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Original Article

Evaluation of the bond strength of chlorhexidine incorporated into the adhesive system composition: A PRISMA guided meta-analysis

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Abstract *Background/purpose:* Composite resin is currently the most widely used dental restoration material. Previous studies have demonstrated that the application of Chlorhexidine (CHX) on the dentin surface after acid etching can result in an improvement in the integrity and stability of tooth restoration through time. In order to better understand whether CHX can help improve the stability of the resin-dentin bond strength, in this study, a comprehensive review of the effect of adding CHX to the adhesive system on the stability of immediate and long-term resin-dentin bond strength was conducted.

Materials and methods: This article was written in accordance with the PRISMA Statement and is registered on the International Prospective Register of Systematic Reviews (registration number CRD42018084962). Six electronic databases including PubMed, Embase, Cochrane library, ISI Web of Science, ClinicalTrials.gov and China National Knowledge Infrastructure (CNKI) were searched up to October, 2018. Ten articles were selected from 340 possible eligible articles for meta-analysis, and 41 sets of data were analyzed in the meta-analysis.

Results: The results indicated that the use of 0.1% and 0.2% CHX does not adversely affect the immediate bond strength ($p > 0.05$), but both 0.1% and 0.2% CHX increased bond strength compared with the control group over 12 months ($p < 0.05$). However, this trend does not represent a longer period of aging.

Conclusion: In these in vitro clinical trials, CHX incorporated into the bonding systems maintained the stability of bond strength.

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Introduction

Composite resin is currently the most widely used dental restoration material. The repair effect and integrity of the composite resin depends on many factors, such as the effect of polymerization shrinkage and light curing factors. When the contractile force of the material on the dentin is greater than the adhesive force, this leads to gaps between the material and the tooth structure.[1] The bond strength of the resin-dentin interface decreases over time, and studies have shown that the decrease in bond strength is associated with the degradation of collagen fibers in the mixed layer.[2,3] For example, after 100 days or 6 months of aging, the bond strength decreases.[4] Degradation of dentin collagen fibers can cause long-term cohesion. Therefore, maintaining the integrity of dentin collagen fibers is a determining factor in the maintenance of long-term adhesion.[3] Dentin contains a class of proteolytic enzymes known as matrix metalloproteinases (MMPs), and MMPs-mediated degradation of dentin collagen fibers is an important endogenous factor leading to degeneration of the dentin bonding interface.[5]

The dentin mineralization mechanism involves a large number of collagen fibers which form a network structure, and when it is demineralized, the collagen fibers collapse. MMPs play an important role in degrading collagen fibers and destroying the adhesive surface.[6] It has been demonstrated that some MMPs in human dentin are responsible for this destruction.[7] Some substances can inhibit these proteases (MMPs inhibitors), and the most commonly used inhibitor is Chlorhexidine (CHX), which can also inhibit the presence of another enzyme (cysteine cathepsin)[8,9] in dentin. The addition of CHX is carried out using the following methods: (1) CHX is added to the etchant (2) CHX is added to the bonding system (primer and bonding agent) (3) CHX as a pretreatment agent is applied on the etched dentin surface by rubbing, to maintain contact with the dentin surface.[10]

Montagner et al.[10] performed a meta-analysis in 2014 to evaluate dentin stability in which CHX was used as a post-etching pretreatment agent to treat the cavity. The results showed that 2% CHX had no adverse effect on the immediate bond strength, and both 0.2% and 2% CHX increased the stability of the bond strength after aging. The use of MMP inhibitors on the surface of dentin or the addition of a bonding system may maintain the integrity of the collagen fibers and the stability of the bond strength.[11–13] CHX can protect collagen in the mixed layer from degradation by MMPs, and can effectively maintain dentin bond interface stability.[14] However, other studies have shown that the addition of CHX in the presence or absence of a bonding system has no effect on long-term dentin bond strength.[15] CHX added to the bonding system can reduce the number of steps and time of the operation. Whether CHX is beneficial in improving the stability of the resin-dentin bond strength is not yet clear.

The purpose of this study was to evaluate the effect of adding CHX, a MMP inhibitor, to the bonding system on the stability of immediate and long-term resin-dentin bond strength of the CHX-stabilized dentin bonding interface. In addition, the results of this investigation may provide a scientific-theoretical basis for resin-dentin bond strength and guide clinical applications.

Materials and methods

Data source

This article was written in accordance with the PRISMA Statement (Systematic Review and Meta-analysis Priority Report)[16] and is registered on the International Prospective Register of Systematic Reviews (Registration Number: CRD42018084962). Six electronic databases including PubMed, Embase, Cochrane library, ISI Web of Science, ClinicalTrials.gov and China National Knowledge Infrastructure (CNKI) were searched. The last retrieval was October, 2018.

The survey strategy (matrix metalloproteinase OR protease inhibitor OR MMPs inhibitor OR chlorhexidine OR CHX) AND (dentin adhesive OR bond adhesive) AND (self-etching primer OR self-etch adhesive OR self-etching adhesive OR self-etching bonding agent OR total-etching bonding agent OR total-etching primer OR total-etch adhesive OR total-etching adhesive OR adhesive system) was employed.

Inclusion criteria

Study type: In vitro randomized controlled trials RCTs.

Research subject: human teeth (first premolar, third molar).

Research subject: CHX, a MMP inhibitor.

Interventions: Addition to full-etching bond systems or self-etching bond systems.

Measured index: bond strength measured by the micro-tensile test and micro-shear test.

Exclusion criteria

(1) All MMP inhibitors other than CHX, including ethylenediaminetetraacetic acid, quaternary ammonium salts, zinc ions and zinc oxide, tetracyclines and their

derivatives, hydroxamic acid inhibitors, crosslinkers and other exogenous inhibitors.

(2) Studies on the bond strength of the fiber post in the bonding system containing CHX.

Literature search, screening

The eligible studies were evaluated independently by two authors. If the decisions by the authors were different, the studies in question were jointly reassessed and the final decisions were determined by consensus.

Data extraction

A data extraction scheme was designed by two authors and one author extracted data from the full text. The second author checked the extracted data.

Inclusion of research risk assessment

For inclusion of research risk assessment, RevMan 5.3 software was applied to assess the risk of bias in the included RCTs according to the Cochrane Systematic Reviewer's Manual 5.1.0.

