Effect of Sodium Hypochlorite on Adhesive Charactersitics of Dentin: A Systematic Review of Laboratory-Based Testing

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Outline

Abstract

Objective: The purpose of this review was to systematically summarize the outcomes of *laboratory-based* studies investigated the effect of sodium hypochlorite application on bond strength of dentin to various materials.

Data: A comprehensive literature search was conducted using PubMed, Google Scholar, Cochrane Library and OpenThesis database. Then a manual search was also carried out for references from identified articles.

Sources: The search followed the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" statement. Two independent reviewers evaluated the collected studies for their eligibility according to the inclusion and exclusion criteria. Data abstraction and evaluation of risk of bias was then performed.

Study Selection: A total of 164 articles were assessed for eligibility. Only 69 met the inclusion criteria. Most included studies presented a low (15.9%) to medium (68.1%) risk of bias. Only 15.9% presented high risk of bias. Because of heterogeneity of the included studies, Meta-analysis was not performed.

Conclusion: The outcome from low or high risk of bias studies revealed that sodium hypochlorite has no effect on bond strength of coronal or root canal dentin. While that from medium risk studies showed a reduction in bond strength of dentin.

Key words: Sodium hypochlorite, bond strength, dentin, root canal fillings/sealers/posts and risk of bias.

1. Introduction

Due to the complex anatomy of root canal, some areas of root canal dentin could remain untouched during instrumentation. Further effective cleaning is therefore an integral step for the success of endodontic treatments (2). Irrigants, rinses or inter-visit medications are commonly used to remove necrotic tissues and produce bacteria-free root canals (3, 4) – Fig. 1 (i). They also act as lubricants (5).

Sodium hypochlorite (NaOCl) has been recognised as an effective antibacterial agent in 1843 when low rates of infection transmission was recorded between patients washed their hands with it. Its use as an irrigant in endodontics dated back to 1902 since then it has been routinely used for such purpose (6). It has an effective antibacterial action (7-10) and dissolves both pulpal remnants (11, 12) as well as the organic component of root canal dentin (3). Increasing the concentration of NaOCl helps to improve the tissue dissolution and debridement capacities (13, 14). Lowering the surface tension of NaOCl also helps to improve its penetration to those uninstrumented areas of root canals (15). Furthermore, NaOCl also helps in removal of the organic component of the smear layer, produced during filing and drilling of root canal (16). This layer is a film of debris attached to root canal dentin; it is composed of shredded dentin, bacteria, bacterial products, remants of pulp tissues and retained irrigants (17). It occludes the orifices of dentinal tubules, so its presence could adversely affect the penetration of root canal sealers and the formation of intertubular tages required for adhesion of filling materials to root canal dentin (18, 19). Also its removal could ensure elimination of bacteria and their products. Hence the survival and reproduction of bacteria under filling materials could be jeopardized. Since NaOCl can dissolve the organic content of the smear layer, a combination of both NaOCl and

EDTA was found to be effective in removing both inorganic and organic content of the smear layer respectively (16). The concentration of both NaOCl and EDTA is very critical; erosion of root canal dentin could occure after the smear layer removal if the concentration is not well adjusted (20).

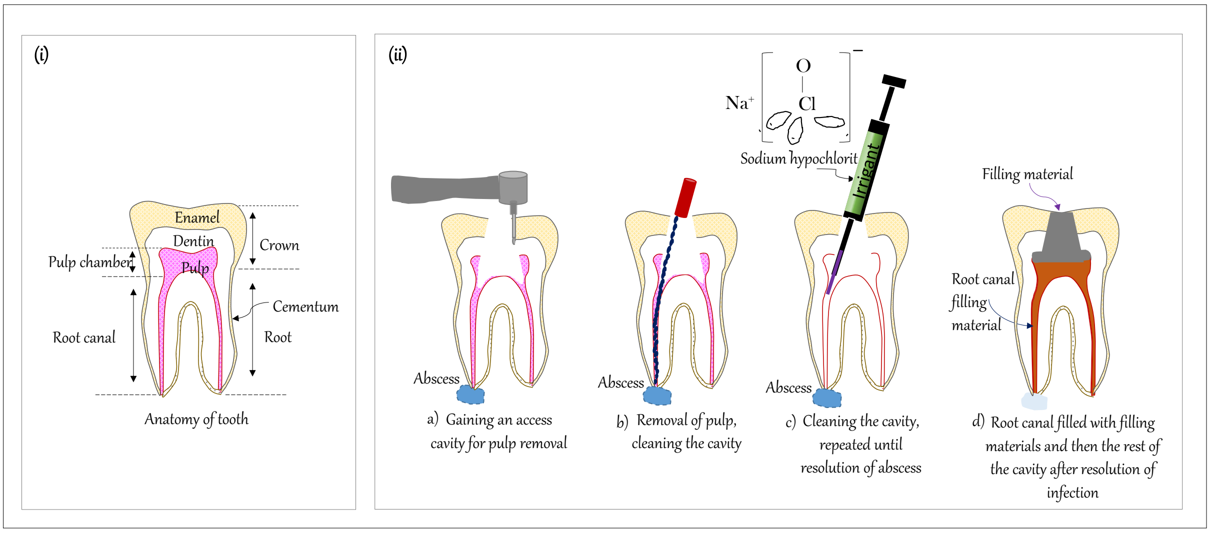


Fig. 1: Diagrammatic representation of (i) normal tooth anatomy. (ii) steps of endodontic treatment of tooth with periapical infection: in presence of infection eg, abscess; an access cavity is prepared a), pulp is then removed b); shaping and cleaning of root canal is repeated till infection subside; during this step NaOCl is usually used for irrigation of the root canal c), finally the root canal is filled with a root canal filling material eg, gutta percha and the rest of cavity is also filled with a restorative material eg composite d).

Dentin is composed of 20 wt% organix matrix (manily type I collagen) which substantially contributes to its mechanical properties. NaOCl is known to breakdown the long peptide chains. It also chlorinates terminal groups of protein which will then break down into other species. NaOCl may therefore adversely affect mechanical properties (eg, microhardness, elastic modulus and flexure strength) of dentin (3). Since NaOCl may alter the composition of dentin, its interaction (eg, bond strength) with the subsequent root filling materials could be affected. The long term success of post/core, for example, depends on the bonding of adhesive cement to root canal dentin. Improvement in bonding to root canal dentin increases the longevity of restorations (21-23). Lack of sealing ability of root canal sealers, used with root canal filling materials, or adhesive cements, used to bond post/core materials, could lead to microleagen and finaly premature failure of endodontic treatement (24).

