



Bonding of Glass-Ionomer Cement and Adhesives to Silver Diamine Fluoride-treated Dentin: An Updated Systematic Review and Meta-Analysis

Tatiana Tambara Fröhlich^a / Graziela Botton^b / Rachel de Oliveira Rocha^c

Purpose: To evaluate through a systematic review and meta-analysis the bonding performance of adhesive materials to silver diamine fluoride (SDF)-treated dentin.

Materials and Methods: Studies located in PubMed, Web of Science, LILACS, and Scopus up to September 2020, which compared the bond strength of adhesives (AD) or glass-ionomer cement (GIC) to SDF-treated and untreated (control) dentin were included. Mean differences were estimated separately by material and dentin condition (sound or caries-affected), with a random-effects model, at a 5% significance level.

Results: Twenty-two studies, including 11 new studies not included in our previous systematic review, met the eligibility criteria, and 21 studies were considered in the meta-analyses. SDF dentin pretreatment did not influence the bonding of GIC ($Z = 0.53$; $p = 0.60$), independent of dentin condition. SDF treatment significantly impaired the bonding of AD ($Z = 2.43$; $p = 0.01$). A rinsing step after SDF eliminated this effect in sound dentin ($Z = 1.82$; $p = 0.07$) and increased the bond strength to caries-affected dentin ($Z = 2.14$; $p = 0.03$).

Conclusion: SDF pretreatment does not influence the bond strength of GIC. A rinsing step after SDF application can improve the bond strength of AD to caries-affected dentin.

Keywords: bond strength, adhesion, glass-ionomer cement, adhesive, silver diamine fluoride.

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Silver diamine fluoride (SDF) has been considered the most effective non-invasive treatment for carious lesions, especially in primary teeth.⁵ SDF has bactericidal properties, inhibits demineralization, and promotes the remineralization of demineralized dentin.⁵⁶ Also, it inhibits collagenases (matrix metalloproteinases and cysteine cathepsins) and protects dentin collagen from destruction.^{30,31}

Due to these properties, SDF has a potential application as an adjunct to restorative treatment to prevent recurrent caries lesions.^{26,53} In vitro studies show that SDF dentin

treatment prior to placing restorations provides greater resistance to the development of new lesions when submitted to cariogenic challenge.^{32,36,57} However, a silver phosphate layer was formed on the SDF-treated dentin surface,⁴⁰ and silver particles extend into the dentinal tubules, totally or partially obstructing them,²² which could impair the adhesion of restorative materials.

A previous systematic review and meta-analysis¹¹ showed that SDF pretreatment does not negatively influence the bond strength of glass-ionomer cement to dentin, but can impair the adhesive bond strength. The rinsing step after SDF application eliminates this adverse effect. However, few studies considered caries-affected dentin at the time of the review, and a separate meta-analysis with these data could not be performed. Worse results can be expected for caries-affected dentin, as chemical and morphological differences (eg, lower mineral content¹ and increased porosity of intertubular dentin³³) jeopardize bonding.¹⁸ Moreover, it is essential to consider that more silver precipitated onto demineralized than sound dentin.²²

Interest in using SDF as a dentin pretreatment has increased since the publication of the systematic review mentioned above.¹¹ Several studies have been published recently which evaluated this effect on caries-affected

^a Graduate Student, Graduate Program in Dental Science, Federal University of Santa Maria, RS, Brazil. Conceived the idea and study design, performed the literature search, extracted data, performed the meta-analysis, wrote the manuscript.

^b Professor, Postgraduate Program of Pediatric Dentistry, Ingá University Center- Uningá, Santa Maria, RS, Brazil. Contributed substantially to discussion.

^c Associate Professor, Department of Stomatology, Federal University of Santa Maria, Brazil. Conceived the idea and study design, contributed substantially to discussion, proofread the manuscript.

Correspondence: Rachel de Oliveira Rocha, Federal University of Santa Maria, Av. Roraima nº 1000, Prédio 26F, Cidade Universitária, Bairro Camobi, Santa Maria, RS, Brazil 97105-900. Tel: +55-55-3220-9264; e-mail: rachelrocha@smail.ufsm.br