Statistical analysis

Data analysis was performed using RevMan 5.3 software. The outcome measure of this study was a continuous variable. Inconsistencies among the trials were estimated using the Chi-square test of heterogeneity (χ^2) and quantified by the I^2 test. Heterogeneity was within the acceptable range ($p > 0.1$ and $I^2 < 50\%$), and the combined effect analysis was performed using the fixed effect model. Otherwise, the random effect model was used. Values of $p \leq 0.05$ were considered statistically significant (Z test). Mean difference (MD) was used for the same numerical measure of the

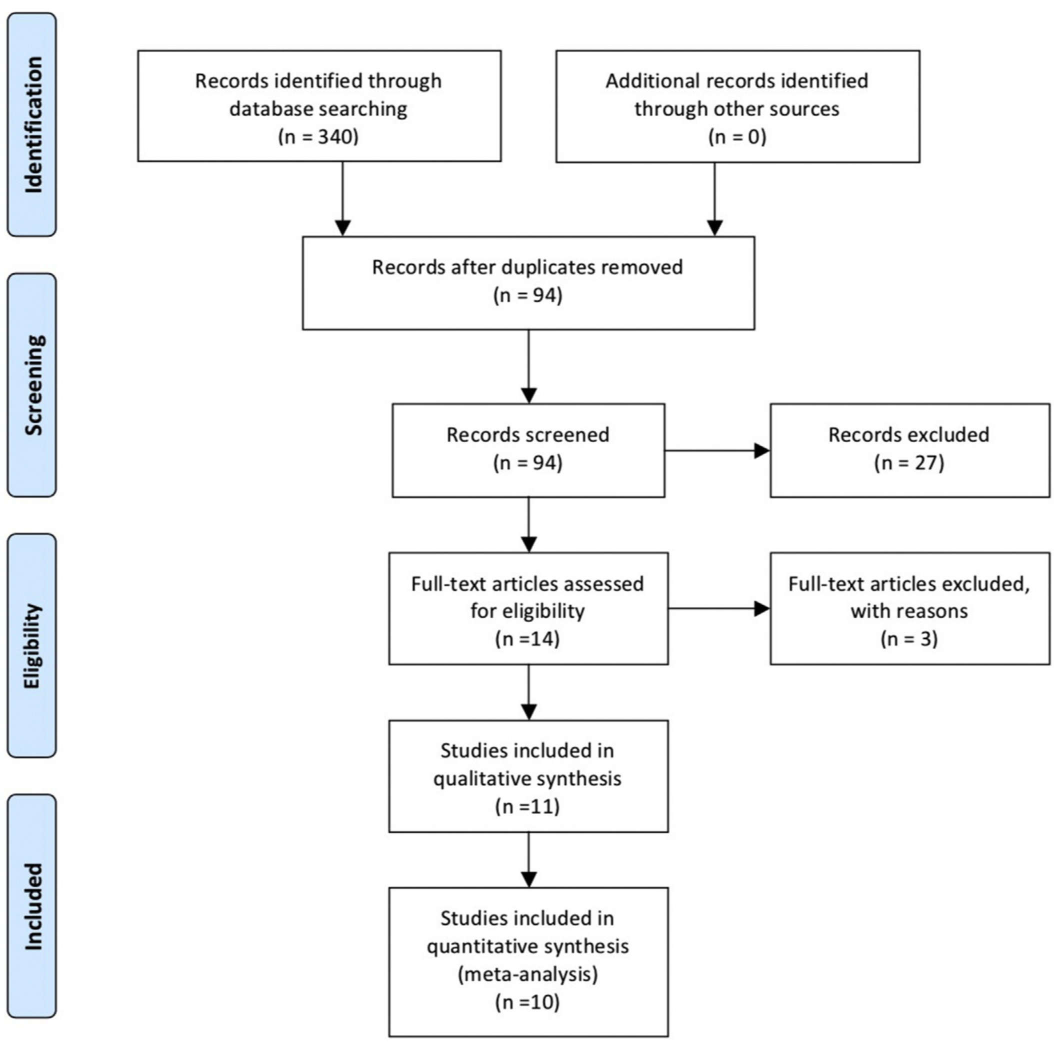

Figure 1 Flow diagram of included studies.

Table 1 Basic information included inthe study (immediately measured bond strength).

Study	Adhesive System	TCHX Concentration (%)	Tsample (n)	Tmean μTBS (MPa)	Tsd μTBS (SD)	CCHX Concentration (%)	Csample (n)	Cmean μTBS (MPa)	Csd μTBS (SD)
Hiraishi et al. 2010[17]	Self-etching primer	1	40	19.81	4.273	0	40	21.43	4.273
	Self-etching primer	2	40	15.14	1.563	0	40	21.43	1.563
Zhou et al. 2010[19]	Self-etching primer	0.05	16	64.75	9.46	0	15	66.49	8.98
	Self-etching primer	0.1	15	69.81	15.41	0	15	70.62	11.83
	Self-etching primer	0.5	16	70.97	3.16	0	15	69.75	3.71
	Self-etching primer	1	16	68.96	14.38	0	16	65.6	12.71
Zhou et al. 2009[20]	Self-etching primer	0.05	16	62.81	9.36	0	16	64.89	9.24
	Self-etching primer	0.1	16	67.88	15.52	0	16	68.6	11.87
	Self-etching primer	0.5	16	68.59	12.69	0	16	67.41	14.4
	Self-etching primer	1	16	66.51	14.39	0	16	63.05	12.75
De Munck et al. 2009[18]	Self-etching primer	0.05	10	55.05	13.21	0	10	69.72	13.21
	Total-etching primer	0.05	10	50.23	8.968	0	10	58.46	8.968
De Munck et al. 2010[13]	Self-etching primer	0.05	4	60.5	16.6	0	4	55.3	21.3
	Total-etching bonding agent	0.05	7	28.5	13.9	0	6	41	12.2
	Self-etching bonding agent	0.05	6	13.9	12.8	0	4	14.2	8.5
Islam et al. 2012[21]	Self-etching primer	0.5	40	70.1	8.7	0	55	74.4	8.8
Sabatini et al. 2013[15]	Self-etching bonding agent	0.2	10	37.4	11.7	0	10	39.5	9.9
	Total-etching bonding agent	0.2	10	46	7.2	0	10	40.6	15.7
Nishitani et al. 2013[22]	Self-etching bonding agent	0.5	10	69.2	14.7	0	10	67.8	10.6
	Self-etching bonding agent	1	10	55.4	13.1	0	10	67.8	10.6
	Self-etching bonding agent	2	10	54.8	10.5	0	10	67.8	10.6
	Self-etching bonding agent	5	10	12.7	2.4	0	10	67.8	10.6
Stanislawczuk et al. 2014[23]	Total-etching bonding agent	0.01	10	56.2	4.3	0	10	54.5	3.9
	Total-etching bonding agent	0.05	10	51.2	4.1	0	10	54.5	3.9
	Total-etching bonding agent	0.10	10	55.3	3.2	0	10	54.5	3.9
	Total-etching bonding agent	0.2	10	54.1	3.8	0	10	54.5	3.9
	Total-etching bonding agent	0.01	10	61.9	5.8	0	10	64.5	2.7
Yiu et al. 2012[24]	Total-etching bonding agent	2	5	19	2	0	5	20.2	2.6

Table 1 (*continued*)

Study	Adhesive System	TCHX Concentration (%)	Tsample (n)	Tmean μTBS (MPa)	Tsd μTBS (SD)	CCHX Concentration (%)	Csample (n)	Cmean μTBS (MPa)	Csd μTBS (SD)
	Total-etching bonding agent	2	5	30.2	3.4	0	5	33.1	2.9
	Total-etching bonding agent	2	5	34.8	2.7	0	5	37.3	1.7

T:Test group, C:Control group.

Table 2 Basic information included in the study (measurement of bond strength after storage for 12 months).