The adhesive ability of any restoration can be used to predict its longevity that can be measured by bond strength test eg, microtensile, shear, pull out and push out test. The validity of these tests and their relevance to the clinical performance of any restoration is still questionable (25). The relevance of these tests to *in vitro* microleakage is also questionable (26). However, due to their simplicity, bond strength tests (eg macrobond) are still in use to measure the adhesion of restorative materials to tooth structures (25). Some of these tests (microtensile and microshear) also correlate better with longevity of restorations than others (macrotensile and macroshear) (27).

Not only the root canal dentin can be affected by irrigation/rinses/medications but also the coronal dentin (34). Furthermore, coronal dentin can be infected during root canal irrigation. Both conditions could affect the way the coronal dentin interact with the adhesive system and restorative materials used to restore the crown portion. Compromising the bond of restorative materials to coronal dentin will jeopridize the sealing ability of coronal restorations (35). A perfectly sealed coronal restoration is essential for increasing the longevity of an endodontically treated teeth. The main purposes behind a highly sealed coronal restoration are to avoid marginal leakage, increase the resistance of remaining tooth structure to fracture and restore the function and esthetics (36). For perfectly sealed coronal restoration, adhesives have been used with composite resins. Total etch and self etch adhesive systems are commonly used for such purpose. With total etch (3 step system), its application usually starts with 37% phosphoric acid etching followed by the primer and then bonding agent. Some total etch (2 step system) combines the primer and bonding agent together. Self etch on the other hand, skips the acid etching step. So the etchant could be combined with the primer (2 step system) or with both primer and bonding agent (one step system). The idea behind the use of dentin adhesives is to produce a strong, durable bond between resin and dentin. This bond will be formed when a monomer, having both hydrophilic and hydrophobic groups, penetrated dentin and polymerizes in situ. This resin-impregnation creates a transitional "hybrid" layer of resin-reinforced dentin. This hybrid layer is responsible for locking dentin with any other material on a molecular level creating a perfect seal against marginal leakage (37). Dentin hybridization, however, is a very sensitive technique (38). Recently, it has been shown that deproteinization of normal or acid etched dentin using sodium hypochlorite could be employed as an alternative method to the commonly used technique-sensitive dentin hybridization (39, 40).

Several studies reported the action of NaOCl on bond strength to dentin; there is however a significant controversy between these studies. Some studies reported that NaOCl improved the bond strength to dentin. They related this improvement to: (a) its deproteinizing action (dissolution and removal of exposed decalcified collagen produced by acid etching) thus producing a fresh mineralized matrix that bonded directly to the adhesive (29, 30) and (b) formation of an unusual bonding mechanism to dentin called a “reverse hybrid layer” where NaOCl can also dissolve collagen fibrils in the mineralized matrix left after acid etching producing submicron porosities into which the adhesive can penetrate forming this layer (30). Other studies suggested the opposite (ie, NaOCl reduces the bond strength to dentin). They related this to: (a) its deproteinizing action that produces a less receptive surface for bonding (31); (b) removal of collagen fibrils prevent the formation of a continuous hybrid layer (32); (c) the presence of remnants of NaOCl may interfere with the penetration of adhesive resins (32) and (c) its oxidizing action and hence an interference with the polymerization mechanism of adhesive resins (33). Accordingly, some authors recommended a delay of bonding for one week after root canal irrigation to provide enough time for elimination of the adverse effect of irrigants/rinses on dentin (28). This delaly in some cases is however impractical. In addition to this major controversy in the results, there are no systematic reviews published on the action of NaOCl on bond strength of dentin. Therefore, this systematic review aimed to summarize the outcomes of *in vitro* studies conducted on bond strength of dentin treated with sodium hypochlorite. It was conducted to answer the following research question (PICO statement is also included): Q1: Does the application of NaOCl have an effect on the bond strength of dentin? **PICO statement:** **P/Population** = dentin (whether coronal or root canal); **I/Intervention** = application of NaOCl; **C/Comparison** = dentin or dentin irrigated with water or saline; **O/Outcome** = effect on bond strength.

2. Methods/Study Design

This review has been conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement.

2.1. Eligibility Criteria

In vitro studies reporting the bond strength to dentin treated with sodium hypochlorite were considered eligible for inclusion in this systematic review. Articles were considered eligible if they:

a) Evaluated the effect of sodium hypochlorite applied (before or after etching) on bond strength (immediate or long term) of dentin (human or bovine; coronal or radicular or pulp chamber or root canal) to different materials (resin cements or endodontic fillings or posts).
b) Have a control group (NaOCl-untreated dentin, dentin irrigated with water or saline).

Articles that did not cover such data were excluded. Also *in vitro* studies that did not report the bond strength and present the control where other chemical irrigants (eg, chlorehexidine) used as controls were excluded. Non- English articles or those having authors' or editorial opinions were also excluded.

2.2. Search Strategy

A web-based search, conducted using PubMed and Google Scholar as research engines, was used to collect the research data. No time limitation was used during the search. The following key words were used for the search: (Sodium hypochlorite OR chemical irrigant OR deprotonizing agent* OR oxidizing agent) AND (Dentin bonding OR dentin adhesive* OR Dent* self-etch adhesive OR Dent* etch and rinse adhesive OR resin cement) AND (resin composite OR endodontic filling OR root canal filling OR endodontic sealer OR root canal sealer). These key words were modified according to the database used for the search. The initial search was conducted in August 2016 and repeated in October 2017 before the final write-up. Furthermore, using a similar search, OpenThesis database was also used to collect relevant theses and dissertations. Reference list of all included studies were hand searched for additional articles. Consultation with endodontic experts was also obtained through personal correspondence. An example of search strategy used is given in Table 1.

Table 1: An example of search strategy conducted in this systematic review (I) and category & subcategory used for data extraction (II).

No.	I. Search key words	Results
#1	Sodium hypochlorite solution * OR sodium hypochlorite gel* root canal irrigation * OR endodontic irrigation* OR hypochlorite*	7385
#2	Dentin bonding* OR dental adhesives* OR dental adhesive* OR adhesive* OR adhesives* OR etch and rinse* OR total etch* OR self etch* OR one step self etch* OR two step self etch* three steps etch and rinse* OR bond strength* OR shear bond strength* tensile bond strength* OR microtensile bond strength*	2237
#3	Endodontic filling* OR root canal filling* OR root canal sealers* OR endodontic sealers* OR endodontic post*	6900
#4	#1 AND#2 AND#3	7

II. Category & sub-category used for data extraction

1. NaOCl:
  a) Form
  b) Concentration
  c) Time of application

2. Type of control

3. Method:
  a) Source of dentin/location/preparation method
  b) Step during which NaOCl applied
  c) Type of adhesive
  d) Materials bonded to dentin
  e) Bond strength test

4. Outcome of NaOCl on bond strength in comparison to control

Two independent reviewers screened the obtained articles by the title. Any duplicate was eliminated and the abstract of relevant articles were further appraised for their eligibility. When the information provided in both titles and abstracts was not sufficient; full text was considered. The inclusion of articles was based on the agreement between the two reviewers. Any disagreement between the two reviewers was solved by discussion.