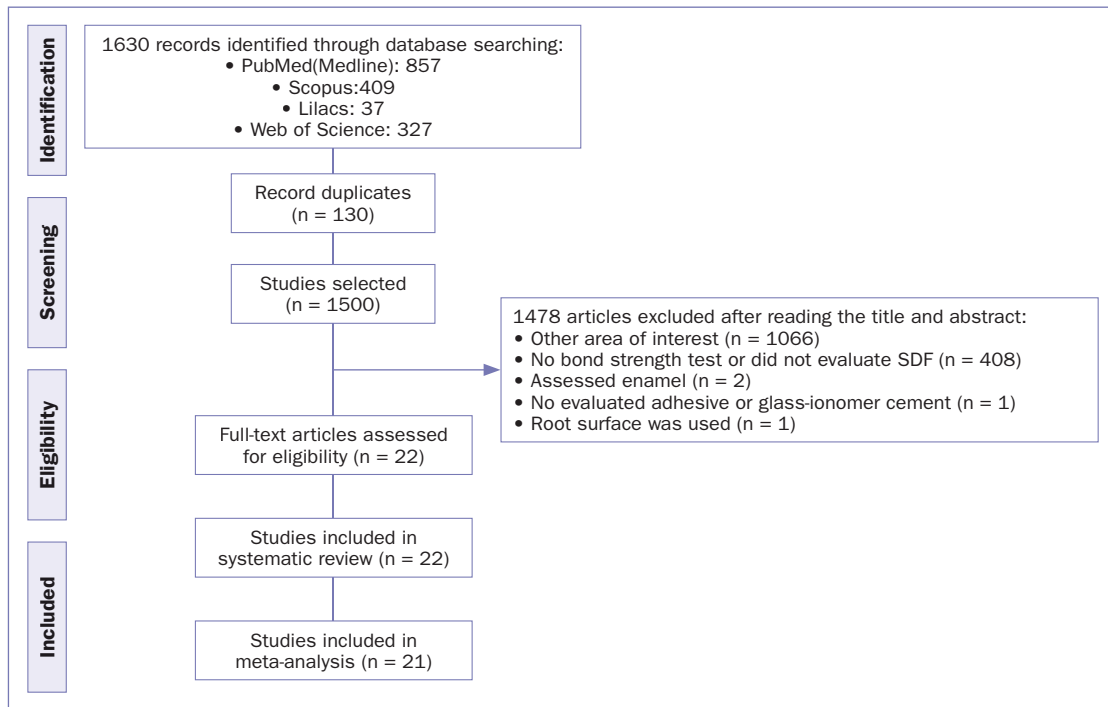


Fig 1 Flowchart diagram of study selection according to the PRISMA statement.

dentin,^{3,9,19,34,46,49,50} a relevant substrate in daily clinical practice. Some authors found that prior SDF application on caries-affected dentin does not diminish bond strength,^{19,50} or can even improve it.^{9,46} In contrast, other studies showed a significant reduction in bond strength.^{3,26} Therefore, this study aimed to update the systematic review and meta-analysis on the influence of silver diamine fluoride on the bonding performance of direct restorative materials to sound and caries-affected dentin. The null hypothesis tested was that SDF pretreatment does not influence the bond strength of glass-ionomer cement and adhesives regardless of the dentin condition – sound or caries-affected.

MATERIALS AND METHODS

This systematic review was written following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.³⁸ The literature approach and search strategy were developed based on the following PICO (participant/problem, intervention, comparator, and outcome) question: does prior application of silver diamine fluoride influence the bond strength of direct restorative materials to sound and caries-affected dentin? The direct restorative materials (glass-ionomer cement and adhesives) was the “participant/problem”, prior silver diamine fluoride application was the “intervention”, no previous application was the “comparator”, and the bond strength was the “outcome”. The systematic review protocol was not previously registered; it can be accessed by contacting the authors.

Search Strategy

A comprehensive literature search was undertaken through the electronic databases PubMed/MEDLINE, ISI Web of Science, Scopus, and LILACS to identify literature up to September 2020, with no language or publication year limits.

The subject search used a combination of controlled vocabulary and text words based on the search strategy developed for the PubMed/MEDLINE database as follows: (((((((((((bond strength) OR microtensile) OR micro shear) OR tensile) OR Tensile Strength[MeSH Terms]) OR tensile strength) OR shear) OR shear strength) OR Shear Strength [MeSH Terms])) AND (composite resins[MeSH Terms]) OR composite resins) OR composite resin*) OR resin composite* OR Adhesives[MeSH Terms] OR adhesive* OR adhesion OR adhesive* OR Dental Bonding [MeSH Terms] OR dental bonding OR Dentin-Bonding Agents[MeSH Terms] OR dentin bonding agent* OR total-etch adhesive* OR total-etch adhesive* OR total-etch OR total-etching OR conventional adhesive OR etch-and-rinse adhesive* OR self-etch adhesive* OR self-etch adhesive* OR self-etch* OR self-etching primer* OR all-in-one adhesive* OR one-bottle adhesive* OR universal adhesive* OR glass-ionomer cements [MeSH Terms] OR glass-ionomer cements OR glass-ionomer cement OR glass polyalkenoate cement* OR resin-modified glass-ionomer cement* OR highly viscous glass-ionomer cement* OR high viscosity glass-ionomer cement AND (((((silver fluoride) OR silver diamine fluoride) OR SDF) OR diamine fluoride). For ISI Web of Science, LILACS and Scopus the following search terms were used: (Silver Diamine Fluoride) OR (Silver Fluoride) AND (Bond Strength).