Study	Adhesive System	TCHX Concentration (%)	Tsample (n)	Tmean μTBS (MPa)	Tsd μTBS (SD)	CCHX Concentration (%)	Csample (n)	Cmean μTBS (MPa)	Csd μTBS (SD)
Hiraishi	Self-etching primer	1				0			
et al. 2010[17]	Self-etching primer	2				0			
Zhou et al. 2010[19]	Self-etching primer	0.05				0			
	Self-etching primer	0.1				0			
	Self-etching primer	0.5				0			
	Self-etching primer	1				0			
Zhou	Self-etching primer	0.05	16	44.71	13.51	0	16	52.75	20.12
et al. 2009[20]	Self-etching primer	0.1	16	68.39	12.28	0	16	57.65	15.94
	Self-etching primer	0.5	16	64.53	13.08	0	16	52.73	16.93
	Self-etching primer	1	16	64.6	11.9	0	16	53.21	13.11
De Munck	Self-etching primer	0.05	10	38.89	1.495	0	10	37.23	1.495
et al. 2009[18]	Total-etching primer	0.05	10	33.56	8.39	0	10	25.86	8.39
De Munck	Self-etching primer	0.05	4	31.3	16.9	0	4	36.8	17.1
et al. 2010[13]	Total-etching bonding agent	0.05	7	6	6.6	0	6	20.7	18
	Self-etching bonding agent	0.05	6	2.9	2.7	0	4	4.8	4.8
Islam et al. 2012[21]	Self-etching primer	0.5				0			
Sabatini et al. 2013[15]	Self-etching bonding agent	0.2				0			
	Total-etching bonding agent	0.2				0			
Nishitani et al. 2013[22]	Self-etching bonding agent	0.5				0			
	Self-etching bonding agent	1%				0			
	Self-etching bonding agent	2%				0			
	Self-etching bonding agent	5%				0			
Stanislawczuk et al. 2014[23]	Total-etching bonding agent	0.01	10	50.8	2.5	0	10	34.8	4.1
	Total-etching bonding agent	0.05	10	49.6	4.2	0	10	34.8	4.1
	Total-etching bonding agent	0.1	10	53.4	4.5	0	10	34.8	4.1
	Total-etching bonding agent	0.2	10	52.9	3.8	0	10	34.8	4.1
	Total-etching bonding agent	0.01	10	47.4	3.2	0	10	35.9	2.8

(*continued on next page*)

Table 2 (*continued*)

Study	Adhesive System	TCHX Concentration (%)	Tsample (n)	Tmean μTBS (MPa)	Tsd μTBS (SD)	CCHX Concentration (%)	Csample (n)	Cmean μTBS (MPa)	Csd μTBS (SD)
	Total-etching bonding agent	0.05	10	45.2	5	0	10	35.9	2.8
	Total-etching bonding agent	0.1	10	54.2	4.3	0	10	35.9	2.8
	Total-etching bonding agent	0.2	10	56.5	4.3	0	10	35.9	2.8
Yiu et al. 2012[24]	Total-etching bonding agent	2	5	16.3	0.9	0	5	12.7	4.6
	Total-etching bonding agent	2	5	26.3	3.3	0	5	25.1	2.5
	Total-etching bonding agent	2	5	24.8	1.7	0	5	13.1	3.4

T: Test group, C: Control group.

outcome measure and 95% confidence interval (95% CI) was used for the interval estimate. Funnel plots were used to detect publication bias. Obvious clinical heterogeneity was evaluated by subgroup analysis, sensitivity analysis or descriptive analysis.

CHX 0.05%, 0.1%, 0.2%, 0.5%, 1%, and 2% were included to determine bond strength. These were the most commonly used data in the selected studies, and were analyzed as follows:

0.05% CHX vs control group (immediate bond strength values);
0.05% CHX vs control group (12 month bond strength values);
0.1% CHX vs control group (immediate bond strength values);
0.1% CHX vs control group (12 month bond strength values);
0.2% CHX vs control group (immediate bond strength values);
0.2% CHX vs control group (12 month bond strength values);
0.5% CHX vs control group (immediate bond strength values);
1% CHX vs control group (immediate bond strength values);
2% CHX vs control group (immediate bond strength values);

As there may have been a high degree of heterogeneity, the studies were divided into whole acid etching and self-etching bonding systems, added to primer and bonding agent for subgroup analysis to determine their effects.

Results

Literature search and screening results

From the 340 possible documents identified, and according to the inclusion and exclusion criteria, a total of 10 articles,[13,15,17–24] were finally included. The literature screening process and results are shown in Fig. 1.

The basic features included in the study

CHX at concentrations of 0.05%, 0.1%, 0.2%, 0.5%, 1%, and 2% were included for immediate bond strength

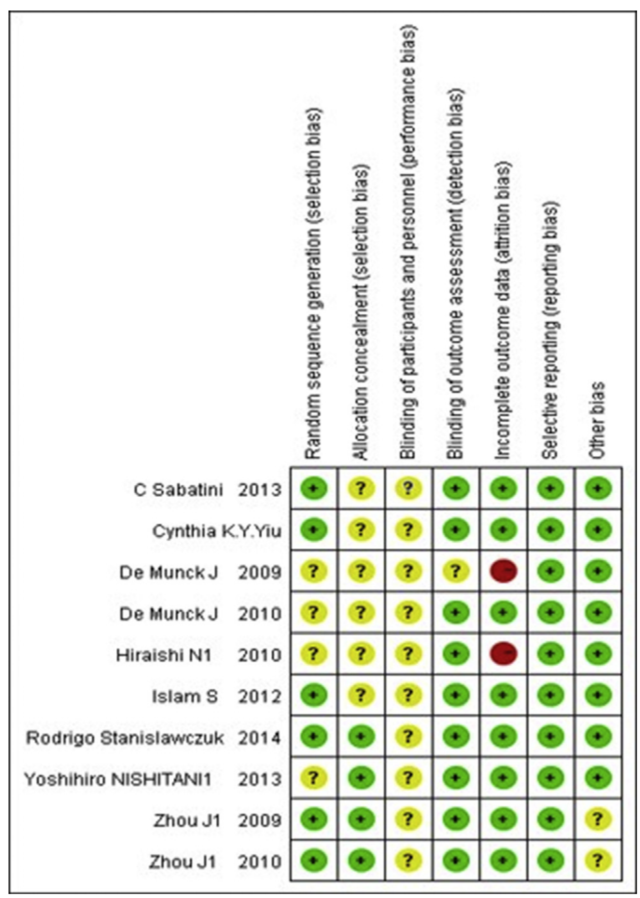

Figure 2 Quality assessment of included studies.

