The effect of desensitizing agents on the bond strength of dentin bonding agents: A systematic review

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Abstract

Background: Dentinal hypersensitivity (DH) is a common dental problem and is treated non-invasively using topical application of various desensitizing agents. When there is loss of tooth structure or tooth preparation is to be followed by a bonded restoration, it requires application of dentin bonding agent. However, the effect of desensitizers on bond strength is still controversial.

Aim and Objective: To evaluate the influence of different desensitizing agents on the bond strength of the dentin bonding agents.

Methods and Materials: PICO strategy was used to formulate the research question. In-vitro studies conducted on human teeth to evaluate the bond strength of dentin bonding agent following the application of desensitizing agent were included. Electronic databases PubMed and Cochrane and google scholar were searched using search terms alone or in combination from the year 2010 till 2020. Search was conducted using the key words and MeSH terms (hypersensitivity, bond strength, dental adhesives, dentin bonding agents). The title and abstract were read to verify the inclusion and exclusion criteria and if further any details required, full article was accessed to check the criteria and then included or excluded. Data extraction was done using a customized data extraction form. The risk of bias was evaluated using modified Cochrane Collaboration Quality Assessment tool.

Results: Total no of studies identified in the search were 146, after scrutiny 23 articles were eligible to be included in this study. Out of 23 articles, 17 articles were of medium bias and 6 articles were of high risk after risk of bias assessment.

Conclusion: According to the various articles included in this study, GLUMA and 8.0%Arginine and CaCO3 when used as desensitizing agents along with different bonding agents, were found to be highly compatible without interfering with the bond strength of the dentin adhesives.

Keywords: Bonding agent; Bond strength; desensitiser; hypersensitivity

INTRODUCTION

Dentinal hypersensitivity (DH) is a common dental problem that occurs as a result of caries, noncarious lesions, or following freshly cut dentin during tooth preparations. The incidence of occurrence of DH varies from 10% to 30% in various populations with the age group varying from 20 to 50 years. The commonly accepted theory is the hydrodynamic theory which states that any stimuli that cause fluid movement within the dentinal tubules, in turn, can stimulate the nerve fiber resulting in a painful response.[1]

Hypersensitivity is treated noninvasively using topical application of various desensitizing agents.
The most commonly used agents are potassium nitrate, fluorides, oxalates, GLUMA-containing agents, bonding agents, calcium phosphate/calcium carbonate, bioactive glass, strontium acetate, and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP). Different lasers are also used in treating DH. These act by plugging the dentinal tubules directly or after the chemical reaction. According to Pashley et al., dentinal permeability and sensitivity are reduced when the dentinal tubules are occluded.\(^2\) However, when there is a loss of tooth structure or tooth preparation is to be followed by a bonded restoration, it requires the application of dentin bonding agents (DBA).

In superficial dentin, which contains fewer tubules, the permeation of resin in the DBA is into intertubular dentin, which will be responsible for most of the bond strength. The dentinal tubules are present in more numbers in deep dentin and the bond strength is increased because of the intratubular resin permeability.\(^3\) However, the effect of desensitizers on bond strength is still controversial. Some studies have demonstrated negative effects\(^4\) and some either positive or no effect.\(^4\) 

**STRUCTURED QUESTION**

Does the application of dentin desensitizers influence the bond strength of DBAs?

**PICO ANALYSIS**

Population is extracted teeth. Intervention is the application of dentin desensitizing agents. Comparison is without application of desensitizing agent (studies with control). Outcome increases or decrease in bond strength of DBA. Study design is *in-vitro* study.

**METHODOLOGY**

**Protocol and registration**

PRISMA 2020 guidelines were followed in this study and the study protocol was registered with PROSPERO (Registration no-CRD42020218931).

**SEARCH STRATEGY**

The electronic databases PubMed, Cochrane, and Google Scholar websites were searched. The keywords used were desensitizer OR desensitizers OR dentin desensitizer OR dentin desensitizing OR desensitizing product OR desensitizing products OR desensitizing agent OR desensitizing agents OR desensitizing paste OR desensitizing pastes AND dentin bond OR dentin bond strength OR bond strength for studies in the English language from the year 2010–2020.

**STUDY SELECTION**

Inclusion criteria were *in-vitro* studies conducted on the coronal dentin surface of human extracted teeth. Exclusion criteria were studies conducted on bovine teeth, on enamel or radicular dentine of human teeth, and reviews.