Table 1 Descriptive data of the included studies – glass-ionomer cement

Study	Country	Number of teeth per group	Silver diamine fluoride (SDF)	SDF protocol*	Restorative material	Type of teeth	Dentin condition	Caries-affected lesion	Bond strength test**
Braz et al, 2020 [3]	Brazil	7	Advantage Arrest < (38%SDF)	Rinsed Not rinsed	Fuji II LC@ Riva Self-Cure&	Permanent teeth	Sound and caries-affected	Artificial (pH-cycling model)	μSBS
François et al, 2020 [10]	France	20	Riva Star& (38% SDF and KI)	Not rinsed	Equia Forte Fil@	Permanent molar	Sound	–	SBS
Gupta et al, 2019 [15]	India	8	Riva Star& (38% SDF and KI)	Rinsed	Gold Label 2 LC@	Permanent molar	Sound	–	SBS
Jiang et al, 2020 [19]	Hong Kong	15	Saforide\$\$\$ (38% SDF)	Not rinse	Ketac-Molar Aplicap #	Permanent molar	Sound and caries-affected	Artificial (microbiological model)	μTBS
Knight et al, 2006 [23]	Australia	10	*** (1.8M SDF and KI)	Not rinsed Rinsed	Fuji VII@	Permanent molar	Sound	–	SBS
Koizumi et al, 2016 [25]	Japan	10	Riva Star& (38% SDF and KI)	Not rinsed	Riva Bond LC&	Permanent molar	Sound	–	μTBS
Ng et al, 2020 [34]	USA	10-12	Advantage Arrest- (38% SDF)	Not Rinsed	Fuji IX GP Extra Capsule@	Permanent molar	Caries-affected	Artificial (demineralizing solution)	SBS
Puwanawiroj et al, 2018 [42]	Thailand	40	Saforide\$\$\$ (38% SDF)	Rinsed	Fuji IX GP Extra Capsule@	Primary molar	Caries-affected	Natural	μTBS
Uchil et al, 2020 [49]	India	9	Fagamin\$\$\$\$ (38% SDF) Lugol's solution 10 wt% (KI)%	Rinsed	Gold Label Ligth-Cure Universal@	Primary molar	Caries-affected	Artificial (microbiological model)	μTBS
Wang et al, 2016 [52]	Hong Kong	4	Saforide\$\$ (38% SDF)	Rinsed	Fuji IX@	Permanent molar	Sound and caries-affected	Artificial (demineralising solution)	μTBS
Yamaga et al, 1993 [54]	Japan	***	Saforide\$ (38% SDF)	Not rinsed	Hy-Bond#	Bovine incisor	Sound	–	SBS
Zhao et al, 2019 [55]	Hong Kong	20	Riva Star& (38% SDF and KI) Saforide\$\$\$ (38% SDF)	Rinsed Not rinsed	Ketac-Molar#	Permanent	Caries-affected	Artificial (demineralising solution)	SBS

* SDF protocol: not rinsed or rinsed after the waiting time; * elapsed time between the placement of SDF and restoration; **SBS: shear bond strength; μTBS: microtensile bond strength; μSBS: microshear bond strength; *** not given; \$ Toyo Pharmaceutical, Tokyo, Japan; # Shofu, Tokyo, Japan; @ GC, Tokyo, Japan; # 3M Oral Care, St Paul, MN, USA; & SDI, Bayswater, Victoria, Australia; \$\$ Morita, Osaka, Japan; \$\$\$ Bee Brand Medico Dental, Osaka, Japan; \$\$\$\$ Tedequim Company, Córdoba, Argentina; < Elevate Oral Care, West Palm Beach, FL, USA; % Nice Chemicals, Kochi, India.

Study Selection

Screening of titles and abstracts of all studies were performed to select studies according to the inclusion criteria: in vitro studies that evaluated the bond strength of direct restorative materials (glass-ionomer cement and adhesives/resin composite) to previously SDF-treated dentin. The full-text of potentially eligible studies was assessed. Those which had no control group (dentin without prior application of silver diamine fluoride), assessed root dentin, or used different application protocols of restorative material between the experimental and control groups, were excluded. The reference lists of all included studies were manually screened to retrieve all relevant papers. The studies were selected by two independent reviewers ($\kappa = 0.90$), and any disagreement regarding eligibility was solved through discussion and consensus with a third reviewer.

Data Extraction

The data were extracted according to a predefined protocol using a form in Microsoft Office Excel 2013 (Microsoft; Redmond, WA, USA). For each paper, the following data were systematically extracted: publication year, country, number of teeth per group, type of teeth, silver diamine fluoride and restorative material used, application protocol, bond strength test, dentin condition (sound or caries-affected), type of carious lesion (natural or artificial), bond strength mean values (in MPa) and standard deviations (SD). The authors were contacted via e-mail at least twice to retrieve the bond strengths that were not presented as means and standard deviation. If the authors did not provide this information, the study was not included in the systematic review.

Table 2 Descriptive data of the included studies – adhesives

Study	Country	Number of teeth per group	Silver diamine fluoride (SDF)	SDF protocol*	Restorative material	Type of teeth	Dentin condition	Type of caries-affected lesion	Bond strength test**
Firouzmandi et al, 2020 [9]	Iran	12	Ancarie Cariostatic ^o (30% SDF)	Rinsed	Adper Single Bond 2%	Permanent molar	Sound and caries-affected	Natural	μSBS
Ko et al, 2020 [24]	Hong Kong	16	Saforide\$\$ (38% SDF) Saforide RC\$\$ (3.8% SDF)	Rinsed	Clearfil SE Bond#	Permanent molar	Sound	–	μTBS
Koizumi et al, 20016 [25]	Japan	10	Riva Star& (38% SDF and KI)	Not rinsed	Optibond FL Optibond Versa Clearfil Liner Bond#	Permanent molar	Sound	–	μTBS
Kucukylmaz et al, 2016 [26]	Turkey	8	Saforide\$ (38% SDF)	Not rinsed	Clearfil SE Bond#	Permanent molar	Sound and caries-affected	Artificial (pH-cycling model)	μTBS
Lutgen et al, 2018 [28]	USA	10	Advantage Arrest< (38% SDF)	Not rinsed Rinsed	Clearfil SE Bond 2# Scotchbond Universal%	Permanent molar	Sound	–	μSBS
Markham et al, 2020 [29]	USA	15	Advantage Arrest < (38% SDF)	Rinsed	Scotchbond Universal% Prime & Bond NT > G-Premio Bond £	Permanent molar	Sound	–	SBS
Quock et al, 2012 [43]	USA	7	Saforide\$ (38% SDF) Ancarie Cariostatic ^o (12% SDF)	Rinsed	Peak SE@ Peak LC@	Permanent molar	Sound	–	μTBS
Selvaraj et al, 2016 [45]	India	18	Riva Star& (38% SDF and KI)	Rinsed	Adper Single Bond 2% Adper Easy One%	Permanent molar	Sound	–	μSBS
Siqueira et al, 2020 [46]	Brazil	5	Riva Star& (38% SDF and KI) Cariestop? (12% SDF)	Rinsed	Clearfil Universal Bond Quick# Scotchbond Universal%	Permanent molar	Caries-affected	Artificial (micro-biological model)	μTBS
Van Duker et al, 2019 [50]	USA	10	Advantage Arrest < (38% SDF) Saturated solution of KI	Rinsed	Scotchbond Universal%	Permanent molar	Caries-affected	Artificial (demineralising solution)	μTBS
Wu et al, 2016 [53]	USA	12	Saforide\$ (38% SDF)	Rinsed	Prime & Bond NT >	Primary molar	Sound	–	μTBS