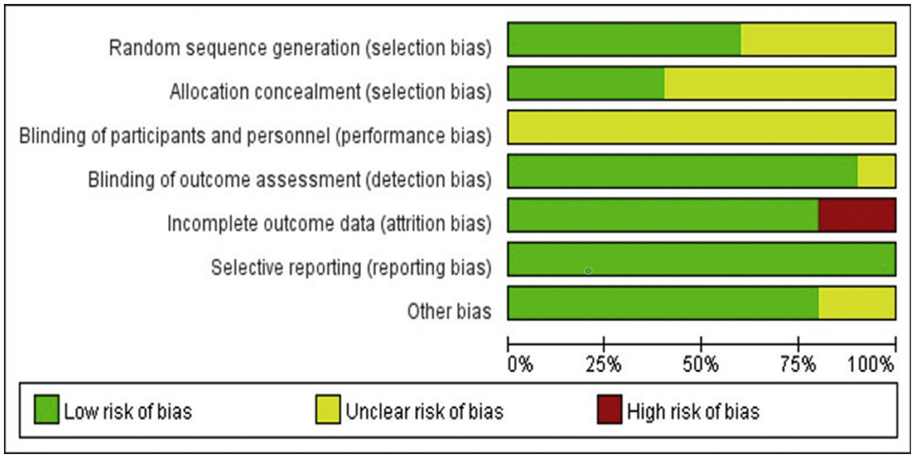

Figure 3 The percentage of risk of bias items in the included studies.

measurements, 0.05%, 0.1%, and 0.2% CHX for bond strength measurements after 12 months storage. The basic features of the studies included are shown in Table 1 (immediate measured bond strength) and Table 2 (measured bond strength after 12 months storage). Quality assessment of the included studies is shown in Fig. 2.

Results of bias risk assessment and publication bias

The results of bias risk assessment in the included studies are shown in Fig. 3.

Funnel plots were used to visually assess the presence of publication bias. Most studies were within the domain, which represents 95% confidence interval limits around the estimate, although some articles exceeded these boundaries, no apparent asymmetry was observed in the funnel plots. https://www.proxydgb.buap.mx:2300/pmc/articles/PMC3366926/figure/pone-0038268-g004/. Fig. 4 illustrates the funnel plots and shows the publication bias of immediate bond strength values of 0.05% CHX incorporated into the adhesive system composition.

Results of the meta-analysis

From the 10 articles, 9 sets of meta-analysis were conducted, and the results are shown in Tables 3 and 4, Figs. 5—13. The studies assessed indicated that MMP inhibitors have different effects on the immediate bond strength values and on the values after storage for 12 months.

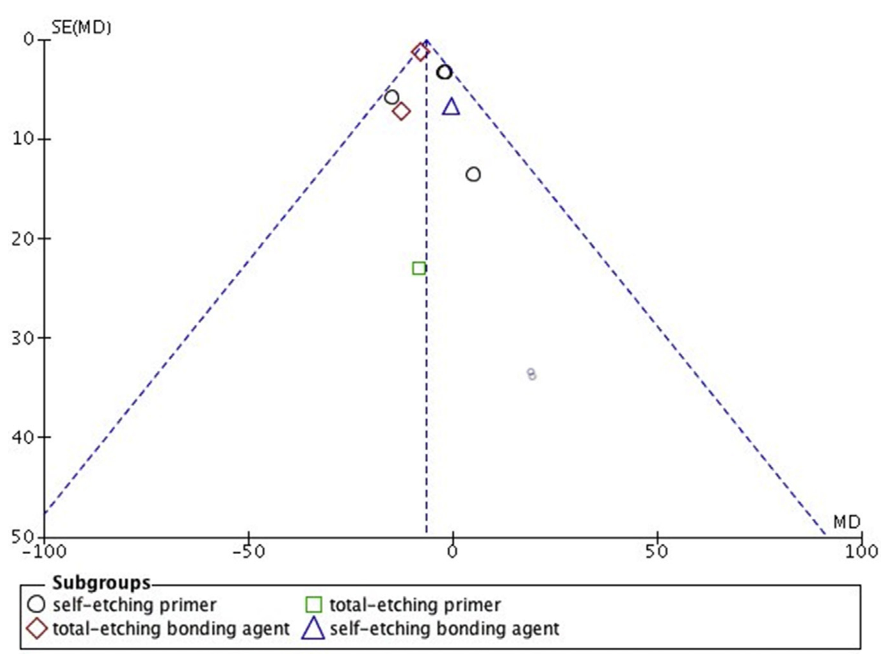

Figure 4 Funnel plots for comparison of immediate bond strength values of 0.05% CHX incorporated into the adhesive system composition and control group.

Table 3 Meta-analysis results (the immediate bond strength values).

CHX concentration	Number of articles	Number of data	Heterogeneity Adhesive system	MD Adhesive system	95% CI Adhesive system	P value Adhesive system	Heterogeneity Self- etching	MD Self-etching	95% CI Self-etching	P value Self-etching	Heterogeneity Total-etching	MD Total-etching	95% Total-etching	P value Total-etching
0.05%	5	9	$P = 0.25$ $I^2 = 23\%$	−5.76	$-9.09 \sim -2.41$	0.0007	$P = 0.22$ $I^2 = 33\%$	−3.94	$-9.60 \sim -1.72$	0.17	$P = 0.52$ $I^2 = 0\%$	−7.95	$-10.45 \sim -5.44$	$P < 0.00001$
0.1%	3	4	$P = 0.98$ $I^2 = 0\%$	0.52	$-1.58 \sim -2.61$	0.63	$P = 0.99$ $I^2 = 0\%$	−0.76	$-7.62 \sim 6.10$	0.83	$P = 0.89$ $I^2 = 0\%$	0.65	$-1.55 \sim 2.85$	0.56
0.2%	2	4	$P = 0.03$ $I^2 = 71\%$	5.62	$-2.59 \sim 13.84$	0.18					$P = 0.34$ $I^2 = 0\%$	10.38	$7.39 \sim 13.37$	$P < 0.00001$
0.5%	4	4	$P = 1.00$ $I^2 = 0\%$	1.23	$-1.08 \sim 3.53$	0.30	$P = 0.99$ $I^2 = 0\%$	1.22	$-1.14 \sim 3.57$	0.31				
1%	3	3	$P = 0.10$ $I^2 = 52\%$	−1.50	$-6.71 \sim 3.70$	0.31	$P = 0.36$ $I^2 = 2\%$	−1.18	$-3.16 \sim 0.80$	0.24				
2%	4	4	$P < 0.00001$ $I^2 = 97\%$	−2.41	$-9.03 \sim 4.20$	$P = 0.47$					$P = 0.61$ $I^2 = 0\%$	2.91	$1.17 \sim 4.66$	$P = 0.001$

Table 4 Meta-analysis results (the bond strength values after 12 months).