2.3. Risk of Bias Assessment

For quality assessment, the evaluation has been based on the presence of the following six parameters: a) presence of control, b) description of sample size, c) randomization of samples, d) procedures carried out by one operator, e) blinding of the operator and f) materials used according to manufacturers' instructions.

If the parameter under interest has been reported, the article had "Y" (ie, Yes); if not the article received "N" (ie, No). Articles reported one or two parameters were classified as "high risk of bias". Those reported three or four were classified as "medium risk of bias", while those reported five or six were classified as "low risk of bias" (41).

2.4. Data Extraction

Full articles with relevant information were obtained and data were extracted by the two reviewers according to specific criteria that were categorized as given in Table 1.

2.5. Statistical Analysis

Descriptive statistics were used to describe the data obtained from this review, but due to heterogeneity of the studies, Meta-analysis was not be performed.

3. Results

There were 234 articles identified through the database searching. After exclusion of duplicate articles, only 164 articles were involved; 95 articles were further excluded after assessing their eligibility. Therefore, there were 69 articles which were assessed qualitatively throughout this review – Fig. 2.

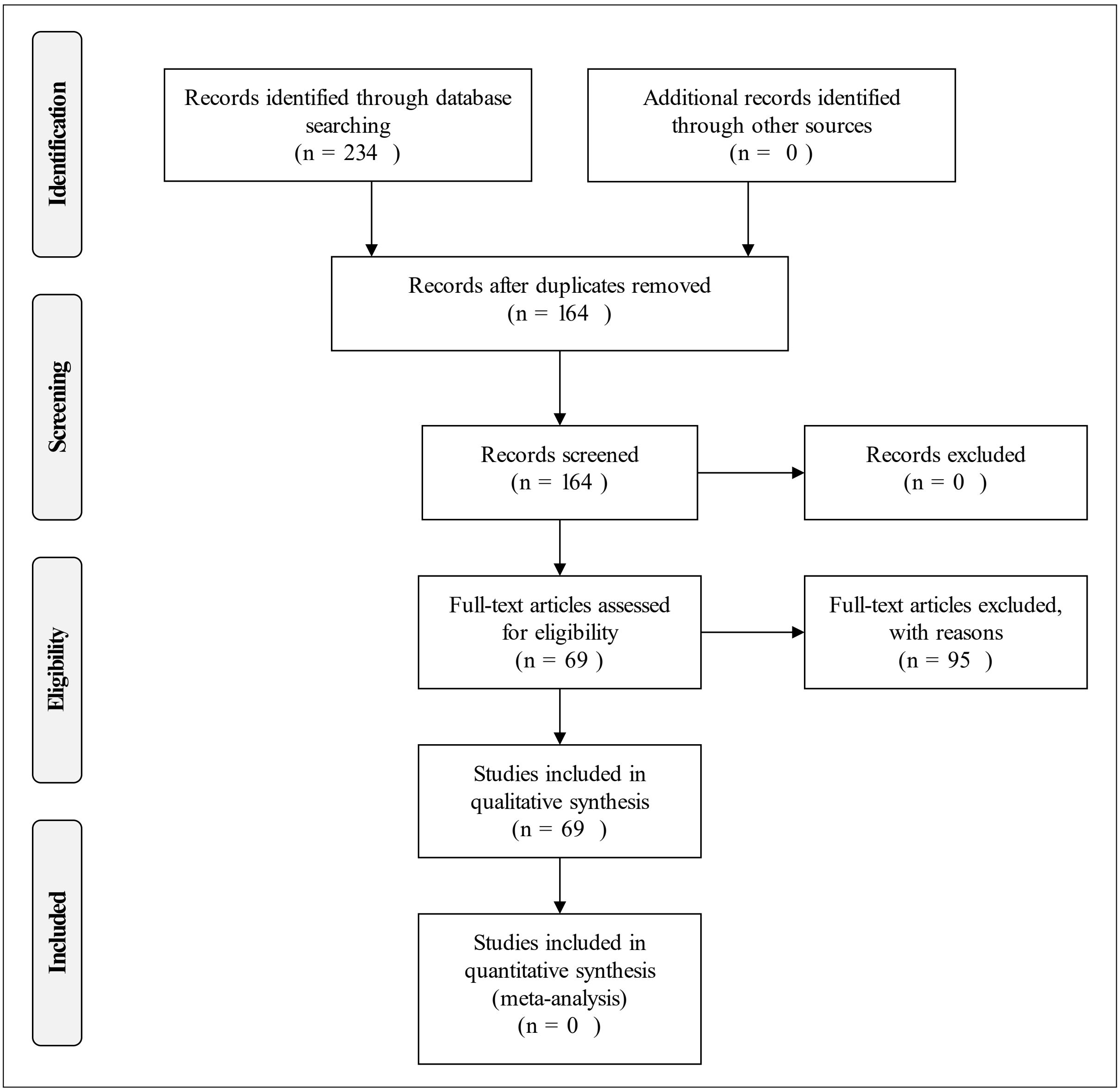


Fig. 2: PRISMA 2009 Flow Diagram

Table 2 summarizes all the work carried out using sodium hypochlorite to treat dentin and highlights various methodologies used (eg, form/concentration/time of application/step during which NaOCl used, test method, type of adhesive used and type of materials bonded to treated dentin). Regardless of the main use of sodium hypochlorite as an irrigant solution for root canal during endodontic treatments, testing its effect on the bond strength to dentin did not only involve the use of root canal dentin but also the coronal or pulp chamber dentin as highlighted above. Furthermore, the use of sodium hypochlorite could be done after etching step. This includes two situations (a) when used with etch and rinse adhesive where etching is a separate step or (b) when used for deproteinization of acid etched dentin as an alterative to the technique-sensitive dentin hybridization (39) as explained above. The use of sodium hypocholorite could also be done before bonding. This includes two situations (a) before the application of self etch adhesive where there is no separate etching step or (b) when used to simulate what happens clinically where coronal dentin can be contaminated with sodium hypochlorie during root canal irrigation.

Diagrammatic representation of the different methods used to prepare samples for testing the effect of NaOCl on bond strength of different materials to dentin is presented in Fig. 3 (i-v).