**DATA EXTRACTION PROCESS**

Both the reviewers screened the abstract of the selected articles based on the inclusion and exclusion criteria. Both the reviewers read the articles and extracted the data such as author, year, DSA used, DBA used, type of bond strength and type of fracture that occurred and the effect of DSA on the bond strength. If there is any disagreement, the common consensus was arrived at after discussion.

**QUALITY ASSESSMENT**

The assessment was carried out using the criteria such as teeth free of caries, similar size sample dimension, sample size calculation, teeth randomization, blinding of the evaluator, storage, thermocycling, thermomechanical aging, fracture investigation following bond strength test. If these criteria were present it was scored “Yes” and not present was marked “No.” Both the reviewers carried out the quality assessment of the studies independently. Overall risk assessment was done with the Cochrane Risk of Bias tool using software (REVMAN 5.4.1).

**RESULTS**

Total articles identified through database search were 146, after removal of duplicates and ineligible articles, records screened were 135, after applying inclusion and exclusion criteria 28 records were retrieved, two full texts could not be retrieved.\(^9,10\) 26 full-text articles were screened and three articles\(^11-13\) on bovine teeth were excluded. Out of seven articles identified from Google Scholar, after screening the full text, no article was eligible. A total of 23 articles were included in the quality analysis. The search process is shown in Figure 1. The data extraction done is shown in Table 1. Then, full-text articles were assessed independently by both the authors for the risk of bias of the included studies individually [Figure 2] and the overall quality of the included studies are given in Figure 3. There is an agreement of 83% between the two authors, arrived using Cohen’s Kappa coefficient.

**ANALYSIS OF RISK OF BIAS**

Following the assessment of different items for the analysis of Risk of Bias, it was found that there was high
risk of bias for sample size calculation, blinding of the evaluator, thermomechanical aging, for which none of the studies had scored Yes, whereas for thermocycling 21 studies have scored No and only two studies had scored Yes. Incomplete outcome data wherein 7 studies had not reported fracture investigation following bond strength tests. 1–3 Yes were considered high risk, 4–6 Yes considered as medium risk, and 7–9 risk as low risk. Out of 23 articles, 17 articles were of medium risk and 6 articles were of high risk after the risk of bias assessment. Since different desensitizing agents, different bonding agents used, and different bond strengths were evaluated in the included studies, meta-analysis could not be performed, thus quantification of heterogeneity by using $I^2$ statistics was not possible.

**DISCUSSION**

Since bond strength studies could not be performed clinically, *in-vitro* studies are at the most important for evaluating the bond strength of different materials even though the same clinical conditions as in the oral cavity could not be mimicked in *in-vitro* studies. Of the 23 articles, nine have studied the macro-strength of which, eight were shear bond strength studies and one was tensile bond strength. Macro tests resulted in cohesive failure and overestimation of bond strength, however, it could be considered because of its simplicity. Fracture investigation was not done in the three studies. Of the rest of the five studies, adhesive failure was prominent in three studies and mixed failure was prominently reported in one study and one study reported equal adhesive and mixed failures. In one study, it is mentioned in material and methodology that fracture investigation was done, but the type of failure was not mentioned in the results.

14 studies have performed the micro-strength tests of which micro-tensile bond strength tests were done in 12 studies and micro-shear bond strength bond tests were done in two studies. More of adhesive failure was reported in eleven studies and mixed failure were reported in seven studies and fracture investigation was not done in seven studies. Adhesive area reduction influenced the bond strength and reduced the cohesive failures in micro-tensile bond strength tests thus advantageous over macro tests to evaluate the adhesive interface.