CHX concentration	Number of articles	Number of data	Heterogeneity Adhesive system	MD Adhesive system	95% CI Adhesive system	P value Adhesive system	Heterogeneity Self- etching	MD Self-etching	95% CI Self-etching	P value Self-etching	Heterogeneity Total-etching	MD Total-etching	95% Total-etching	P value Total-etching
0.05%	4	8	$P < 0.00001$ $I^2 = 90\%$	−3.51	$-1.46 \sim 8.48$	0.17	$P = 0.24$ $I^2 = 30\%$	−0.72	$-6.89 \sim 5.44$	0.82	$P < 0.00001$ $I^2 = 93\%$	−7.95	$-0.97 \sim 8.48$	$P = 16.14$
0.1%	2	3	$P = 0.33$ $I^2 = 10\%$	17.98	$15.62 \sim 20.34$	$P < 0.00001$					$P = 0.91$ $I^2 = 0\%$	18.42	$15.99 \sim 20.86$	$P < 0.00001$
0.2%	1	2	$P = 0.43$ $I^2 = 0\%$	19.95	$17.21 \sim 22.68$	$P < 0.00001$					$P = 0.43$ $I^2 = 0\%$	19.95	$17.21 \sim 22.68$	$P < 0.00001$

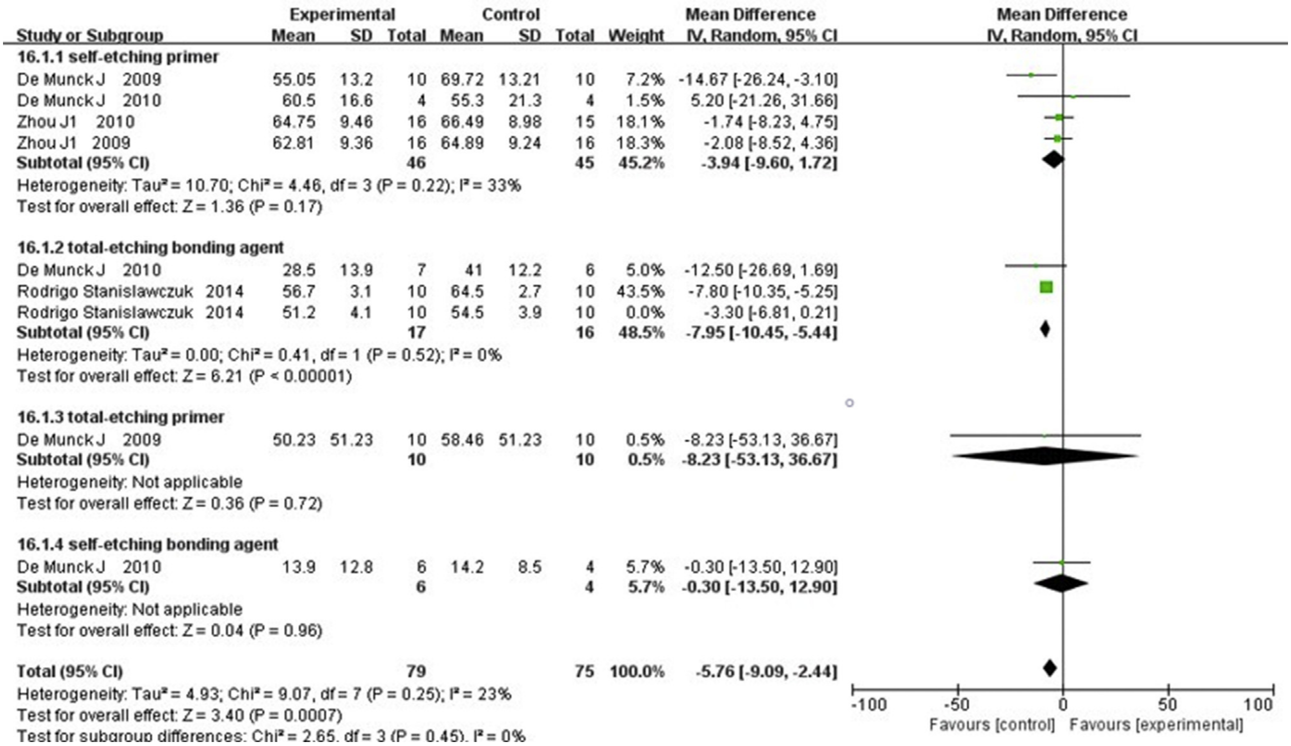

Figure 5 Forest plots for comparison of immediate bond strength values of 0.05% CHX incorporated into the adhesive system composition and control group.

The statistical results showed that: (1) When 0.05% CHX was added to the bonding system, the immediate bond strength value decreased compared with the control group ($p < 0.05$). The effects of CHX 0.1%, 0.2%, 0.5%, 1%, and 2% were similar to those in the control group ($p > 0.05$). When the bond strength value was measured after 12 months of storage, 0.05% CHX had no effect on the bond strength ($p > 0.05$), and both 0.1% and 0.2% CHX increased the bond strength ($p < 0.05$). (2) When 0.05%, 0.5%, and 1% CHX were added to the self-etching primer, whether the bond strength value was measured immediately or after 12 months of storage, the bond strength values were unaffected compared with the control group ($p > 0.05$), and the other three concentrations could not be measured due to

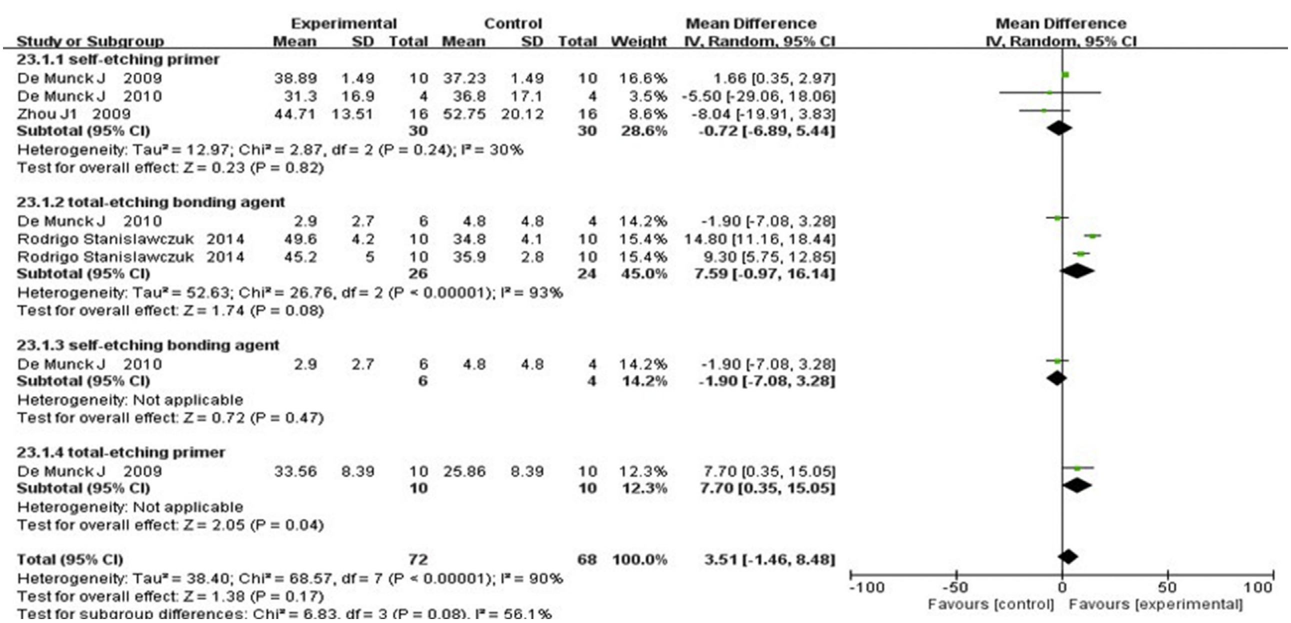

Figure 6 Forest plots for comparison of 12 month bond strength values of 0.05% CHX incorporated into the adhesive system composition and control group.