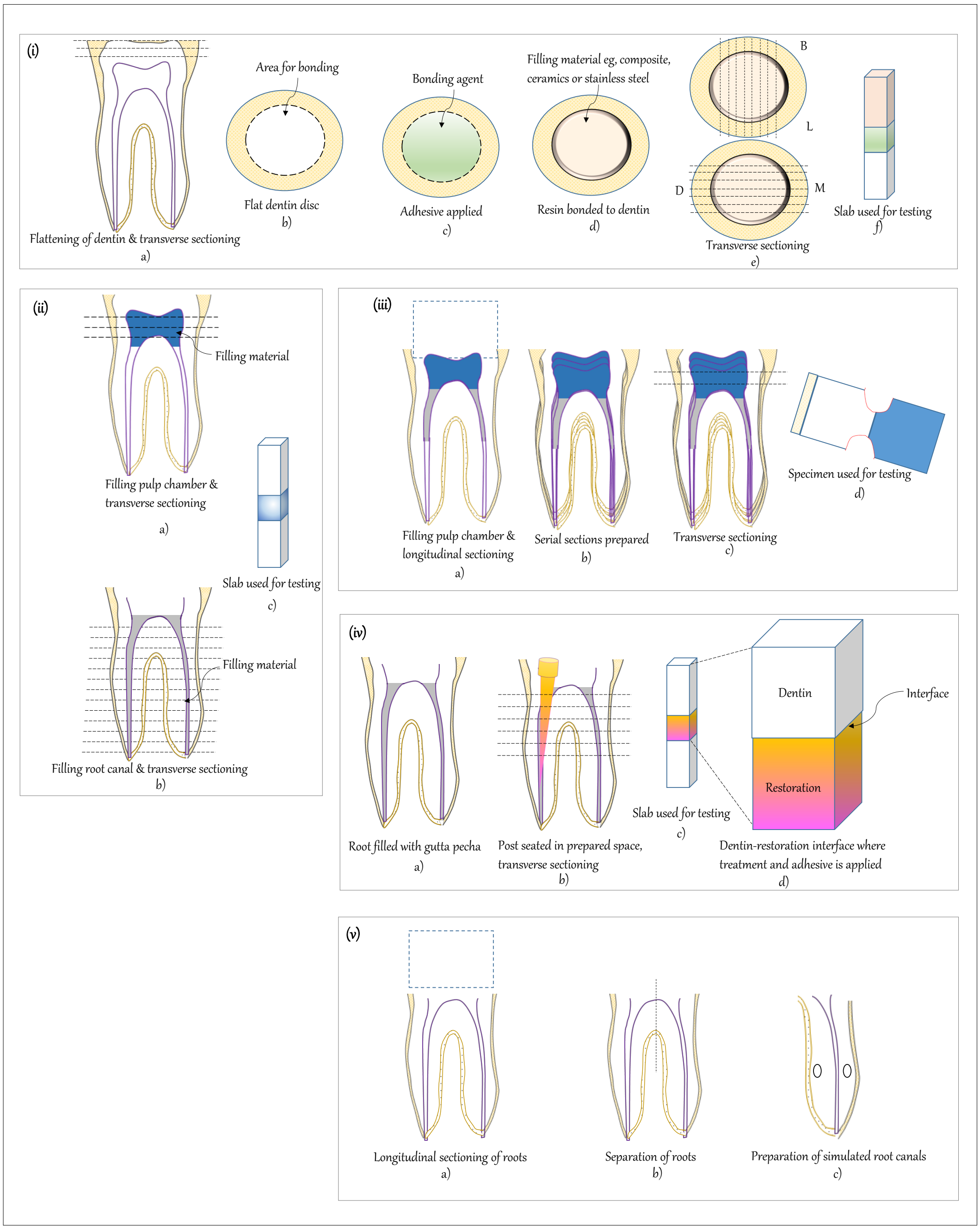


Fig 3: Different methods used to prepare samples for testing the adhesion of filling materials to NaOCl-treated dentin; (i) This can be done by using coronal dentin after its flattening a) and preparing discs b) upon which the adhesive is applied c) then the filling material bonded to it d) then sectioning bucco-lingually or mesio-distally e) to prepare slabs used for testing f); (ii) Others rely on filling the pulp chamber a) or root canal b) then transvers sectioning is carried out to prepare slabs used for testing c); (iii) Sometimes longitudinal sections are performed after filling the pulp chamber a) to prepare serial sections b) that further cut transversally c) to prepare hourglass specimens used for testing d). (iv) Also, the root canal can be filled with gutta percha a), then a preparation is made within filled root canal to receive a post b), and then transverse sectioning is done to prepare slabs for testing c). In all cases, at the restoration-dentin interface, the dentin treatment and adhesive systems are performed d). (v) In some cases, simulated root canal cavities were prepared in radicular dentin at an equal distance between the dentin and root canal wall (a-c).

Fig. 4(a) summarizes the distribution of number of cases according to the site from which dentin was used for testing the effect of NaOCl on bond strength ie, whether it is coronal (CD), pulp chamber (PCD) or root canal dentin (RCD). As seen 51% of cases used coronal dentin; 43% used root canal dentin and only 6% used pulp chamber dentin. Fig. 4(b) shows the distribution of the number of cases according to the step during which NaOCl was applied. Generally, 69% of cases applied NaOCl before the application of the adhesive (bonding system) to dentin; 31%, applied NaOCl after etching (the first step of bonding) of dentin. When coronal dentin was used, most of the cases applied NaOCl after etching (45%); the opposite is true for root canal dentin (ie, 20% of cases utilized NaOCl after etching). NaOCl-treated coronal dentin was usually bonded to filling materials (eg, composites); NaOCl-treated root canal dentin was usually bonded to root canal filling materials eg, gutta percha (42), resin cements (43) or posts (44).

