Are self-etch adhesives reliable for primary tooth dentin? A systematic review and meta-analysis

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Abstract
The purpose of this study was to systematically evaluate the dentin bond strength of etch-and-rinse and self-etch adhesives to primary teeth. In this study, PubMed, ISI (all databases), Scopus, and Cochrane Database were searched according to the selected keywords up to May 11, 2016. The full texts of published articles that appeared to meet the primary criteria for inclusion in this study were obtained. Due to the variation in the methods used, the studies were divided into 2 groups: Group 1 – studies that evaluated the micro-tensile bond strengths (MTBSs) of two-step etch-and-rinse adhesives and two-step self-etch adhesives and Group 2 – studies that evaluated the MTBSs of two-step etch-and-rinse adhesives and one-step self-etch adhesives. The initial search yielded 1447 publications. After a methodological assessment, 8 publications were selected. The results of this study showed that the MTBS of the etch-and-rinse adhesives and the two-step self-etch adhesives were similar (P = 0.34), and both were significantly higher than that of the one-step self-etch adhesive (P = 0.001). This meta-analysis showed that the application of two-step self-etch adhesives performs well when used for primary dentin and can be used to save time in pediatric dentistry.

Keywords: Adhesive; micro-tensile bond strength; primary dentin

INTRODUCTION
Bond strength to enamel or dentin is an important indicator of an adhesive systems’ effectiveness. However, bonding to dentin depends not only on the adhesive system but also on the dentin substrate.[1] Although enamel bonding is quite reliable, dentine is considered a complicated and challenging substrate for bonding. There are several differences in the chemical composition of primary and permanent teeth. Primary dentin appears more reactive to acidic conditioners due to the reduced degree of mineralization observed in primary dental hard tissues.[2] In addition, primary dentin has a greater tubule density and diameter, resulting in a reduction of the intertubular dentin area available for bonding. Differences in intrinsic humidity and permeability can also affect the bond strength of adhesive systems in primary dentin.[3] In addition, conflicting results regarding hybrid layer formation in primary teeth represent an area of controversy.[4] Because less chair-side time has an important role in behavior management in pediatric dentistry, self-etch bonding may be considered the best resin-bonded material. In contrast to the etch-and-rinse system, which requires a separate etching protocol, self-etching adhesives reduce the number of steps and application time required. These adhesives have been classified into 2 main categories: (1) acidic monomers that are combined with a primer, requiring a separate bond application (the two-step self-etching system) and (2) an acidic primer and bond that are combined in a single clinical step (the one-step self-etching system).[5] As mentioned...
above, these adhesives may be more useful in pediatric dentistry and may reduce possible handling defects.\[^{[6]}\] In addition, these materials are based on acidic monomers that are of lower acidity than phosphoric acid, which is used in the total etch system. This prevents excessive loss of the dentinal matrix and apatite crystals around the collagen network, especially in primary teeth that have lower mineralization and a higher reactivity to acid etching. As demineralization and resin monomer infiltration occur simultaneously, the collapse of the demineralized dentin will decrease; therefore, fewer potential discrepancies and gap formations may be observed.\[^{[7]}\]

In addition, from a clinical point of view, dentin bonding has several advantages. The bonding layer may not only reduce the polymerization shrinkage stress of the composite restoration but also avoid gap formation due to occlusal forces in stress-bearing areas. Thus, a bonding prevents microleakages, secondary caries, and postoperative sensitivity.\[^{[8]}\] Many studies have already evaluated the bond strength of self-etch adhesive systems to permanent dentin.\[^{[9]}\] Moreover, the measurement of bond strength to primary teeth is controversial; some studies have demonstrated a lower bond strength to this substrate,\[^{[10]}\] whereas others have found similar\[^{[11]}\] or higher primary dentin values compared to permanent dentin.\[^{[12]}\] Therefore, it is important to clarify the effectiveness of self-etch adhesive systems for primary dentin. The purpose of this meta-analysis was to systematically evaluate the existing data to verify the effectiveness of self-etch adhesives compared to etch-and-rinse adhesives for primary teeth dentin.