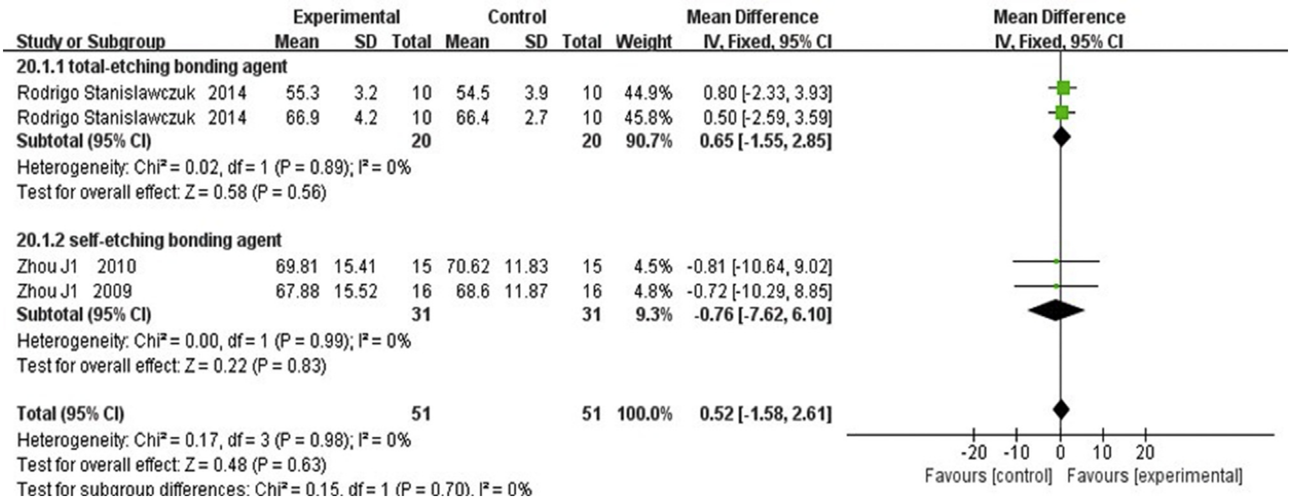

Figure 7 Forest plots for comparison of immediate bond strength values of 0.1% CHX incorporated into the adhesive system composition and control group.

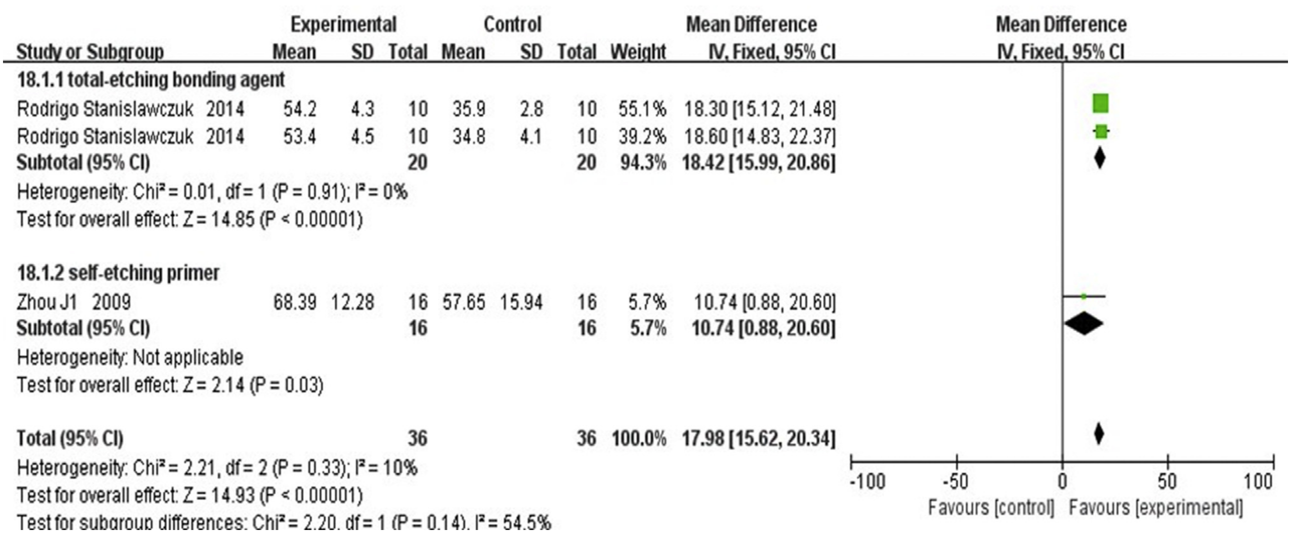

Figure 8 Forest plots for comparison of 12 month bond strength values of 0.1% CHX incorporated into the adhesive system composition and control group.

data issues. (3) When CHX was added to the total-etching primer, and the bond strength value was measured immediately, 0.1% CHX did not affect the bond strength value compared with the control group ($p > 0.05$), and the bond strength value was decreased by 0.05% CHX compared with the control group ($p < 0.05$). Both 0.2% and 2% CHX increased the bond strength value compared with the control group ($p < 0.05$).The bond strength value was measured after 12 months of storage, 0.05% CHX had no effect on the bond strength ($p > 0.05$), and both 0.1% and 0.2% CHX increased the bond strength ($p < 0.05$).

In the heterogeneity test, some data led to a high heterogeneity, and were excluded from the statistical analysis as follows: when the immediate bond strength was measured, and 0.05% CHX, 0.2% CHX was added to the total-etching primer, a set of data from the study by Rodrigo Stanislawczuk et al.[23] was excluded; when 0.5% CHX was added to the self-etching primer, a set of data by Sofiqul Islam et al.[21] was excluded; when 2% CHX was added to the total-etching primer, a set of data by Cynthia K.Y. Yiu et al.[24] was excluded. All excluded data were due to high heterogeneity in the sensitivity analysis. However, when 0.05% CHX was added to the total acid etching binder, and the bond strength measured after 12 months, the high heterogeneity was still present following sensitivity analysis.

Discussion

We conducted an extensive search and rigorous screening of the literature to reduce data heterogeneity during this meta-analysis. Unfortunately, five sets of data still showed high heterogeneity, which may have been due to the different types of bonding systems. Subgroup analysis and