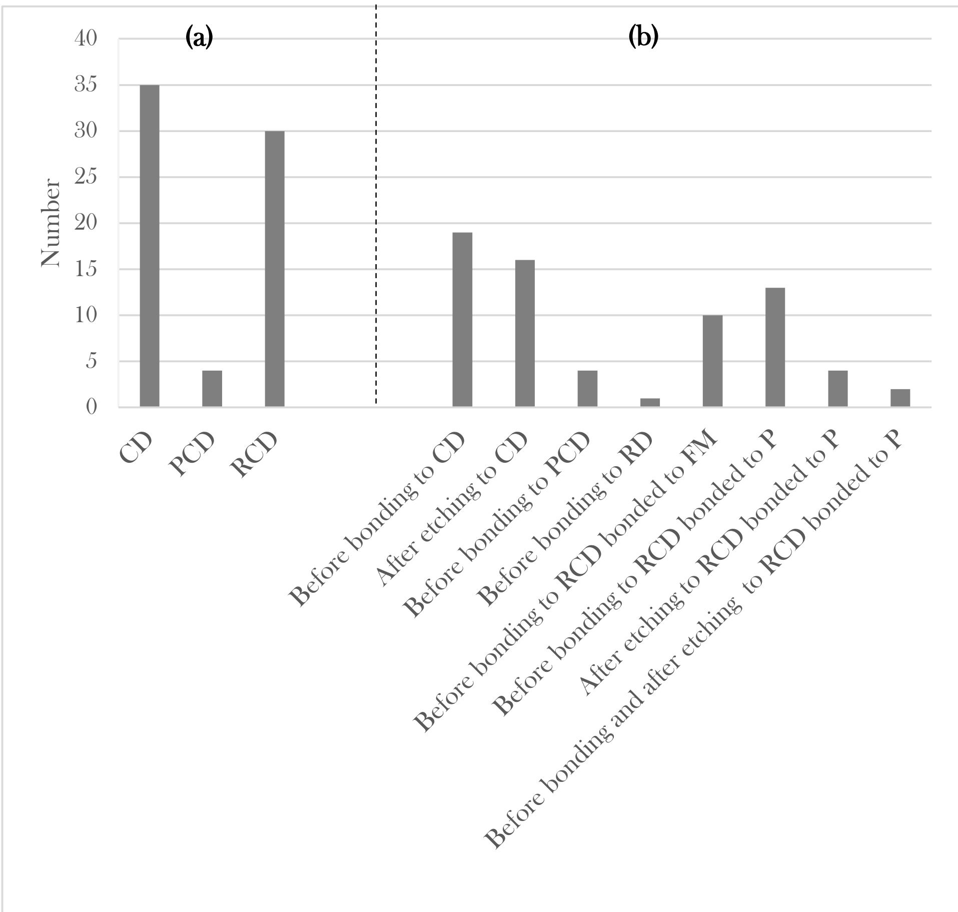


Fig. 4: Distribution of cases according to the site from which dentin was used ie, whether it is coronal (CD), pulp chamber (PCD) or root canal dentin (RCD) (a); steps during which NaOCl was applied (b). RD: radicular dentin (ie, simulated root canals). FM: filling materials. P: posts.

Table 2: The effect of NaOCl application on bond strength to dentin. HF: hydroflouric acid. CEJ: cemento-enamel junction. + identifies all factors under bond strength testing methods while * identifies all factors under NaOCl.

Author	+Step during which NaOCl used	*Form of NaOCl	*Concentration of NaOCl (%)	*Time of application of NaOCl (min)	Type of Control	+Bond strength test	+Source of dentin, location & preparation method	+Type of adhesive	+Material bonded to dentin	Outcome of NaOCl on bond strength in comparison to control
Francescantonio et al., (45)	After etching with H3PO4	Gel	10	1	Etched dentin	Microtensile	Human 3rd molars, coronal dentin	One Step Plus (etch & rinse)	Aelite LS	Decrease
								Clearfil Photo Bond (etch & rinse)	Clearfil Majesty	Decrease
								Clearfil SE Bond (self-etch)	Clearfil Majesty	No change
Prati et al., (30)	After etching with 35%H3PO4 for 20s	Gel	1.5	2	Etched dentin	Shear (immediate)	Human 3rd molars, coronal dentin	Optibond FL	Z100 (composite resin)	Increase
								Scothcbond MP		Decrease
								Single Bond		Decrease
								Prime & Bond 2		No change
Uceda-Gomez et al., (46)	After etching with 32% H3PO4	Solution	10	1	Etched dentin	Microtensile	Human molars, coronal dentin, longitudinal sections of teeth (superficial vs deep dentin ie apical vs occlusal dentin)	One Step	Z100 (composite resin)	Decrease
Osorio et al., (47)	After etching with 35% H3PO4 for 15s	-	5	2	Etched dentin	Shear	Human 3rd molars, coronal dentin	Single Bond	Z100 (composite resin)	Decrease
Yiu et al.,(48)	After etching	-	5	10	Etched dentin	Microtensile	Human 3rd molars, coronal dentin	One Step (single bottle)	Renamel Sculpt (composite resin)	Decrease
								Gluma Comfort Bond + Desensitizer (single bottle)		
Saboia et al., (49)	After etching with 35% H3PO4 for 15s	Solution	10	1	Etched dentin	Microtensile	Human 3rd molars, coronal dentin	XP-Bond (2-step etch & rinse)	Filtek Z250 (mcirohybrid composite resin)	Decrease
Baseggio et al., (50)	After etching with 35% H3PO4 gel for 20s	-	10	1	Etched dentin	Microtensile	Human 3rd molars, coronal dentin	Single Bond	Z100 (composite resin)	Decrease
dos Santos et al., (51)	After etching with 35% H3PO4 for 15s	Solution	10	1	Etched dentin	Shear	Bovine incisors, coronal dentin	Single Bond	Z100 (composite resin)	Decrease
Perdigão et al., (52)	After etching with 34% H3PO4 for 15s	Gel	10	¼, ½ & 1	Etched dentin	Shear	Bovine, coronal dentin	Prime&Bond NT (total-etch)	Surefil (composite resin)	Decrease with time
								Single Bond (total-etch)	Z100 (composite resin)	
Uceda-Gomez et al., (53)	After etching with 37% H3PO4	Solution	10	1	Etched dentin	Microtensile	Human 3rd molars, coronal dentin	Single Bond (etch & rinse)	Z250 (composite resin)	No change
	After etching with 32% H3PO4							One Step (etch & rinse)		
Manjunath & Vinutha (54)	After etching with 35% H3PO4 for 15s	-	5.25	1	Etched dentin	Shear	Human premolars, coronal dentin	Adper Single Bond 2 (single bottle)	Z100 (composite resin)	Increase
								Excite (single bottle)	TeEconom (composite resin)	
Correr et al., (55)	After etching with 35%	Solution	10	1	Etched dentin	Shear	Human primary molars, coronal dentin	Single Bond	Filtek Z250 (composite resin)	No change
								Prime & Bond 2.1		