### MATERIALS AND METHODS

The guidelines developed and recommended by PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) were employed in this systematic review. The PICOS was identified as Table 1.

#### Search strategy

The following keywords were used in searches of PubMed, SCOPUS, the Cochrane Database of Systematic Reviews and ISI (All Databases, including Web of Science core collection, Biosis Previews, Biosis Citation index, Current Content Connect, Data Citation Index, Derwent Innovation Index, CI-Korean Journal Database, Russian Science Citation Index, MEDLINE, SciELO Citation Index, and Zoological Record) up to May 11, 2016, without any language or time limitations.

The following keywords were used (MeSH): (teeth OR tooth OR dent*) AND (primary OR deciduous OR milky) AND (bonding OR adhesive).

Published studies that met the inclusion criteria were selected. The investigation was completed with an additional manual search of the references of the selected articles. All studies were imported to an EndNote library (Endnote X7, Thomson Reuters, San Francisco, CA), and all duplicate studies were removed.

#### Statistical analysis

Due to considerable heterogeneity among the included studies, we used the random-effects model to pool the data. The Cochrane Q test was used to assess heterogeneity. We set the significance level at $P = 0.05$. Furthermore, we used the $I^2$ index to quantify the degree of heterogeneity. To compare possible differences between the adhesive system types (i.e., etch-and-rinse or self-etching), we selected studies in which the investigators had compared both the etch-and-rinse and self-etching adhesive systems. Comprehensive Meta-Analysis Version 2 (Biostat Inc., Englewood NJ, USA) was used for the statistical analyses.

#### Inclusion and exclusion criteria

1. Due to the differences in stresses created at the adhesive interface between test methods, only studies that reported the micro-tensile bond strength (MTBS) of etch-and-rinse and self-etch adhesives to primary dentin were selected. Articles with other bond strength tests were excluded
2. All studies compared the effects of both etch-and-rinse and self-etch adhesives on primary dentin
3. The adhesives were applied according to the manufacturers’ recommendations (without any extra dentin preparation, such as air abrasion or the use of lasers)
4. The bond strength studies were conducted at least 24 h after the bonding procedure without any thermocycling
5. The studies used appropriate statistical tests to analyze the bond strength data, and the sample size, $P$ value, mean and standard deviation are reported in the results. As described under the heading “author contact process,” we attempted to contact the authors of studies with inadequate information
6. The number of eligible studies required to conduct a meta-analysis is at least 3.

#### Author contact process

The authors of articles with insufficient data were contacted through E-mail to retrieve the missing data and

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**Table 1: Search strategy using PICOs analysis**

| PICOS | Definition |
|-------|------------|
| Participants | Primary teeth dentin that underwent bonding application with resin restoration |
| Innervation | Etch-and-rinse bonding |
| Comparison | Comparisons |
| Comparison | Self-etch bonding |
| Outcomes | Not applicable |
| Study design | All included |

PICOs: Participants, Innervation, Comparison, Outcome, Study design
information. If no answer was received within 2 weeks of the initial E-mail contact, a second E-mail was sent. One month after the first contact, if no answer or an incomplete answer was received from the authors, the article was excluded.

To select eligible articles, two reviewers (AS and ME) independently screened the literature and assessed the studies based on the inclusion/exclusion criteria. In cases of a difference of opinion, the subject was resolved by discussion with the third reviewer (AJ).

