesive 2 (Primer) + 2% CHX (without rinsing) + adhesive 2 (bond) (20)	Molars	0.1% Thymol + water	Adhesive: 1 – Adper™ Single Bond 2 – Clearfil™ SE Bond Resin: Filtek™ Z250	G_1: 25.43±12.94 G_2: 39.96±21.75 G_3: 66.45±8.3 G_4: 39.02±23.29 G_5: 47.83±19.83 G_6: 53.36±18.05 G_7: 46.25±9.34 G_8: 56.4±22.18 G_1*/G_3

	G_8 – Adhesive 2 (primer) + 2% CHX (without rinsing) + adhesive 2 (bond) (3months) (20)				
Mohammadi *et al*, 2020[23]	37% phosphoric acid + G_1 – PBS (15) G_2 – 2% CHX (without rinsing) (15) G_3 – 2% Doxycycline (without rinsing) (15) G_4 – 17% EDTA (15) + adhesive	Anterior teeth	-	Adhesive: Adper™ Single Bond 2 Resin: Filtek™ Z250	G_1: 6.20±2.11 G_2: 5.60±2.69 G_3: 8.82±3.29 G_4: 7.50±3.94 G_2*/G_3

CHX – Chlorhexidine; EDTA – Ethylenediaminetetraacetic Acid; GIC – Glass-Ionomer Cement; NaOCl – Sodium hypochlorite; NA – Not answered

Table 5 – Modified CONSORT checklist for reporting *in vitro* studies of dental materials.

Author, year	Item									
	1 Abstract	**2a Introduction** (Background)	**2b Introduction** (Objectives)	**3 Methods** (Intervention)	**4 Methods** (Outcomes)	**10 Methods** (Statistical Methods)	**11 Results** (Outcomes and estimation)	**12 Discussion** (Limitations)	**13 Other information** (Funding)	**14 Other information** (Protocol)
Vieira *et al*, 2003[13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	No	No
Correr *et al*, 2004[25]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	No	No
Monghini *et al*, 2004[19]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	No	No
Ersin *et al*, 2009[26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	No	No
Ricci *et al*, 2010[27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	Yes	No
Leitune *et al*, 2011[28]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	No	No
Scatena *et al*, 2011[29]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	No	No
Manfro *et al*, 2012[24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	No	No
Lenzi *et al*, 2012[30]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	Yes	No
Aras *et al*, 2013[32]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	Yes	No
Lenzi *et al*, 2014[31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	Yes	No

Oznurhan *et al*, 2015[33]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	Yes	No
Yildiz *et al*, 2015[20]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	Yes	Yes	No
Bahrololoomi *et al*, 2017[21]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	Yes	No
Ebrahimi *et al*, 2018[22]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	No	Yes	No
Mohammadi *et al*, 2020[23]	Yes	Yes	Yes	Yes	Yes	Yes	Yes[a]	Yes	Yes	No

[a] No confidence interval

Discussion

A cavity disinfectant must not only have a strong antimicrobial effect but also not compromise the adhesion of the restorative material to the dental substracts.[8,35] The majority of the studies on this topic reports results on permanent teeth but the structural and mechanical properties of the primary teeth make it necessary to carry out experimental protocols testing this type of teeth.[36,37] Compared to permanent teeth, primary teeth have thinner enamel and dentin, are less mineralized due to their lower concentration of calcium and potassium ions, have a hybrid layer more prone to be degraded[38] and its dentin has a lower tubule density.[26,39,40] This may explain why bond strength values of composite materials in primary teeth are lower to those of permanent teeth.[41]

Dental adhesion may not only be affected by the cavity disinfectant used but also by the dental substract. In order to minimize its effect, it is recommended to perform adhesion tests in superficial dentin of healthy teeth, ideally without restorations.[42] Deep dentin is mainly composed of dentinal tubules and a small percentage of intertubular dentin. Superficial dentin has a higher percentage of organic components (collagen) and of intertubular dentin and a lower number of dentinal tubules.[43–45]

The differences between healthy and caries-affected dentin should also be underlined. The caries-affected dentin is more porous and softer due to its partial demineralization which leads to a less effective adhesion.[46–48] In fact, some of the articles included in this systematic review evaluated the effect of a cavity disinfectant in healthy and affected dentin[26,30,31] and Lenzi *et al*[30,31] reported significant lower bond strength values for the affected-dentin groups.

All of the studies reported the use of a storage medium before the samples were submitted to the experimental protocol. The ISO/TS 11405/2015 (Dentistry – Testing of adhesion to tooth structure)[42] provides guidance for testing adhesion between dental substracts and restorative materials. This ISO/TS recommends the use of a 0.5% chloramine solution or of distilled water as a storage medium for the extracted teeth. If chloramine is chosen, it should be replaced by distilled water after one week. Despite these recommendations, some authors used other solutions, such as thymol[13,22,26]. The use of other solutions is not recommended by the ISO/TS 11405/2015, since it may affect dentin's mechanical properties. In fact, Santana *et al*[49] reported that the use of thymol as a storage medium lead to an impaired adhesion.

After the restorations were made, all authors stated that the samples were kept in water, which is exactly the recommendation of the ISO/TS 11405/2015 (ISO 3696:1987, grade 3)[50].

Almost all authors reported results on adhesion to molars, which is also in line with the recommendations of the ISO/TS 11405/2015[42]. However, Monghini *et al*[19] and Mohammadi *et al*[23] used anterior teeth.