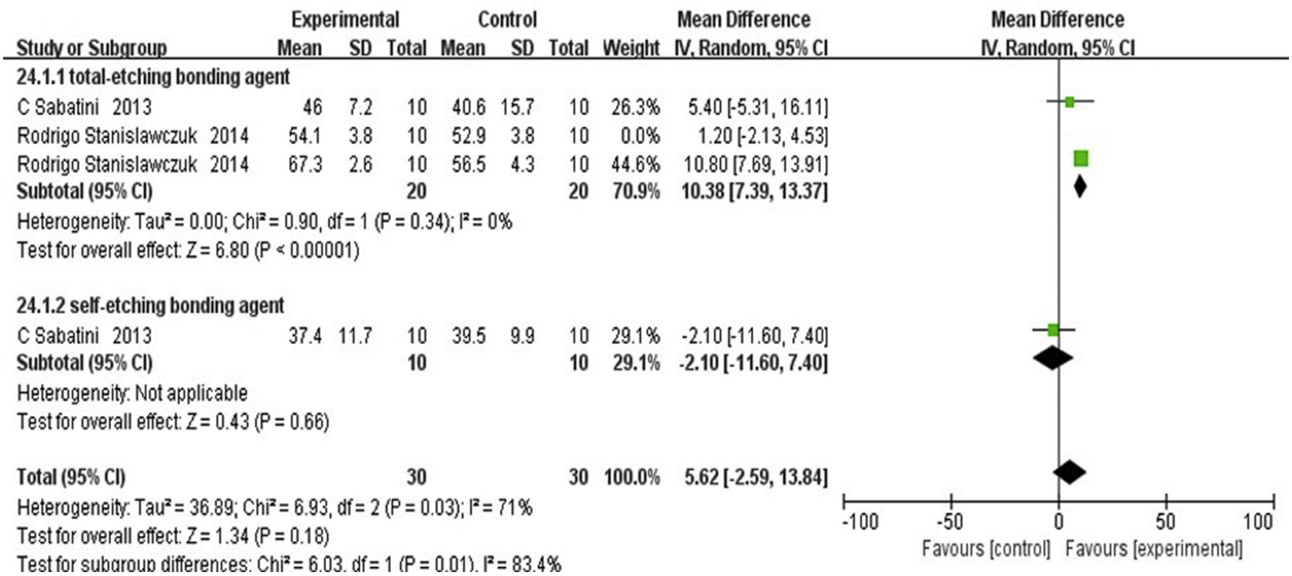

Figure 9 Forest plots for comparison of immediate bond strength values of 0.2% CHX incorporated into the adhesive system composition and control group.

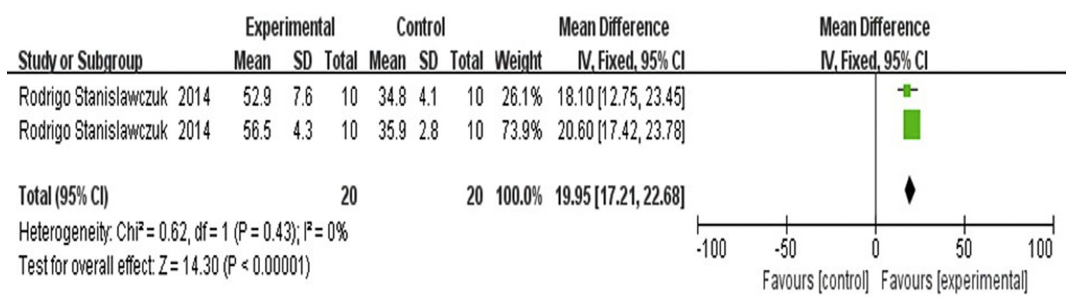

Figure 10 Forest plots for comparison of 12 month bond strength values of 0.2% CHX incorporated into the adhesive system composition and control group.

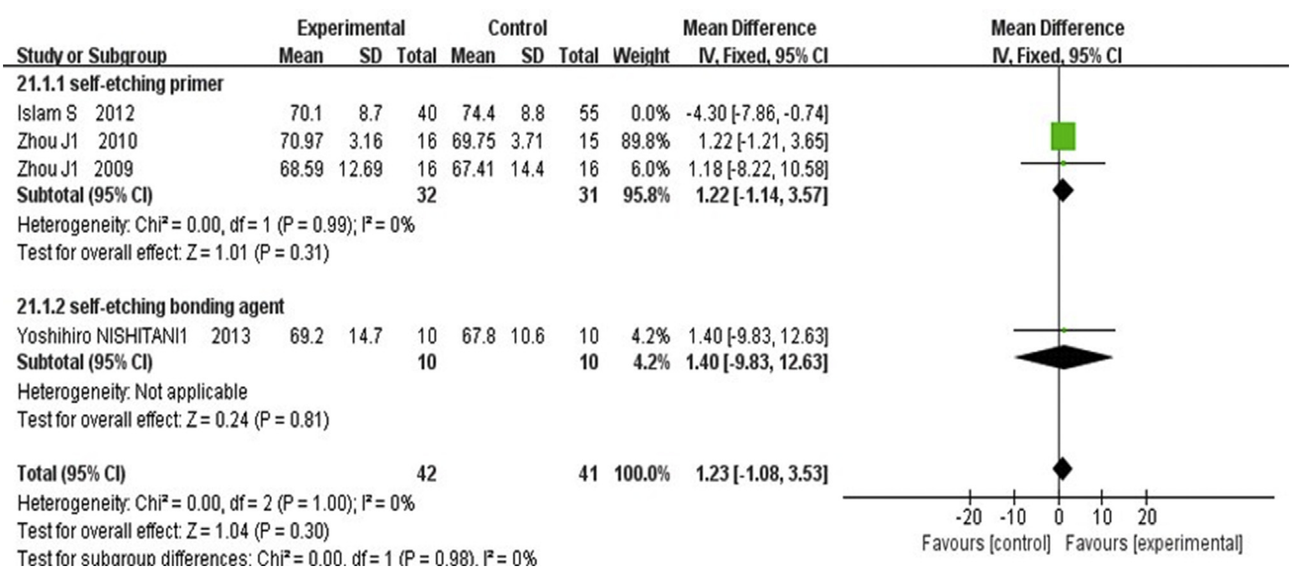

Figure 11 Forest for comparison of immediate bond strength values of 0.5% CHX incorporated into the adhesive system composition and control group.

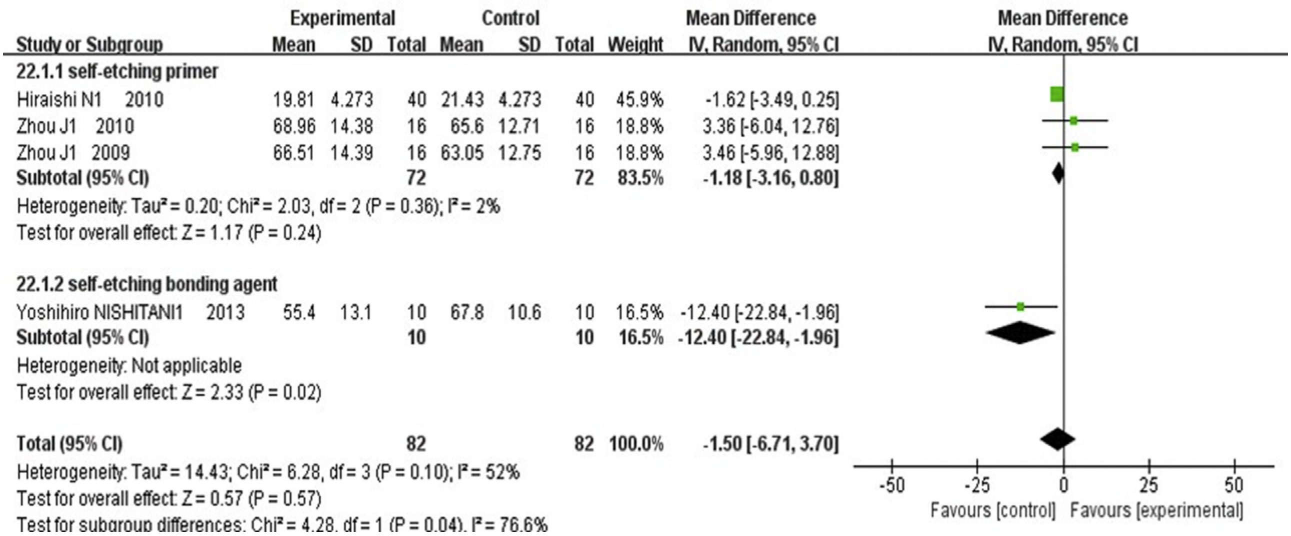

Figure 12 Forest plots for comparison of immediate bond strength values of 1% CHX incorporated into the adhesive system composition and control group.