	H3PO4 for 15s									
Montagner et al., (56)	After etching with 35% H3PO4 for 15s	Solution	10	1	Etched dentin	Push out	Human 3rd molars, coronal dentin (circular cavities in superficial & deep occlusal & proximal surfaces)	Adper ™ Single Bond 2 (etch & rinse) Clearfil ™ SE Bond (self-etch) Adper ™ SE Plus (self-etch) G-Bond ™ (self-etch)	Filtek ™ Z250 (composite resin)	No change
Lisboa et al., (57)	After etching with 34% H3PO4 for 15s	-	5	2	Untreated dentin	Shear	Human 3rd molars, coronal dentin	Rely X Unicem (self-adhesive resin cement)	Rely X Unicem (self-adhesive resin cement)	No change
								BisCem (self-adhesive resin cement)	BisCem (self-adhesive resin cement)	Increase
Aguilera et al., (58)	After etching with 35% H3PO4	Solution	5	2	Etched dentin	Shear	Human 3rd molars, coronal dentin	Prime & Bond NT	Tetric Ceram (composite resin)	No change
de-Souza et al., (59)	After etching with 35% H3PO4 for 15s	Solution	5	2	Etched dentin	Microtensile	Human 3rd molars, coronal dentin	Single Bond™ (total etch)	Filtek™ Z250 (composite resin)	Decrease
	After etching with 34% H3PO4 for 15s							Prime & Bond NT™ (total etch)	Esthet® X (composite resin)	Increase
	After etching with 15% H3PO4 for 30s							One Coat Bond (total etch)	Fill Magin (composite resin)	No change
	After etching with 35% H3PO4 for 15s							PQ1™	Vit-l-escence™	Increase
Sauro et al., (60)	After etching with 35% H3PO4 for 15s	-	0.5	1/2	Etched dentin	Microtneisle	Human 3rd molars, coronal dentin	Schotchbond 1XT (etch & rinse) Optibond Solo Plus (etch & rinse)	Filtek Supreme XT™ (flowable composite resin)	No change
Goncalves et al., (61)	After etching with 37% H3PO4 for 15s	Solution	10	1	Etched dentin	Microtensile	Bovine incisors, coronal dentin	Prime & Bond NT	TPH Spectrum (microhybrid composite resin)	No change
Arias et al., (62)	After etching with 36% H3PO4 for 20s	Gel	10	1	Etched dentin	Shear	Bovine incisor, coronal dentin	Gluma One Bond Prime & Bond 2.1 Single Bond Prime & Bond NT	Z100 (composite resin)	No change
		Solution						Gluma One Bond		Increase
								Prime & Bond 2.1 Single Bond Prime & Bond NT		No change
Taniguchi et al., (63)	Before bonding	Solution	6	1/4	Dentin rinsed with water	Microtensile	Human molars, coronal dentin	Bond Force (self-etch)	Clearfil AP-X (composite resin)	Increase for caries affected dentin No change for normal dentin
				1/2				Clearfil Protect Bond (self-etch)		No change for caries affected dentin) Decrease for normal dentin
								Variolink II (total-etch)		N0 change
								Cealrfill SA Cement (self-etch)		Decrease

Stevens et al., (64)	Before bonding	Solution	6	20	Untreated dentin	Shear (immediate)	Human molars & premolars, coronal dentin	Clearfill Esthetic Cement EX (self-etch)	Ceramic rod etched with 4.9 % HF acid for 20s and silanated with Monobond Plus for 1min	N0 change
								SpeedCEM (self-etch, self-adhesive)		Decrease
								Multilink (self-etch, self-adhesive)		No change
Cecchin et al., (65)	Before bonding	Solution	1	5 ml every 5min for 60min	Untreated dentin	Microtensile	Human 3rd molars, coronal dentin, hourglass samples	Xeno III (self-etch)	Z250 (composite resin)	Increase
Hassan et al., (66)	Before bonding	-	4	1/3	Untreated dentin	Shear	Human molars, coronal dentin	Adper Easy One	TPH (microhybrid composite resin)	Increase
									Tetric Evoceram (nanohybrid composite resin)	
								Prime and Bond 2.1	TPH (microhybrid composite resin)	
									Tetric Evoceram (nanohybrid composite resin)	
Ebrahimi-Chaharom et al., (67)	Before bonding	Solution	5.25	10	Untreated dentin	Shear	Human premolars, coronal dentin	Clearfil S^3 Bond	Z100 (composite resin)	Decrease
								Adaper Easy Bond		
Gönülol et al., (68)	Before bonding	Solution	5.25	10	Dentin irrigated with distilled water	Microtensile	Human 3rd molars, coronal dentin	Clearfil SE Bond (2-step self-etch)	Filtek Z550 (core build up composite resisn)	Decrease
Farina et al., (69)	Before bonding	Solution	1	40	Untreated dentin	Microtensile	Human 3rd molars, coronal dentin	Clearfil SE Bond (self-etch)	Z250 (composite resin)	Decrease
Nassar et al., (70)	Before bonding	Solution	5	10	Dentin irrigated with deionized water	Shear	Human 3rd molars, coronal dentin	Ephiphany self-etch root canal sealer	Ephiphany (self-etch root canal sealer)	Decrease
Abo et al., (71)	Before bonding	Solution	0.5 v	60	Dentin irrigated with water	Shear	Human molars, coronal dentin	OptiBond FL (3-step etch & rinse)	Filtek Supreme (composite resin)	Decrease
								EL#628 (2-step etch & rinse)		
								OptiBond SOLO Plus (2-step self-etch)		
								Clearfil SE Bond (2-step self-etch)		
								AdheSE (2-step self-etch)		
								iBond (1-step self-etch)		
								Adper Prompt L-Pop (1-step self-etch)		
								Xeno (1-step self-etch)		
Saber & El-Askary (72)	Before bonding	Solution	2.5	-	Untreated dentin	Shear	Human molars, coronal dentin	Clearfil S^3 bond (1-step self-etching)	TPH™ Spectrum (composite resin)	Decrease
Kunawarote et al., (73)	Before bonding	Solution	6	1/12	Dentin irrigated with running water	Microtensile	Human molars, coronal dentin	Clearfil SE Bond (2- step self-etch)	Clearfil AP-X (composite resin)	No change
				¼						Decrease
				½						
Kambara et al., (74)	Before bonding	Solution	6	1/12	Dentin irrigated with running water	Shear	Human molars, coronal dentin	Clearfil SA luting (self-adhesive cement)	SUS-304 (stainless steel rods that had been sandblasted using 50 μm alumina	Decrease
								Breeze (self-adhesive cement)		
								Rely X Unicem clicker (self-adhesive cement)		
				¼				Clearfil SA luting (self-adhesive cement)		
								Breeze (self-adhesive cement)		