**Data extraction and analysis**

The following data were recorded for each included study:

- Statistical data, such as the sample size, mean, and standard deviation
- Details of the bonding protocol, such as the adhesive system, bonding substrate, conditioning before bonding application, thermal or mechanical cycling, and bond strength test type
- To assess individual risk of bias of each study, 6 methodological criteria were evaluated as follows: Teeth randomization, Use of caries or restoration free teeth, Use of materials according to the manufacturer’s instructions, Performance of restorations by the same operator, Description of calculation of sample size, and blinding of the operator who test the samples. If the authors reported the criteria, the paper got a Y (yes) on that criteria; if the authors didn’t reported the criteria, the paper had a N (no) on that parameter. Papers that reported 1 or 2 items were classified as high risk of bias, 3 or 4 as medium risk, and 4–6 as low risk.

**RESULTS**

**Risk of bias**

Of the 8 studies included, only 3 presented low risk of bias, while 3 studies showed medium risk of bias and 2 showed high risk of bias. The results are described in Table 2.

**Study search**

The database search and study inclusion process are presented in Figure 1. After removing duplicates, the databases and manual searching yielded 1447 potentially eligible studies. An initial assessment of the articles led to the exclusion of 1421 records; hence, 26 publications that met our inclusion criteria were included for scientific and methodological accuracy [Table 3]. Finally, 8 articles were included in the final qualitative analysis and were categorized into two main groups. Group A compared the MTBS achieved using a two-step etch-and-rinse adhesive (Single bond, 3M ESPE, USA) with a two-step self-etch adhesive (Clearfil SE bond, Kurary, Japan), and Group B compared Single bond with a one-step self-etch adhesive (One Up bond F, Tokuyama, Japan).

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**Table 2: Risk of bias considering aspects reported in the materials and methods section**

| Study            | Teeth randomization | Teeth free of caries or restoration | Materials used according to the manufacturer’s instructions | Adhesive procedures performed by the same operator | Sample size calculation | Blinding of the operator | Risk of bias |
|------------------|---------------------|------------------------------------|------------------------------------------------------------|---------------------------------------------------|-------------------------|--------------------------|--------------|
| Miranda (2010)   | No                  | Yes                                | Yes                                                        | Yes                                               | No                      | No                       | Medium       |
| Sanabe (2009)    | Yes                 | Yes                                | Yes                                                        | Yes                                               | No                      | Yes                      | Low          |
| Osorio (2010)    | Yes                 | No                                 | Yes                                                        | Yes                                               | No                      | No                       | Medium       |
| Soares (2003)    | Yes                 | Yes                                | Yes                                                        | Yes                                               | No                      | No                       | Low          |
| Nakornchai (2005)| Yes                 | Yes                                | Yes                                                        | Yes                                               | Yes                     | No                       | Low          |
| Aguirra (2012)   | No                  | Yes                                | Yes                                                        | No                                                | No                      | No                       | High         |
| Rocha (2007)     | No                  | Yes                                | Yes                                                        | No                                                | No                      | No                       | High         |
| Lenz (2013)      | Yes                 | No                                 | Yes                                                        | Yes                                               | No                      | No                       | Medium       |

**Table 3: Detailed summary of studies included in the meta-analysis**

| Study            | Storage time | Group | Sample size | Bond strength (MPa), mean±SD | Speed (mm/min) |
|------------------|--------------|-------|-------------|------------------------------|----------------|
| Miranda et al.[13]| 24 h water storage | Single bond | 8            | 23.27±4.78                  |                |
| Sanabe et al.[14] | 24 h water storage | Single bond | 2            | 49±12.9                     | 0.5            |
| Osorio et al.[15] | 24 h water storage | Single bond | 2            | 29.38±11.5                  | 0.5            |
| Soares et al.[16] | 24 h water storage | Single bond | 5            | 70.1±3.8                    | 1              |
| Nakornchai et al.[13] | 24 h water storage | Single bond | 5            | 12.9±5.13                   |                |
| Aguirra et al.[14] | 24 h water storage | Single bond | 2            | 29.38±11.5                  | 0.5            |
| Rocha et al.[17]  | 24 h water storage | Single bond | 5            | 33.81±2.45                  | 1              |
| Lenz et al.[18]   | 24 h water storage | Single bond | 6            | 44.2±6.8                    | 0.5            |

*Data used for the first part of the meta-analysis; † data used for the second part of the study. SD: Standard deviation
A summary of the included studies is presented in Table 2. Mean difference was used as it would indicate the difference of bond strength in micro-tensile units. To assess the presence and extent of statistical heterogeneity, Cochran Q test and I² index were used respectively. Accordingly, \( P > 0.1 \) indicated the presence of heterogeneity and I² values >50% possibly indicated considerable heterogeneity among the studies.