** SDF protocol: not rinsed or rinsed after the waiting time; * elapsed time between the placement of SDF and restoration; **μTBS: microtensile bond strength; μSBS: microshear bond strength; ^o Maquira Dental Products, Maringa, PR, Brazil; \$ Toyo Seiyaku Kansei, Osaka, Japan; \$\$Bee Brand Medico Dental, Osaka, Japan; @ Ultradent, South Jordan, UT, USA; & SDI, Bayswater, Victoria, Australia; ^ Kerr, Orange, CA, USA; # Kuraray Noritake Dental, Tokyo, Japan; % 3M Oral Care, St Paul, MN, USA; ? Biodinâmica, RJ, Brazil; < Elevate Oral Care, West Palm Beach, FL, USA; > Dentsply Caulk, Milford, DE, USA; £ GC, Tokyo, Japan.

Risk of Bias Assessment

The risk of bias was based on and adapted from a previous study.⁴⁴ The domains considered were: random sequence generation of the teeth for experimental groups, sample size calculation, the same number of teeth per group, failure mode evaluation, silver diamine fluoride and restorative materials applied following manufacturers' instructions, materials and testing procedures performed by a single operator, and specimens tested by a blinded operator. If the parameter was described in the text, the study received a "yes," otherwise, it received a "no" or "unclear" (no information or

uncertainty about the potential for bias). The risk of bias was classified according to the sum of "yes" answers received, as follows: 1–3 = high; 4–5 = intermediate; 6–8 = low risk of bias. If needed, authors were contacted via e-mail (at least two attempts were made) for missing or unclear information.

Data Analysis

Through a random-effects meta-analysis, the pooled-effect estimates were obtained by comparing the standardized mean difference between the bond strengths of SDF treated dentin and control groups separately for each restorative

material considered. Subgroup analyses were carried out according to the SDF application protocol (including or excluding the rinsing step after the SDF application time) and dentin condition (sound or caries-affected). $p \leq 0.05$ was considered statistically significant (Z-test). For studies that evaluated more than one adhesive, it was necessary to combine the obtained bond strengths (regardless of the etching strategy) into one mean and one standard deviation using a formula suggested by the Cochrane Statistical Guidelines.¹⁷ Only the immediate bond strengths were considered for analysis. Forest charts were created to illustrate the meta-analysis. Statistical heterogeneity of the treatment effect among studies was assessed using the Cochran Q test and inconsistency (I^2), with a p-value of 0.1.¹⁷ All analyses were performed using Review Manager Software 5.3 (The Cochrane Collaboration; Copenhagen, Denmark).

RESULTS

Search and Selection

The search strategy identified 1630 potentially eligible studies in all databases. Duplicates were removed, and 1500 studies remained for further examination regarding the inclusion criteria. After screening titles and abstracts, 1478 studies were excluded. With this, 22 studies remained after the full-text assessment. For the meta-analysis, 21 studies were included because one of the studies⁵⁴ did not present means and standard deviation, and the missing data were not provided by the authors through e-mail. A flowchart of the study selection process according to the PRISMA statement³⁸ and the reasons for exclusion are shown in Fig 1.

Descriptive Analysis

Tables 1 and 2 show the descriptive data of the included studies separately by restorative material, glass-ionomer cement, and adhesives. Studies were published between 1993 and 2020, all in English. Almost all of the included studies are from the last eight years, except two^{23,54} evaluating glass-ionomer cement bonding.

For glass-ionomer cement, 12 studies were included.^{3,10,15,19,23,25,34,42,49,52,55} The studies come mainly from 3 countries/regions – Japan, India, and Hong Kong. SDF concentrations of 30% or 38% associated with potassium iodide solution were evaluated. The majority of the studies evaluated glass-ionomer cement modified by resin or high viscosity; only three used conventional glass-ionomer cement.^{3,23,52} Five studies evaluated the bonding of glass-ionomer cement to sound dentin,^{10,15,23,34} four considered caries-affected dentin,^{34,42,49,55} and three evaluated the two substrate conditions.^{3,19,52} Of the studies that assessed caries-affected dentin, most used artificial lesions; only one study⁴² used natural lesions. The majority assessed permanent teeth, and only two studies used primary molars.^{42,49} The shear bond strength test was the most frequently employed mechanical method, followed by the microtensile bond strength test.