Potassium nitrate-containing desensitizing agents, apart from interfering with the nerve conduction, also blocks...
Table 1: Data extraction from the included studies

| Author/year | Desensitizing agents | Etch and rinse DBA | Self etch DBA | Type of bond strength/ failure | Conclusion |
|-------------|----------------------|-------------------|--------------|-------------------------------|------------|
| SMA Silva et al./2010 | Potassium oxalate DSA | E and R DBA | Adper Single Bond, One-Step and Scotchbond Multi-Purpose | MTBS/equal among mixed and cohesive failure | BS with DSA |
| Can-Karabulut DC/2011 | Diode laser | Clearfil Tri S Bond | SBS/- | Short term use of diode laser and smart protect didn't interfere with the bond strength |
| Yahya Orcun Zorba et al./2010 | CPP-ACP (Tooth mousse), KNO3 (Ultra-Eze), Cervitec plus (Chlorhexenedene) DSA | One E and R- XP Bond | 3 SEA AdheSE, Adper Prompt L-pop, GBond | SBS/equal of adhesive and mixed | DSA'S doesn't affect the SBS |
| HD Arisu et al./2011 | Resin, glutaraldehyde, K fluoride and oxalate, bonding agent with Nd-YAG laser | SEA - Clearfil SE primer and bond | MTBS/more of adhesive | BS was reduced except Bonding agent with Nd:YAG laser |
| Shekar Bhatiya et al./2012 | Ca, sodium phosphosilicate containing Novamin and K No3 | 2 E and R Prime N Bond NT and Single Bond | SBS/ adhesive | Sensodent increased the BS of Prime N Bond NT where - As with Novamin no change in BS |
| Yousry M/2012 | Oxalate desensitizer-D/Sense crystal | Single bottle E and R adhesive (single bond and Optibond S) | MSBS/mostly adhesive and mixed | Compromises bond strength in re-etching after oxalate treatment |
| Yake Wang, et al./2012 | 8% Arginine and calcium carbonate (sensitive pro-relief) | SEA single G-Bond and two step SEA Fl Bond 2 | MTBS/- | No adverse effect of the DSA on the bonding performance to dentin when using SEA containing functional monomer such as 4 MET like G-Bond |
| Hongye yang et al./2013 | 8% arginine and calcium carbonate - (sensitive pro-relief) | E and R adhesives | Adper singlebond2 Adper scotchbond multipurpose | MTBS/- | 8% arginine and calcium carbonate didn’t affect the MTBS of E and R adhesives to dentin |
| Dandan pei et al./2013 | 8% Arginine | Mild SEA’S G-Bond and Clearfil SE bond | MTBS/mostly adhesive failure | CPP-ACP didn’t influence BS of both SEA’S, ARG-CaCo3 and Hydroxy apatite paste | BS of G-Bond and variable result for S bond |
| Yang H and Pei D/2014 | Arginine - Ca Co3 Sensodyne repair and protect with Novamin | Two etch and rinse DBA Adper single bond 2 and Adper Scotchbond | MTBS/mostly adhesive failure | Didn’t affect the bond strength |
| Sameer makkar et al./2014 | Thermokind F gel, Er:YAG LASER | Selfetch adhesive (3 m | TBS/- | Er-YAG laser and F1 dentrifice lowered the BS |
| Meng Ding et al./2014 | Gluma, Co2 laser | SEA-Adper single bond2 | MTBS/adhesive and mixed | GlumaBS for eroded and sound dentin |
| Luciene Santana et al./2014 | Sensitive pro-relief, Aqueous biosilicate | E and R- Scotchbond multipurpose 2s SEA-clearfil SE bond | MSBS/mixed | Arginine didn’t influence but biosilicate increased BS |
| Erhan Dilber et al./2014 | Gluma, Nd-YAG, Gluma+ Nd-YAG | Two-step adhesive procedure (Clearfil® SE Bond, Kuraray Co. Ltd, Osaka, Japan) | SBS/mixed | Nd-YAG laser RX following Gluma DSA could be an effective RX for hypersensitivity and doesn’t affect the BS |
| C Sabatini Z Wu et al./2015 | Gluma, Micro prime B (HEMA and Benzalkonium chloride) and pulpdent desensitizer (Glutaraldehyde and sodium fluoride) | SEA’S - Optibond XTR, SBS/adhesive IBond, Xeno IV | Desensitizing agents can be used in combination with self-etching adhesives to control hypersensitivity without adversely affecting their bond strength to dentin |

Contd...
the dentinal tubules following repeated application, thus reducing the bond strength[25] but according to authors[16,18] there is no interference with the bonding.

OXALATES

Oxalates application on the dentin results in the formation of calcium oxalate crystals in the dentinal tubules, which in turn interferes with the resin infiltration.[39] Oxalates are applied after acid etching since the oxalates like Bisblock have a pH of 1.5–1.8, causes an additional etching effect and thus leading to the extent of demineralization and penetration depth of the resin mismatch.[40] Compared to ethanol/water-based adhesives, acetone-based adhesives are more sensitive to moist bonding techniques, and in only one study[40] oxalates are compatible with the adhesive, i.e., Adper Single Bond.