								Rely X Unicem clicker (self-adhesive cement)		Increase
Ayad & Garcia-Godoy (75)	Before bonding	Solution	5	1	Untreated dentin	Push-out	Human mandibular 3rd molars, coronal dentin	Epiphany primer	Epiphany sealer	Increase
Kasraei et al., (76)	Before bonding	Solution	2.5	¼	Untreated dentin	Microtensile	Human premolars, coronal dentin	Clearfil S3 (self-etch) I-Bond (self-etch)	Z100 (composite resin)	No change
Sasafuchi et al., (77)	Before bonding	Solution	5	1	Untreated dentin	Tensile	Bovine incisors, coronal dentin	Super-Bond C&B (resin cement) Panavia F (resin cement)	Composite resin rods	Decrease No change
Prasansuttiporn et al., (78)	Before bonding	Solution	6	1/2	Dentin irrigated with distilled water	Microtensile	Human 3rd molars, coronal dentin	Clearfil Protect Bond (2-step self-etch)	Clearfil AP-X (composite resin)	Decrease
Vongphan et al., (79)	Before bonding	Solution	5.25	10	Pulp chamber irrigated with distilled water	Microtensile	Human 3rd molars, pulp chamber dentin (cavity in pulp chamber was filled & sectioned vertically into 0.8mm thick slabs that were trimmed into dumbbell shaped specimens)	Single Bond (total-etch)	Z250 (composite resin)	Decrease
Bhat Gorwish et al., (80)	Before bonding	Solution	3	1	Pulp chamber irrigated with distilled water	Microtensile	Human mandibular 3rd molars, pulp chamber dentin (cavity in pulp chamber was filled then sectioned)	Single Bond 2 Prime & Bond NT Adhes SE	Solitaire (posterior composite resin)	Decrease
Ozturk & Ozer (81)	Before bonding	Solution	5	1	Unirrigated pulp chamber	Microtensile	Human mandibular 3rd molars, pulp chamber dentin (cavity in pulp chamber was filled then sectioned)	Clearfil SE Bond Prompt-L Pop Prim & Bond NT Schotbond Multipurpose Plus	Clearfil AP-X Hytac TPH Filtek Z250	Decrease
Santos et al., (82)	Before bonding	Solution	5.25	30 (renewed every 3)	Pulp chamber irrigated with 0.9% saline	Tensile	Bovine incisors, pulp chamber dentin (cavity in pulp chamber was filled)	Clearfil SE Bond (self-etch)	Filtek Z250 (composite resin)	Decrease
Shretha et al., (83)	Before bonding	Solution	1.3 5.2	1	Dentin irrigated with distilled water	Micropush-out	Human single rooted teeth, simulated (vertically oriented truncated) canals were prepared in middle of radicular dentin in longitudinal slices cut below CEJ and filled	RealSeal SE (self-etching adhesive sealer)	RealSeal SE (self-etching adhesive sealer)	Increase
Morris et al., (84)	Before bonding	Solution	5	15-20	Root canals irrigated with 0.9% saline	Tensile	Human maxillary incisors and mixed canines, root canal dentin (after filling root canal, they were sectioned into 1 mm thick slabs from CEJ to apex)	C&B Metabond	C&B Metabond	Decrease
Manimaran et al., (85)	Before bonding	Solution	5.25	15-20	Root canals irrigated using 0.9% saline	Microtensile	Human single rooted teeth, root canal obturated with root a canal sealer	Adper™ (self-etch)	RelyX™ (resin cement)	Decrease
Erdemire et al., (21)	Before bonding	Solution	5	1	Root canal irrigated with water	Microtensile	Human single rooted teeth, root canal dentin (after filling root canal, they were sectioned into	C&B Metabond	C&B Metabond	Decrease

							1 mm thick slabs from CEJ to apex)			
Gu et al., (43)	Before bonding	Solution	5.25	1	Root canals irrigated using 0.9% saline	Push-out	Human single rooted teeth, root canal obturated with gutta percha and AH Plus, then a post space was prepared and filled with a resin cement	Panavia F resin cement	Panavia F (resin cement)	Decrease
Ari et al., (86)	Before bonding	Solution	5	5	Root canal irrigated with water	Microtensile	Human single rooted tooth, root canal dentin (after filling root canal, they were sectioned into 1 mm thick slabs from CEJ to apex)	C&B Metabond PanaviaF Variolink II Rely-X	C&B Metabond PanaviaF Variolink II Rely-X	Decrease No change
Stelzer et al., (87)	Before bonding	Solution	3	4	Root canal irrigated with 0.9% saline	Push-out	Human teeth, root canal obturated with a filling material and a sealer	AH Plus (sealer) RealSealSE (sealer)	Gutta percha Resilon	No change Decrease
Haragushiku et al., (88)	Before bonding	Solution	1	30	Root canal irrigated with distilled water	Push-out	Human maxillary canines, root canal obturated with a root canal sealer, then a post space was prepared and filled with a resin cement	- - Epiphany-self etching primer Epiphany-self etching primer	Apexit Plus AH Plus Epiphany-auto mixed Epiphany-hand mixed	No change
Ishizuka et al., (89)	Before bonding	Solution	6 v/v	1,5 & 10	-	Push -out shear	Bovine mandibular 1st & 2nd incisors, root canal dentin (after filling root canal with gutta-percha, a truncated cone cavity of 4 mm diameter & 2.5mm height within coronal part of the root was prepared. Cavity was then filled and sectioned into 1mm thick slabs)	Clearfil Mega Bond (self-etch primer) Single Bond (total-etch)	Clearfil AP-X (composite resin)	Decrease N0 change
Rocha et al., (42)	Before bonding	Solution	2.5	3	Root canal irrigated with 0.9% saline	Push -out	Bovine central incisore, root canal obturated	Epiphany (sealer) AH Plus (sealer)	Resilon Gutta percha	Increase Decrease
Weston et al., (31)	Before bonding	Solution	5.25	15-20	Root canals irrigated with 0.9% saline	Tensile	Human maxillary incisors and mixed canines, root canal obturated with C&B Metabond	C&B Metabond	C&B Metabond	Decrease
Bournziniat et al., (90)	Before bonding	Solution	-5.25 (10 ml during root canal shaping)	1	Root canal irrigated with normal saline	Pull-out	Human mandibular premolars teeth, root canal obturated with gutta percha and AH-26 sealer, then a post space was prepared and filled with a post.	Panavia F2 (self-etch resin cement) Embrace (self-adhesive resin cement)	White Post DC3 (fiber reinforced composite posts)	Decrease
Lacerda et al., (91)	Before bonding	Solution	2.5	-	Root canal irrigated with normal saline	Push-out	Bovine incisors, root canal obturated with gutta percha and calcium hydroxide sealer (Sealer 26), then a post space	Futurabond DC (self-etch dual-cure adhesive) + Bifix QM (epoxy-based dual-cure resin)	Glass fiber posts	Decrease