For adhesives, eleven studies were included.^{9,24-26,28,29,43,45,46,50,53} The studies come mainly from the USA. The

majority of studies used SDF concentrations of 30% or 38%, associated with potassium iodide solution. Only two studies^{43,46} evaluated both SDF 38% and SDF 12%, and one study²⁴ assessed SDF 38% and 3.8%. Therefore, data based on concentrations of 12% and 3.8% were not considered. Sound dentin was the bonding substrate considered in most studies; only four studies^{9,26,46,50} evaluated the bond strength to caries-affected dentin. Of the studies that assessed caries-affected dentin, most used artificial lesions and only one study⁹ used natural lesions. Only one study considered bonding to primary dentin.⁵³ The microtensile bond strength test was the most commonly used mechanical test.

Meta-Analysis

Glass-ionomer cement

Figure 2 shows the results for the meta-analysis considering glass-ionomer cement. No significant difference was found between control and SDF groups ($Z = 0.53$; $p = 0.60$) in the overall meta-analysis, with moderate heterogeneity (chi-squared test; $p = 0.04$; $I^2 = 41\%$). SDF pretreatment does not affect the bond strength to sound dentin, with ($Z = 0.93$; $p = 0.35$) or without the rinsing step ($Z = 1.11$; $p = 0.27$). The data showed heterogeneity for rinsing subgroups (chi-squared test; $p = 0.03$; $I^2 = 65\%$) and no heterogeneity for subgroups without a rinsing step (chi-squared test; $p = 0.43$; $I^2 = 0\%$). Similarly, pretreatment with SDF did not jeopardize the bond strength to caries-affected dentin, with ($Z = 0.99$, $p = 0.32$) or without a rinsing step ($Z = 0.92$, $p = 0.36$). The data show moderate heterogeneity for rinsing subgroups (chi-squared test; $p = 0.16$; $I^2 = 39\%$) and no heterogeneity for subgroups without rinsing (chi-squared test; $p = 0.82$; $I^2 = 0\%$).

Adhesives

Figure 3 shows the results of meta-analysis for adhesives. SDF applied prior to the adhesive significantly impaired the bond strength to dentin in overall meta-analysis ($Z = 2.43$; $p = 0.01$) and in the sound dentin subgroup without rinsing ($Z = 2.93$; $p < 0.01$). The data were heterogeneous (chi-squared test; $p < 0.01$; $I^2 = 98\%$ and $p < 0.01$; $I^2 = 95\%$). The rinsing step eliminated the negative effect of SDF application in sound dentin ($Z = 1.82$; $p = 0.07$) and increased the bonding of adhesives to caries-affected dentin ($Z = 2.14$, $p = 0.03$). Data were heterogeneous in both sound and caries-affected dentin, with rinsing step subgroup analysis (chi-squared test; $p < 0.01$; $I^2 = 97\%$; chi-squared test; $p = 0.1$; $I^2 = 72\%$).

Risk of bias

The results of the risk-of-bias assessment are described in Table 3. One study could not have its risk of bias assessed,⁵⁰ as it was not obtained in the full version, and some domains could not be evaluated. The majority of the included studies presented intermediate (10 studies) or high (8 studies) risk of bias. The parameters that most often received “no” were: the description of sample size calculation, a single operator during the specimen preparation, and operator blinded during the tests.