The results obtained for each group are as follows:

Group 1: The comparison of the MTBS achieved using a two-step etch-and-rinse adhesive (Single bond) with that achieved using a two-step self-etch adhesive (Clearfil SE Bond) to the primary dentin is shown in Figure 2. No significant difference was observed in the MTBS obtained for these adhesive systems. However, the \( \mu \)TBS values

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**Figure 1:** PRISMA flowchart of the included studies and the search strategy used. All 8 included studies were used for the first part of the meta-analysis, and 3 of these were eligible to be used for the second part of the study.

**Figure 2:** Forest plot comparison of the micro-tensile bond strength obtained using a two-step etch-and-rinse adhesive with that achieved using a two-step self-etch adhesive to the primary dentin.
obtained using Single bond were higher than those obtained using Clearfil SE Bond ($P = 0.341$).

Group 2: A comparison of the MTBS obtained using a two-step etch-and-rinse adhesive (Single bond, 3M ESPE, USA) with that obtained using a one-step self-etch adhesive (One Up bond, Tokuyama, Japan) to the primary dentin is shown in Figure 3. A significant difference was observed between the MTBSs obtained using these adhesive systems, and the μTBS values obtained using Single bond were significantly higher than those obtained using One-Up bond ($P = 0.001$).

**DISCUSSION**

The results of this meta-analysis showed that the MTBS achieved using 2-step self-etch systems is comparable to that obtained using conventional total-etching systems, and the bond strength values achieved using Clearfil SE Bond were similar to those obtained using Single bond ($P = 0.341$; Figure 2) for primary dentin. These results are also supported, regardless of the testing technique used, by those obtained by Senawongse et al., who evaluated the microshear bond strength of these materials to primary teeth.

Furthermore, this analysis showed that the 1-step self-etching system (One-Up Bond F) results in significantly lower bond strength compared to the etch-and-rinse system. Thus, this study showed that when following the manufacturers’ recommendations, the MTBS values obtained using the etch-and-rinse adhesive (SB) and the two-step self-etch adhesive (SEB) were similar and were significantly higher than that obtained using the one-step self-etch adhesive (OUB), However, Nakornchai et al. reported achieving lower bond strengths for Single bond in comparison with Clearfil SE Bond for sound primary dentin.

In an earlier meta-analysis, Lenzi et al. demonstrated that the performance of etch-and-rinse adhesives in primary teeth was superior to that of self-etch systems. According to the findings of that study, the articles included in the meta-analysis exhibited high heterogeneity and a high risk of bias. The inclusion criteria used in that study were not specified; thus, a wide range of studies using different methodologies (such as different bond strength tests) was included in the analysis.

In the present study, we collected articles that evaluated bond strength to primary dentin. After categorizing the different types of bond strength (shear, tensile, and MTBSs), only studies in which the micro-tensile strength was evaluated were found to have critical point of the meta-analysis assessment. This test leads to more adhesive failures (i.e. true bond strength values) and fewer cohesive failures, allows for the collection of many samples from one tooth and permits the evaluation of bond strength in small, specific areas, such as areas of affected or sclerotic dentin.

In the present study, all eligible studies applied adhesive systems according to the manufacturers’ recommendations. The effects of different adhesive system parameters on bond strength are discussed below:

**Hybrid layer**

Many studies have shown that despite differences in the mineral concentration of these 2 substrates, the thickness of the hybrid layer in primary dentin is the same as that in permanent dentin, which confirms that hybrid layer thickness does not influence bond strength values. More relevant than the hybrid layer thickness is its favorable and uniform interaction with the adjacent tooth substrate. In Clearfil Se Bonds, the etching and bonding of dentin occur simultaneously such that a homogeneous hybrid layer is formed and a better stress distribution along the adhesive area is achieved.