Gluma (Glutaraldehyde and HEMA).

In eroded dentin, the glutaraldehyde in GLUMA fixes the collagen fibrils[43] exposed and HEMA helps in the infiltration of resin monomers into the collagen[43] thus increasing the bond strength.[25] When the bonding agent containing HEMA follows the application of GLUMA, the acidic effect of HEMA is repeated, thus favoring better penetration of the resin monomer achieving a greater bond strength.[44]

LASERS

Lasers work by the mechanism of thermal energy absorption,[40] thus, occluding and narrowing of dentinal tubules and melting of hydroxyapatite in the dentin.[46] These morphological changes interfere with the penetration of resin thus compromising the bond strength. Nd:YAG laser decreased the bond strength by creating morphological changes in the dentin.[47]

According to Yazici et al. Nd:YAG lasers did not interfere with the bonding.[48] Rolla JN reported that Nd:YAG laser irradiation promoted the micro-mechanical retention for self-etch adhesives, whereas did not interfere with the bonding of Universal adhesive such as Single Bond, Co2, Er:YAG, and Diode lasers decreased the bond strength of the adhesives studied.[46,52] Short-term use of red wavelength diode laser did not interfere with the bond strength when

Table 1: Contd...

| Author/year | Desensitizing agents | Etch and rinse DBA | Self etch DBA | Type of bond strength/ type of bond failure | Conclusion |
|-------------|----------------------|-------------------|-------------|------------------------------------------|------------|
| Cortiano FM et al./2016[29] | Bisblock (oxalate), Desensibilize Nano P (capo4) | 2 step E and R Adper Single Bond Plus (SB) and OSP | MTBS/predominantly mixed | Oxalate DSA of one of the adhesive whereas Capo4 containing didn’t affect the dentin bonding |
| Shafiei F et al./2017[30] | CPP-ACP tooth paste | Resin modified GIC and self-adhering composites | SBS/adhesive | Improved bond strength |
| Siso et al./2017[31] | TMD | Clearfil Universal Bond (self-etch/etch and rinse) | MTBS/mostly adhesive | TMD group showed lower MTBS than control group |
| Gupta et al./2017[32] | BG, hydroxyapatite, and diode laser | One step self-etch adhesive (Bond Force) | SBS/- | BG and hydroxyapatite increased SBS, whereas Diode laser decreased the bond strength. |
| Mushtaq et al./2017[33] | Systemp (poly ethylene glycol dimethacrylate) | E and R adhesive (Prime and Bond NT), 2 SEA (Xeno V+, and Futurabond DC) | SBS/- | Systemp increased the BS for Prime and Bond NT DBA and decreased it for Xeno V+ and Futurabond DC |
| Hongye Yang 1/2018[34] | CPP-ACP and Novamin | E&R adhesive - Adper ScotchBond Multi-Purpose | MTBS/adhesive followed by mixed | DSA were compatible with adhesives |
| Pei D et al./2019[35] | Pure nano hydroxyl apatite and Bio-repair Dentodont HAP mixture | SEA-G-Bond and Clearfil S Bond | MTBS/mixed followed by adhesive | Pure nano hydroxyl apatite resulted in comparable bond strength and other agent decreased bond strength |
| Jung JH/2019[36] | Ag-BioGlass Nano @ Mesoporous Silica Nanoparticles | Clearfil SE Bond | MTBS/- | DSA didn’t interfere with the bond strength |

BG=Bioglass, DBA-Dentin Bonding Agent, MTBS-Micro- tensile Bond Strength, BS- Bond Strength, MSBS-Micro-shear Bond Strength, Nd:YAG- Neodymium doped Yttrium Aluminium Garnet, CPP-ACP - Caesin Phosphopeptide, HAp- Hydroxy Apatite, TMD- Teethmate desensitizer, GIC- Glass Ionomer Cements, DC- Dual Curing, SEA- Self-etch Adhesive, Er:YAG- Erbium doped Yttrium aluminium garnet
used with Clearfil Tri S Bond.\textsuperscript{[15]} When Carbon dioxide laser was used, the adhesive could not infiltrate the dentin substrate that is denatured with \textsuperscript{CO2} laser adequately, hence decrease in bond strength\textsuperscript{[34]} Er:YAG laser decreased the bond strength,\textsuperscript{[35]} since the adhesives micro-mechanical retention to the irradiated dentin is affected.\textsuperscript{[49]}