Most authors[13,22–24,26,30,31,34] evaluated the effect of chlorhexidine as a cavity disinfectant. Chlorhexidine has been widely used in dentistry, mainly because of its antimicrobial properties, including against *Streptococcus mutans*, and of its antiplaque effect.[51–54] Chlorhexidine is also well known for its ability to inhibit matrix-metalloproteinases due to its strong collagenolytic activity, reducing the degradation of the hybrid layer[48,55], which may justify the positive results reported by almost all authors. Although only Ersin *et al*[26] evaluated the effect of chlorhexidine on the adhesion to a glass-ionomer material, the authors also reported positive results.

Similar results were previously reported for permanent teeth[56], which makes chlorhexidine the most consensual cavity disinfectant to be used in clinical practice. Not only adhesion to dentin is adequate after its use but as stated by some authors[57,58] it can even be enhanced. As so, chlorhexidine presents as a safe and effective product to be used as a cavity disinfectant.

Sodium hypochlorite is commonly used as a cavity disinfectant due to its favourable properties: antibacterial action against aerobic bacteria, such as *S. mutans*, wettability and deproteinization.[59–63] Although all authors studying the effect of the use of sodium hypochlorite as a cavity disinfectant in primary teeth reported positive results, only three articles[21,25,32] were identified. Since there are just a few studies reporting results on primary teeth and that the use of sodium hypochlorite as a cavity disinfectant in permanent teeth is still a matter of discussion[56], caution is required when choosing this product as a cavity disinfectant.

Initially presented as an alternative to the use of burs for cavity preparation, the Erbium:Ytrium (Er:YAG) laser was first introduced in 1989 by Hibst and Keller.[64] From then on lasers have been used in numerous dentistry fields such as oral surgery, periodontics, endodontics and prosthodontics.[65,66] However, similarly to what was reported for permanent teeth[56], there is no consensus regarding the use of lasers as cavity disinfectants with some authors reporting an impairment of the adhesion[19] and others reporting a maintenance or even an enhancement of the bond strength values[20,29].

Moreover, even though some authors did not report secondary side effects[66,67], lasers may lead to an overheating of the dental structures which may induce pulp injuries, hydroxyapatite changes and excessive dentin dehydration.[68–71] Given the results, the use of lasers as a cavity disinfection method should be avoided.

Both gaseous ozone and ozonated water have been recently introduced as alternatives to cavity disinfection due its known antimicrobial and strong antioxidant properties. Polydorou *et al*[72] reported that gaseous ozone eliminated 99.9% of the microorganisms in carious lesions in 20 seconds. In addition to its great antimicrobial activity (including against *S. mutans*) ozone also has antifungal and antiviral properties.[73] Authors analysing the effect of either ozonated water or gaseous ozone on adhesion reported positive results[33], which may be justified by the opening of the dentinal tubules caused by the oxygen.[74–78] Although there is limited information about the use of ozone as a cavity disinfectant in primary teeth, it looks like a promising alternative.

EDTA is an organic compound responsible for chelating calcium and potassium ions and for selective removal of hydroxyapatite crystals, which allows for the maintenance of the collagen matrix.[79,80] It is widely used in endodontics to improve shaping of the entire root canal system and to dissolve the inorganic components of the smear layer.[81] Although the reported results were positive (no differences on bond strength values after using it as a cavity disinfectant), only one study[23] evaluated it. A few articles on permanent teeth[56] also showed that EDTA presents as a promising alternative but there is a clear need for further research.

Aqua-prep™ [20], 2% doxycycline[23], and 30% propolis[33] were all evaluated by studies included in this review and the reported results were positive but only one article was included for each product. Given the limited scientific evidence associated with these products (even in permanent teeth[56]), its use as cavity disinfectants should be avoided.

Further studies with standardized protocols should be developed to allow solid conclusions and recommendations concerning this issue. Furthermore, no clinical studies on the topic were identified and such studies are essential to analyse the effects of the different cavity disinfectants when applied in the oral cavity. Also, there is no information on the best application time and on durability of bond interfaces over time. The effect of the incorporation of the cavity disinfectants into adhesive systems must also be evaluated since it may reduce clinical steps which is of great importance in paediatric dentistry.

Conclusion

Chlorhexidine is the most studied cavity disinfectant and according to the results, its use does not compromise adhesion to primary dentin.

Sodium hypochlorite is a promising alternative but more research on its use is required to clearly state that it can safely be used as a cavity disinfectant for primary teeth. Although other disinfectants were studied, there is a low-level evidence attesting its effects on adhesion and so their use should be avoided.

There is a clear need for researchers to conduct well-designed *in vitro* and clinical studies so more options can be identified and its long-term effect on adhesion can be evaluated.

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“Agora que vou embora,

Sinto a dor de te deixar

Sei que te levo, Coimbra,

Tudo o que me deste,

Para sempre vou recordar”

(TFMUC – Tuna Feminina de Medicina da Universidade de Coimbra, *“Cidade de Amor”*)

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Attachments

I – PRISMA 2009 Checklist[17]

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	6
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	8,9
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	9
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	9,10
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	11
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	12
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this	11

		information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	11
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	-
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	-
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	12
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	21, 22
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	15 – 20
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	-
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	-
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	-
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	23
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	25
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	26
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	-