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**Meta Analysis**

| Study name       | Statistics for each study | Std diff in means and 95% CI |
|------------------|---------------------------|-------------------------------|
| Sosio (2010)     | 2.065 1.238 1.533 -0.362 4.492 1.558 0.055 |                      |
| Soares (2005)    | 4.909 1.287 1.665 2.428 7.392 3.875 0.000 |                      |
| Aguilera (2012)  | 2.182 1.263 1.565 -0.203 4.658 1.728 0.084 |                      |
|                  | 3.042 0.925 0.856 1.228 4.655 3.287 0.001 |                      |

**Heterogeneity:** Cochrane Q value: 3.257; P-value: 0.196; $I^2$: 38.601

**Figure 3:** Forest plot comparison of the micro-tensile bond strength obtained using a two-step etch-and-rinse adhesive with that obtained using a one-step self-etch adhesive to the primary dentin.
However, when using One-up Bond F, the simultaneous etching, primer, and bond application can limit the permeation of the monomers through the substrate during demineralization, which promotes poor infiltration and results in areas without dentin hybridization. An SEM evaluation found a very thin and discontinuous hybrid layer was formed compared to that formed by Single bond, which may explain the low bond strength values for this adhesive system.

**Adhesive pH**

The depth of dentin demineralization achieved using self-etching primers might differ depending on pH. Previous studies have shown that aggressive versions of simplified self-etch adhesives completely dissolve the smear layer and form relatively thick hybridized complexes and thick resin tags.

Because the Clearfil SE Bond has a relatively high pH, the resulting MTBS, and intertubular roughness were not affected by etching time; therefore, the smear layer was partially dissolved by the primer, and hydroxyapatite remnants were available for chemical interaction with the adhesive’s functional monomers. SEM identified fully resin-infiltrated intertubular dentin with numerous resin tags occluding the dentin tubules.

In comparison with the Clearfil SE Bond, the One-up Bond contains strong acidic agents (with a low pH), which might cause stripping (and therefore destabilization) of the collagen from the surface, leading to a greater depth change. On the other hand, the movement of water outward through the dentin will be increased, leading to dilution of the adhesive components, phase separation, and poor polymerization. This effect was previously observed by Uekusa et al. when using self-etching adhesives on primary dentin. The authors suggested shortening the etching time in these adhesive systems to increase the bond strength.

For etch-and-rinse adhesives, some authors have suggested reducing the etching time for primary dentin by half to create hybrid layers with a thickness similar to that of permanent teeth.

**The functional monomer of the adhesive**

The bonding performance obtained using the self-etch adhesive systems varies considerably depending on the composition and more specifically, on the functional monomer included in the adhesive formulation. The differences between the self-etch adhesive systems evaluated in this study are attributed to the functional monomer and solvent system provided, consisting of a mixture of water-ethanol or water alone. The concentrations of individual monomers in the adhesive system and their interactions determine the extent of the infiltration, ionization, and cross-linking obtained during polymerization and the subsequent mechanical properties of the adhesive system.

The main functional monomer in the Clearfil SE bond is 10-MDP, which was originally synthesized and patented by Kuraray (Osaka, Japan). This monomer is hydrophobic and is mainly used as an etching monomer due to the dihydrogen phosphate group, which can dissociate in water to release two protons, causing minimal dissolution of the smear plugs and limited tubule opening. The submicron hybrid layer produced by this adhesive might more easily promote the diffusion of resin monomers, regardless of the etching time used.