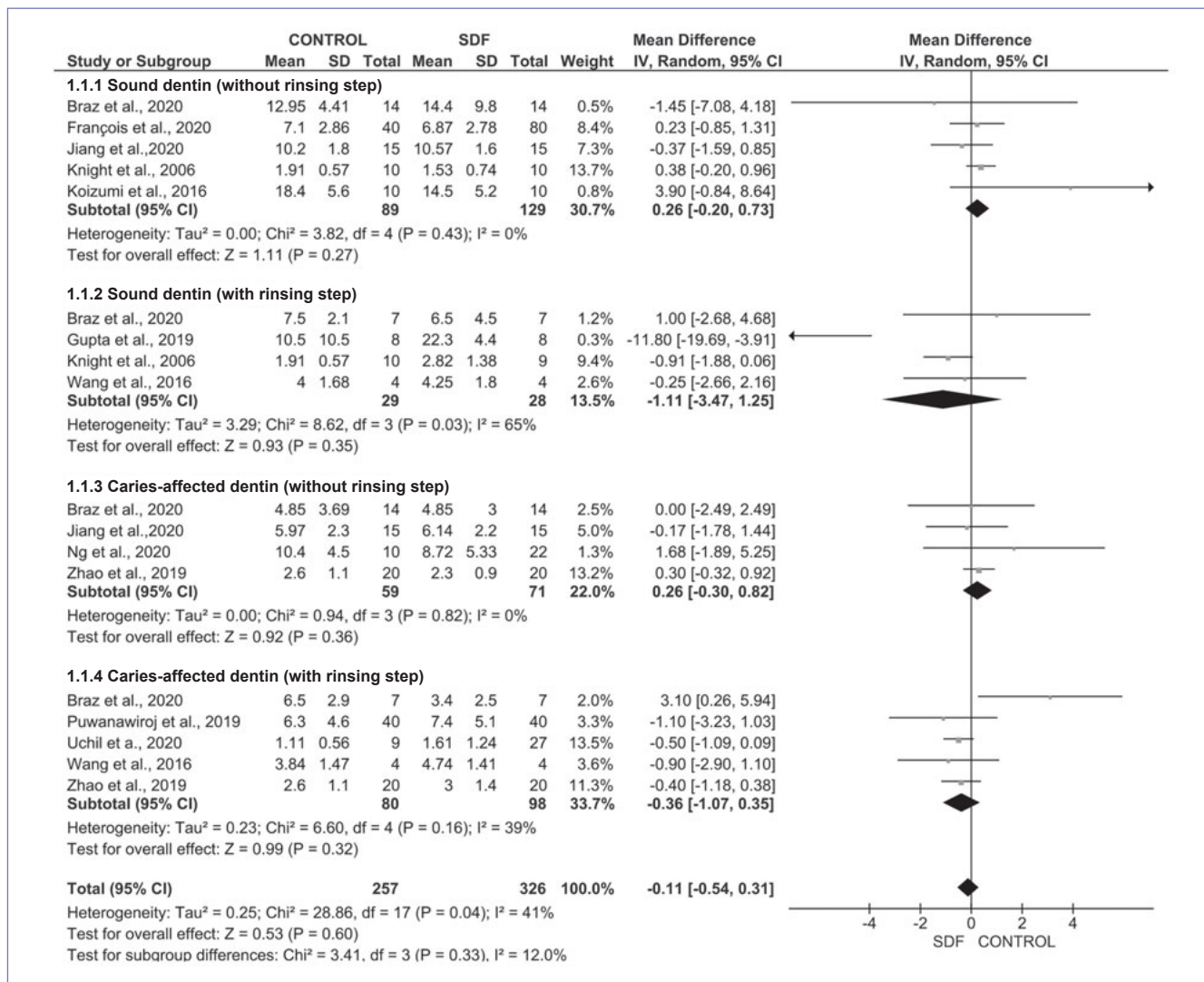


Fig 2 Meta-analysis findings comparing the bond strength of glass-ionomer cement to SDF treated (SDF) and untreated (control) dentin according to SDF protocol (with or without rinsing step) and dentin condition (sound or caries-affected).

DISCUSSION

The present study updates a previous systematic review and meta-analysis on the influence of silver diamine fluoride application on dentin bond strength of glass-ionomer cement and adhesives.¹¹ The first review¹¹ included 11 studies, the majority of them evaluating SDF pretreatment on sound dentin, so that an independent analysis with data of caries-affected dentin could not be investigated. This updated systematic review, conducted by the same research group, included 22 studies; 10 studies that evaluated caries-affected dentin substrate were eligible for this review (6 new studies); this is a more relevant substrate in daily clinical practice. Another systematic review was recently

published, but without including the total of studies considered in this review.²⁰

According to our previous systematic review,¹¹ the effect of SDF application on dentin bonding was material-dependent, as it does not influence the bonding of glass-ionomer cement but can impair the bond strength of adhesives if SDF is not rinsed after application. Therefore, new subgroup meta-analyses were performed considering studies that assessed the SDF effect in caries-affected dentin. As in the previous review, SDF pretreatment in caries-affected dentin does not impair the bond strength of glass-ionomer cement. Likewise, SDF application followed by rinsing, does not jeopardize adhesives' bond strength. Therefore, considering the obtained results, the hypothesis of this updated review was partially accepted.