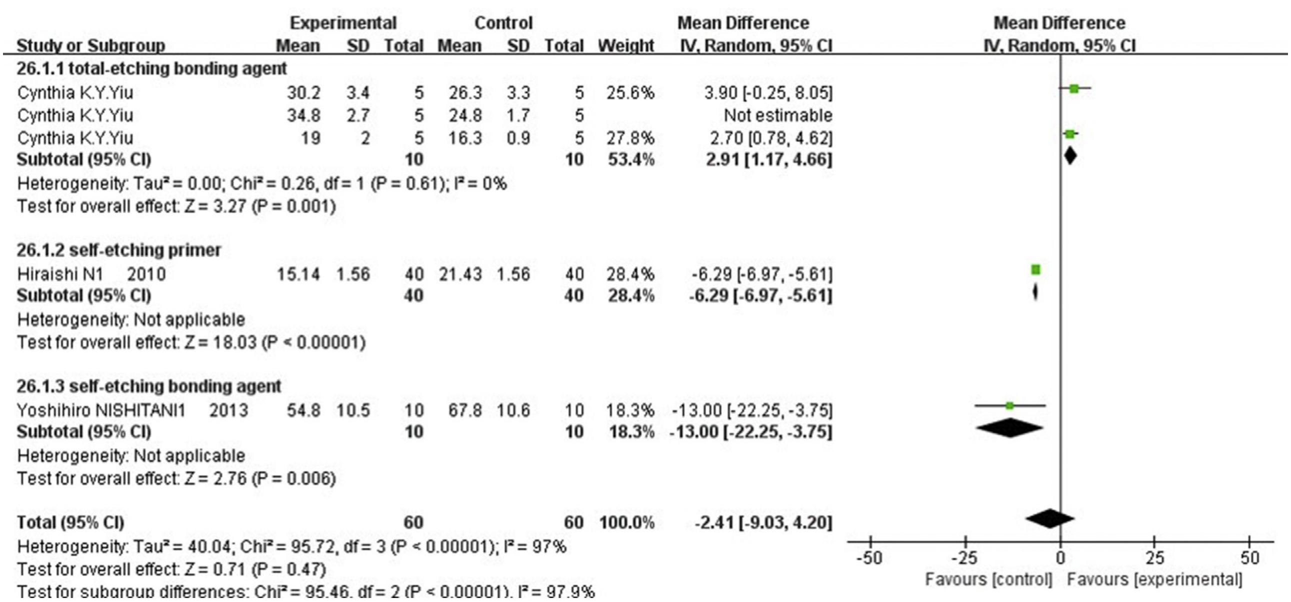

Figure 13 Forest plots for comparison of immediate bond strength values of 2% CHX incorporated into the adhesive system composition and control group.

sensitivity analysis were conducted for this reason. The bonding system used was divided into four subgroups: self-etching pretreatment agent, self-etching adhesive, total-etching pretreatment agent, and total-etching adhesive. The results show that the type of bonding system affected the heterogeneity of the data, and after subgroup analysis and sensitivity analysis, there were four groups with data heterogeneity reduction. However, the heterogeneity of the bond strength value measured after 12 months was not reduced when 0.05% CHX was added to the bonding system. After re-reading the text, the possible reason for the high heterogeneity was analyzed, and it was found that there was also a high degree of heterogeneity in two groups in the same article. This high heterogeneity may have been related to the brand of binder, or to the different storage methods used for the samples, including deionized water and water.

Our study determined the different effects of CHX on the bond strength of dentin in the four subgroups. However, there was a lack of some research data, as most studies only investigated the effect of CHX added to the self-etching pretreatment agent and the full-etching adhesive on the bond strength of dentin, and only one subgroup analyzed the addition of CHX. The addition of 0.1% CHX did not affect the bond strength value of the etching adhesive compared with the control. CHX was added to the self-etching pretreatment and 0.05%, 0.5%, and 1% CHX had no effect on the immediate dentin bond strength. In addition, 0.05% CHX had no effect on the dentin bond strength after 12 months of aging; however, some studies suggested that a CHX concentration greater than 0.1% could increase the bond strength after one year.[9] Due to insufficient study data, further studies on this issue are required.

CHX is a potent, non-specific MMP inhibitor,[6,11,25] and previous studies have shown that the application of CHX can prevent degradation of the mixed layer of collagen fibers and improve the stability of the long-term resin-dentin interface bond strength,[5,10,26] consistent with the results of our meta-analysis. However, the results of studies on whether CHX concentration affects the bond strength of dentin are inconsistent. Some research indicated that the inhibitory effect of CHX on MMPs is related to the concentration,[27] and even low concentrations of CHX can exert inhibitory effects on MMP2, 8 and 9.[10] However, some studies have shown no clear relationship between CHX concentration and bond strength.[28] The present meta-analysis proved that 0.1% and 0.2% CHX increased long-term bond strength stability, and provided statistical evidence for the clinical inclusion of CHX in the bonding system.

This study focused on the in vitro effects of CHX concentration, time and bonding system on dentin bonding strength; however, in addition to the above factors, mechanical stress due to chewing force changes, temperature, pH, water absorption, resin shrinkage and enzymatic action can also affect the bond integrity to varying degrees. In addition, only data from in vitro studies were analyzed in this meta-analysis, and attention should be paid to the link and gap between clinical and laboratory results.[29] Bond strength can directly affect the bonding effect of dentin. Over time, CHX can inhibit the activity of protoplasts and increase the clinical effect of composite resin restorations. In contrast, another study showed that the addition of 2% CHX, and particularly 5% CHX, to the binder significantly reduced the bond strength,[21] therefore, a longer clinical observation period is required.

In summary, this study systematically evaluated the effect of CHX in the bonding system on the resin-dentin bond strength. The randomized controlled trials included were carried out in various research sites, including Europe, America and Asia. However, only 10 randomized controlled trials were included in the meta-analysis, and these studies generally had problems such as unspecified allocation concealment and blinding methods, which reduced the reliability of the results to some extent. Therefore, it is recommended that future research should be strictly designed, and the implementation of testing should be based on strict quality control, in order to achieve higher quality evidence. In conclusion, the use of 0.1% and 0.2% CHX did not adversely affect the immediate bond strength. Both 0.1% and 0.2% CHX maintained the stability of the bond strength for 12 months. In these in vitro clinical trials, CHX maintained the stability of bond strength when added to both self-etching.

Declaration of Competing Interest

All authors declare that there are no personal or professional conflicts of interest.

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