However, Yoshida et al. showed that this monomer can form strong ionic bonds with calcium due to the low dissolution rate of the resulting Ca salt in its own solution. Van Landuyt et al. considered 10-MDP the most promising monomer for chemical bonding to hydroxyapatite in enamel or dentin, as opposed to 4-MET and Phenyl-P. The good in vitro and clinical outcomes of the Clearfil SE Bond may be partly attributed to its intense chemical adhesion with tooth tissue.

MAC-10 is the main functional monomer in the One-up bond, which was patented by the Japanese manufacturer Tokuyama. Similar to 10-MDP, MAC-10 is used as an etching monomer, but its pH is lower than that of 10 MDP; therefore, etching occurs more aggressively relative to 10–MDP. This monomer is relatively hydrolytically stable, and information about this monomer in the literature is very scarce.

Manabe et al. reported that contraction gap formation was promoted when an adhesive monomer, such as 10-MDP, was omitted from the dentin bonding agent, whereas the tensile bond strength was not affected by the presence or absence of the adhesive monomer in the dentin bonding agent. Thus, it is possible to speculate that contraction gap formation was prevented by the chemical interaction between the calcium in the dentin and the functional monomer in the dentin bonding agent.

**Adhesive solvent**

The solvent or medium present in the bonding agent has also been known to affect bond strength. Different solvents present in simplified bonding agents are responsible for either carrying excess water out of or infiltrating resin monomers into interfibrillar dentin. Self-etching adhesives contain more water than total-etch adhesives and need water to ionize acidic monomers to effectively demineralize hard dental tissues. Not all residual water entrapped in the hybrid and adhesive layers is removed, which is harmful because adhesive polymerization is
negatively influenced by the presence of water. As more residual water is entrapped in the hybrid and adhesive layers, the polymer’s mechanical properties are compromised, thus reducing bond strength values.

Conversely, the primer solvent exerts one of the greatest impacts on the manipulation and performance of total-etch adhesive systems. Primers containing water are less susceptible to handling variables than those containing acetone or alcohol. Single bond contains water and ethanol; therefore, the adhesion of Single bond is more vulnerable to water content at the dentin surface after acid etch and provides more stability to the solution.

The results of this study showed that the MTBS values of the etch-and-rinse adhesive (SB) and the two-step self-etch adhesive (SEB) were similar. The high percentage of camphorquinone, the absence of a discrepancy between the depths of demineralization and infiltration, and the protective effect of both resin-coated collagen and the formed calcium salts of MDP may explain the high bond strength achieved in this study. The authors of the current study suggest the use of simplified adhesives (two-step self-etch adhesive) in pediatric dentistry to save time and to achieve high bond efficacy. Some valuable studies may have been missed in this meta-analysis due to our search strategy. We attempted to omit this bias by duplicating our search and by contacting the study authors to obtain necessary information. In addition, we recognize that the selection and qualitative synthesis of eligible studies are ultimately subjective. However, having two reviewers conduct the screening procedure independently using a standardized form to extract the data, and assessing the methodological quality of the studies using a validated checklist helped to ensure objectivity in our search strategy. Another limitation of our study was the omission of studies that evaluated the durability of bond strengths. Incomplete resin infiltration, inadequate polymerization, and the presence of acidic monomers or residual water can compromise the hybridization process, thereby allowing nanoleakage and reducing the longevity of the resin-dentin bond. However, Amstrup claimed that the efficacy of dentin adhesives should be examined in a three-dimensional dentin cavity and that it is essential to evaluate the interaction between the efficacy of the dentin adhesives and the polymerization contraction stress of the resin composite.

**CONCLUSION**

This in vitro based meta-analysis showed that the application of a two-step self-etch adhesive (Clearfil SE Bond) for primary dentin achieves desirable outcomes similar to those with two-step and rinse adhesives (Single bond). Based on the results of this study, the one-step self-etch adhesive (One-Up Bond) may not be suitable. However, the results of in vitro studies should be used in clinic with caution.

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**Conflicts of interest**

There are no conflicts of interest.

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