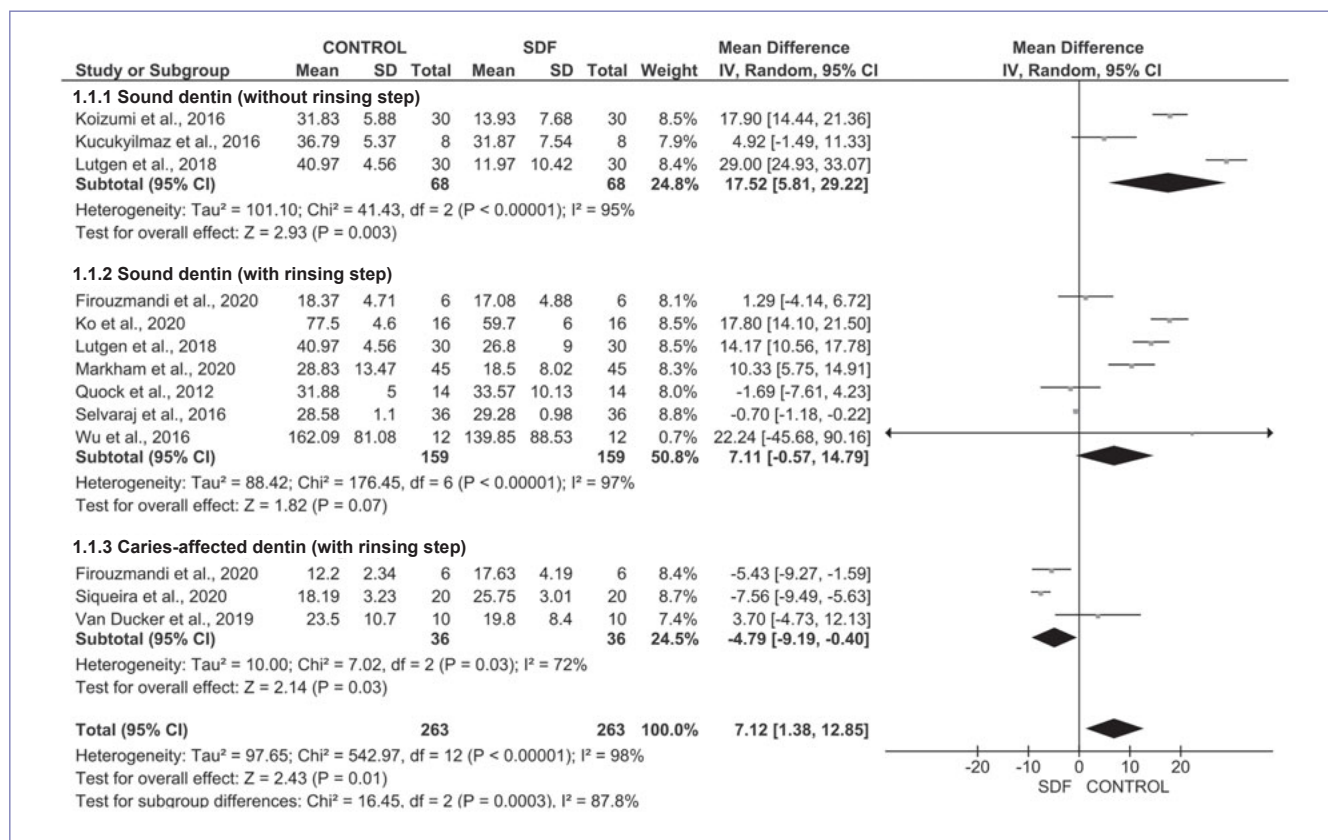


Fig 3 Meta-analysis findings comparing the bond strength of adhesives to SDF treated (SDF) and untreated (control) dentin according to SDF protocol (with or without rinsing step) and dentin condition (sound or caries-affected).

The present findings show that regardless of dentin condition (sound or caries-affected), the bonding of glass-ionomer cement was not affected by SDF pretreatment. This may be explained by the bonding mechanism of glass-ionomer cement, which is based on a chemical reaction between polyacrylic acid from glass ionomer and calcium ions mainly from hydroxyapatite.¹⁴ The SDF protocol (with or without the rinsing step) did not influence dentin bond strength to either substrate. However, even in studies that did not carry out the rinsing step immediately after SDF application, a conditioner, such as polyacrylic acid,^{3,10,19,25} was applied before restoration. Thus, the rinsing step or the application of polyacrylic acid can be necessary for proper adhesion of glass-ionomer cement to SDF-treated dentin to eliminate the silver precipitate excess and increase the ion exchange for an acid-base reaction.

In contrast to the glass-ionomer cement results, the bond strength of adhesives to dentin could be impaired by SDF pretreatment. The silver precipitate formed on the dentin surface and in dentin tubules could adversely affect the bonding of the adhesive, as the bonding mechanism of adhesives is based on micromechanical retention and hybrid layer formation in dentin.^{4,16} As in the first review, this up-

date considered the adhesives in the same group, regardless of the etching strategy (etch-and-rinse or self-etch), as in other reviews,^{2,7,41} considering that the main goal was to evaluate the influence of SDF on dentin bonding.

The negative effect of SDF on the bonding of adhesives was eliminated when rinsing was performed, even in caries-affected dentin. The worst result was expected in caries-affected dentin due to the chemical and morphological differences^{1,33} as well as more silver precipitating onto demineralized dentin,²² but this was not confirmed in this systematic review. On the contrary, pretreatment with SDF followed by rinsing could increase adhesives' bonding to caries-affected dentin. Only one study²⁶ assessed prior SDF application on caries-affected dentin without the rinsing step, so this subgroup analysis could not be performed. Even so, according to this earlier study,²⁶ SDF application jeopardized dentin bond strength. Immediately after SDF application, rinsing can eliminate the excess of silver precipitate from peritubular and intertubular dentin,²⁸ favoring adhesion. Besides, SDF can remineralize the caries-affected dentin,⁵⁶ improving the mechanical properties of this altered substrate. However, this finding is based on only three studies;^{9,46,50} thus, more investigations evaluating

Table 3 Risk of bias assessment for each included study

Study	Random sequence	Sample size calculation	Same number of teeth per group	Failure mode evaluation	SDF application protocol according manufactures	Restorative material application protocol according manufactures	Single operator	Blinded operator	Risk of bias
Glass-ionomer cement									
Braz et al, 2020 [3]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Low
François et al, 2020 [10]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Gupta et al, 2019 [15]	No	No	Yes	No	Yes	Yes	No	No	High
Jiang et al, 2020 [19]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Knight et al, 2006 [23]	No	No	No	No	Unclear	Unclear	No	No	High
Koizumi et al, 2016 [25]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Ng et al, 2020 [34]	Yes	No	No	No	Yes	Yes	No	No	High
Puwanawiroj et al, 2018 [42]	Yes	No	Yes	Yes	Unclear	Unclear	No	No	High
Uchil et al, 2020 [49]	Yes	Yes	Yes	Yes	Unclear	Yes	No	No	Medium
Wang et al, 2016 [52]	Yes	No	Yes	Yes	Yes	Unclear	No	No	Medium
Yamaga et al, 1993 [54]	No	No	Yes	Yes	No	No	No	No	High
Zhao et al, 2019 [55]	Yes	No	Yes	Yes	Unclear	Unclear	No	No	High
Adhesives									
Firouzmandi et al, 2020 [9]	Yes	No	Yes	Yes	Unclear	Yes	No	No	Medium
Ko et al, 2020 [24]	Yes	No	Yes	Yes	Unclear	Yes	No	No	Medium
Koizumi et al, 20016 [25]	Yes	No	Yes	Yes	Yes	Yes	No	No	Medium
Kucuklymaz et al, 2016 [26]	Yes	No	Yes	Yes	Unclear	Unclear	No	No	High
Lutgen et al, 2018 [28]	No	No	Yes	Yes	Yes	Yes	No	No	Medium
Markham et al, 2020 [29]	No	No	Yes	Yes	Unclear	Yes	No	No	High
Quock et al, 2012 [43]	Yes	No	Yes	Yes	No	Yes	No	No	Medium
Selvaraj et al, 2016 [45]	Yes	No	Yes	Yes	No	Yes	No	No	Medium
Siqueira et al, 2020 [46]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Low
Wu et al, 2016 [53]	No	No	Yes	Yes	Unclear	Yes	No	No	High

the bonding mechanism of adhesives to SDF-treated caries-affected dentin are necessary to confirm this result.