**8.0% ARGinine AND CA-CO$_3$**

Calcium and phosphate ions precipitate in the alkaline environment created by the Ar-Ca-Co3 and block the dentinal tubules thus exhibiting desensitizing action.\textsuperscript{[50,51]} The acidity of 4MET in adhesives is likely to solubilize the precipitate, thus reopening the tubules to permit the formation of resin tags to improve the bond strength.\textsuperscript{[52]} Acidic pH of the G Bond yielded favorable bond strength whereas the S3 bond decreased the bond strength since it has a higher pH than G Bond.\textsuperscript{[22]}

**CASEIN PHOSPHOPEPTIDE-AMORPHOUS CALCIUM PHOSPHATE**

CPP-ACP favors re-mineralization over demineralization which might resist the conditioning of the dentin during dentin bonding, reducing the bond strength.\textsuperscript{[53]} On the contrary, CPP-ACP yielded favorable bonding with self-etch adhesives.\textsuperscript{[16,54]} The application of CPP-ACP makes the surface more wet and reduces contact angle, thus favoring mechanical interlocking and adhesion.\textsuperscript{[55]} All the studies concluded either CPP-ACP did not interfere with the bonding or increased the bond strength.

**CALCIUM PHOSPHATE/BIO-SILICATE**

The bond strength results are variable with different adhesives, acetone-based adhesives like Prime and Bond NT achieved favorable bond strength with Denshield because of the high vapor pressure and better penetration of acidic monomers.\textsuperscript{[10]} Ethanol/water-based adhesives decrease the bond strength because of the water tree phenomenon\textsuperscript{[56]} which in turn leads to incomplete polymerization\textsuperscript{[57]} of the adhesive following the application of Denshield. Calcium phosphate-containing DSA did not interfere with the bonding of Etch and Rinse adhesives.\textsuperscript{[58]} Clearfil Universal bond in Etch and Rinse mode achieved reduced bond strength with Teeth Mate Desensitizer\textsuperscript{[31]} G Bond resulted in higher bond strength since 4MET can interact with calcium that is present in the hydroxylapatite that is formed following the application of calcium-containing DSA, whereas in Clearfil S3 bond, the higher pH gets neutralized by the DSA.\textsuperscript{[36]}

**DENTIN ADHESIVES**

Systemp desensitizing agent increased the bond strength, when followed by the application of Prime N Bond NT, because the system acted as rewetting agent,\textsuperscript{[59]} again with the adhesive may yield optimal wetting, thus dual wetting contributing to improved better strength. Xeno V+ was used, Systemp re-wetting combined with the acrylic acid present in the adhesives wetting resulted in phase separation of hydrophobic components leading to resin globule formation resulting in unfavorable bond strength.\textsuperscript{[60]} Futurabond DC also decreased the bond strength, since it contains ethanol which leads to over wetting,\textsuperscript{[61]} leading to the weakening of the resin dentin interface thus unfavorable bond strength.
ANTIBACTERIAL DSA
Chlorhexidine varnish reduced the bond strength, whereas chlorhexidine in gel form did not have any adverse effect on the self-etch and etch and rinse adhesives. Cervitec did not interfere with the bonding of the different adhesives. This review has included most of the studies evaluating the commonly used DSA and DBA and different bond strength tests, however, the limitation is data extraction limited to studies from 2010 to 2020 and studies in the English language only. In future, these types of studies have to be conducted simulating closer to the clinical conditions as far as possible, by creating hypersensitivity models, subjecting the specimens to thermocycling, thermomechanical aging. Blinding of the evaluators has to be performed to reduce the detection and performance bias.

CONCLUSION
According to the various articles included in this study, GLUMA and 8.0% arginine and Ca-CO3 when used as desensitizing agents along with different bonding agents, were found to be highly compatible without interfering with the bond strength of the dentin adhesives. For other desensitizing agents, compatibility with the different DBAs should be checked before the clinical use for successful bonding.

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Conflicts of interest
There are no conflicts of interest.

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