The application of SDF to prevent recurrent caries is a new and off-label approach; therefore, few studies evaluating its effect on bond strength of restorative materials are available, which explains the relatively low number of eligible studies. However, it is essential to note that shortly after the publication of the first systematic review,¹¹ twice as many articles could now be included in this update, demonstrating the growing interest in the use of SDF. Despite the considerable increase in the number of studies, only one new study evaluating primary teeth was included.⁴⁹ Thus, although SDF is most commonly used for arresting caries in primary teeth,⁵ few studies assessed the influence of prior SDF application on the bond strength of re-

storative materials in these teeth (two assessed glass-ionomer cement^{42,49} and only one considered an adhesive).⁵³ Hence, a separate meta-analysis cannot be performed yet. Considering that bond strength evaluations can measure one specific parameter, controlling the other variables, more laboratory investigations should be conducted to evaluate the effect of SDF on bonding to primary dentin.

SDF can inhibit matrix metalloproteinases (MMPs), thus avoiding dentin collagen degradation.^{30,31} It is known that the intrinsic degradation (proteolysis) of collagen fibers in dentin by enzymes such as MMPs can compromise the bonding interface, decreasing the bond strength of restorative materials in the long term.^{37,39} The use of MMP inhibitors has been considered an effective strategy to improve the longevity of adhesive restorations.^{37,48} However, only

one included study evaluated the bond strength of an etch-and-rinse adhesive to SDF-treated dentin after 6 months of water storage;⁹ therefore, the influence of aging could not be evaluated through a meta-analysis. That study⁹ found that prior SDF application on sound dentin limited the effect of water storage on the bond strength; however, on caries-affected dentin, a significant reduction of bond strength after water storage was shown in the SDF-treated group. Therefore, long-term studies are needed to determine the effect of silver diamine fluoride on bond strength after aging.

The present systematic review assessed the influence of SDF on bonding, mainly in concentrations of 30% and 38%, as previous studies demonstrated that products with the highest concentrations are more effective in arresting caries lesions.^{12,13} Only two studies assessed 12% SDF.^{43,46} Moreover, 9 studies evaluated dentin pretreatment with 38% SDF associated with potassium iodide (KI) before restoration placement.^{10,15,23,25,45,46,49,50,55} The subsequent application of KI is suggested to minimize the inherent disadvantage of SDF turning treated areas dark.⁴⁰ A previous study⁵⁷ suggests that the association SDF+KI is not as effective as SDF alone in preventing secondary caries, while another²³ reported that this association was more effective in inhibiting the migration of *Streptococcus mutans* through dentin than SDF alone. Thus, there are doubts regarding the effectiveness of SDF with KI for caries prevention.

As found in this systematic review, high heterogeneity is a common finding in meta-analyses of laboratory studies,^{6,27,44,47} and in this case, may have been influenced by the SDF application protocol, restorative material, different methods of producing caries-affected dentin and bond strength testing. Besides, most studies included presented a high or intermediate risk of bias. Although there is a guideline for conducting and reporting in vitro studies on dental materials,⁸ it seems that it has not been commonly used, so this finding in systematic reviews of laboratory studies is common.^{6,27,47}

This systematic review evaluated the bond strength of glass-ionomer cement and adhesives to silver diamine fluoride-treated dentin. Bond strength tests are commonly used to evaluate restorative materials to predict their performance and the influencing variables – such as prior application of SDF. Although the relationship between in vitro studies and clinical performance is difficult to establish,⁵¹ a material's adhesive ability is an indicator of restoration longevity; superior laboratory performance is probably indicative of better clinical performance.³⁵ Nevertheless, the results of in vitro studies should ideally be confirmed by long-term laboratory studies and randomized clinical trials, evaluating not only the effect of SDF pretreatment on bonding but also considering interface integrity, secondary caries, and staining. At the moment of this review, there was only one randomized clinical trial with 24 months of follow-up which evaluated the prior application of SDF on cavitated dentin caries lesions in primary teeth before atraumatic restorative treatment (ART).²¹ That clinical trial found that SDF did not jeopardize the success rate of the restorations.

The present systematic review pointed out that pretreatment with silver diamine fluoride does not influence the

bond strength of glass-ionomer cement to dentin, regardless of whether it is sound or caries-affected. In contrast, SDF application can impair the bonding of adhesives. However, rinsing after SDF application seems to eliminate this adverse effect in sound dentin and improved the bond strength to caries-affected dentin.

CONCLUSION

Based on the results of this systematic review and meta-analysis of in vitro studies, it can be concluded that the SDF pretreatment does not jeopardize the bonding of glass-ionomer cement to dentin. The same is valid for adhesives only if a rinsing step after SDF application is performed, which can even improve the adhesion of this restorative material to caries-affected dentin.

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Clinical relevance: Dentin pretreatment with silver diamine fluoride does not affect the adhesion of glass-ionomer cements. If a rinsing step after SDF application is not carried out, the bonding of the adhesive to dentin may be compromised.