							was prepared and filled with a post.			
Khoroushi et al., (92)	Before bonding	Solution	-2.5 (during root canal shaping)	1	Root canal irrigated with normal saline	Pull-out	Human single rooted teeth, root canal obturated with gutta percha and AH26 sealer, then a post space was prepared and filled with a silica-coated and Rocatic system (ESPE Sil)-silanized post.	Ceramic Bond + Bifix SE (1-step self-etch cement)	Stainless steel spreaders #55 with handles	Decrease
			-2.5 (after preparation of post space)	2						
Arisu et al., (93)	Before bonding	Solution	-2.25 (during root canal shaping)	-	Root canal irrigated with distilled water	Push-out	Human mandibular premolars, root canal obturated with gutta percha and AH26 sealer, then a post space was prepared and filled with a post	Panavia F 2.0 (resin cement)	Mirafit White (glass fiber posts)	Decrease
			-2.25 (5ml after preparation of post space)	1						
Alkhudhairy & Bin-Shuwaish (94)	Before bonding	Solution	2.5	-	Root canal irrigated with NaCl	Push-out	Human incisors, root canal obturated with gutta percha with AH-26 sealer, then a post space was prepared and filled with post	MultiCore Flow (core build-up)	No.3 RelyX (fiber post)	Increase +++
								RelyX-UniCem (self-adhesive resin cement)		Increase ++
			5.25	-				MultiCore Flow (core build-up)		Increase +
								RelyX-UniCem (self-adhesive resin cement)		Increase +
Faria-e-Silva et al., (95)	Before bonding	Solution	-2.5 (during root canal shaping)	-	Root canals received no irrigation	Push-out	Bovine incisors, root canal obturated with gutta percha and resin sealer (Sealer-26), then a post space was prepared and filled with an etched (24% H2O2 for 10min) & silanated post.	BisCem (self-adhesive resin cement)	FRC post (glass fiber reinforced epoxy posts)	Increase
			- 5 (after preparation of post space)	1				RelyX Unicem clicker (self-adhesive resin cement)		
Bueno et al., (96)	Before bonding	Solution	- 2.5 (25 ml during root canal shaping)	-	Root canal irrigated with saline solution	Push-out shear	Bovine mandibular incisors, root canal obturated with gutta percha and AH Plus sealer, then a post space was prepared and filled with an etched (37% H3PO4 for 15s) & silanated pos	Schotbond Multipurpose + RelyX ARC (resin cement)	Reforpost No.3 (glass fiber posts)	No change
								ED Primer + Panavia F (resin cement)		
								RelyX U100 (resin cement)		
			-5.25 (during root canal shaping)					Schotbond Multipurpose + RelyX ARC (resin cement)		
								ED Primer + Panavia F (resin cement)		
								RelyX U100 (resin cement)		Decrease
Bitter et al., (97)	Before bonding	Solution	-1 (1ml during root canal shaping)	-	Root canals irrigated with distilled water	Push-out	Human maxillary central incisors, root canal obturated with gutta percha and AH Plus, then a post space was prepared and filled with a post	AdheSE (self-etch adhesive)	Post FRC Postec and MultiCore Flow as core material	No change
			-1 (5ml after preparation of post space)	1				XP Bond (etch & rinse) & self-cure activator	Post X Post and the core material Core X Flow	Increase
								SmartCem2 (self-adhesive resin cement)	Post X Post	
			-1 (1ml during root canal shaping)	-				AdheSE (self-etch)	Post FRC Postec and MultiCore Flow as core material	No change
			-5.25 (5ml after preparation of post space)	1				XP Bond (etch & rinse) & self-cure activator	Post X Post and the core material Core X Flow	
								SmartCem2 (self-adhesive resin cement)	Post X Post	

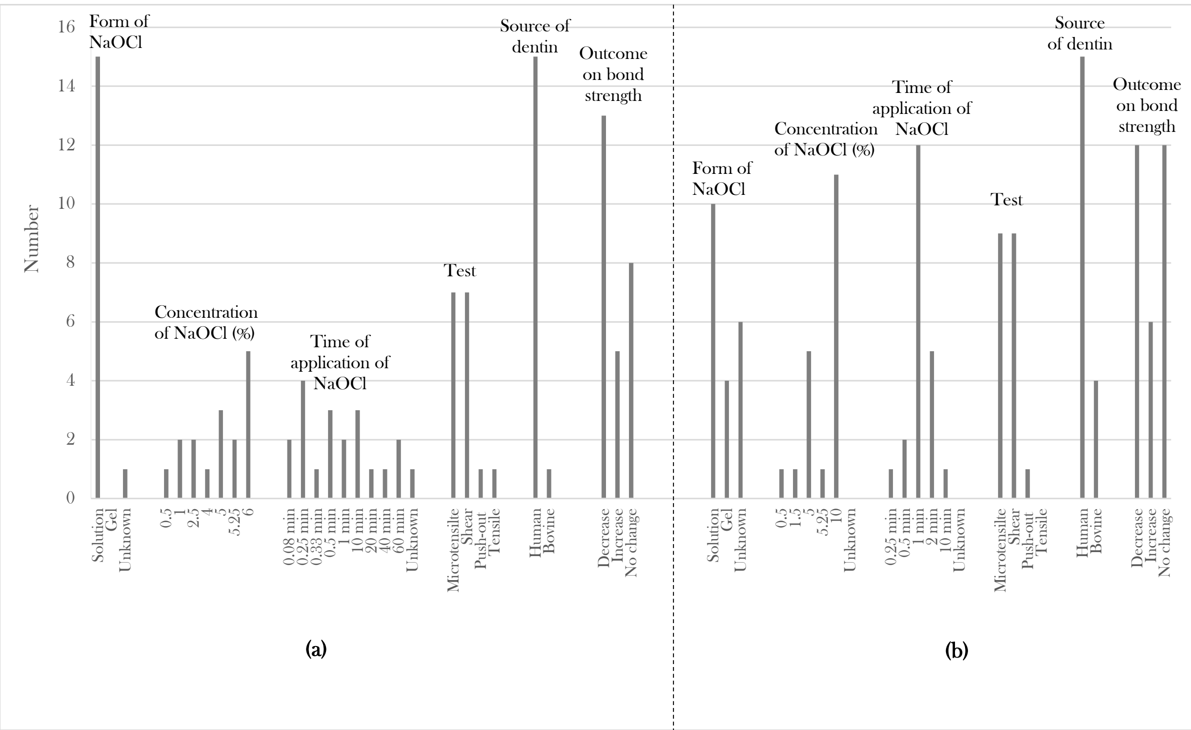
Ertas et al., (98)	Before bonding	Solution	-2.5 (1 ml during root canal shaping) -5.25 (5 ml after preparation of post space)	- 5	Root canals irrigated with 0.9% saline	Push-out	Human single rooted teeth, root canal obturated with gutta percha and AH Plus, then a post space was prepared and filled with a post	Bifix SE (dual-cure resin cement)	Fiber posts	Increase
Pelegrine et al., (99)	Before bonding	Solution	-1 (2o ml during root canal shaping) - 2.5 (2o ml during root canal shaping) - 5.25 (2o ml during root canal shaping)	-	Root canals irrigated with 0.9% saline	Tensile	Bovin teeth, root canal obturated with M gutta perch and AH Plus sealer, then a post space was prepared and filled with a H3PO4 etched and silanized (using Clearfil Porcelain Bond Activator & Clearfil SE Primer) post	Clearfil SE Bond (2-step self-etch) + RelyX ARC (resin cement)	Glass fiber post	No change
Haragushiku et al., (100)	Before bonding	Solution	2.5	1	Root canals irrigated with distilled water	Push-out	Human maxillary canines, root canal obturated with gutta percha, accessory MF cones and AH Plus sealer, then a post space was prepared and filled with a silanized (Prosil) – post.	Ambar FGM (2-step etch & rinse) + AllCem (dual-cure resin-based cement)	WhitePost DC2 (glass-fiber post)	No change
Kaif and Raj (101)	Before bonding	Solution	-5.25 (5 ml during root canal shaping) -5.25 (after preparation of post space)	-	Root canals irrigated with distilled water	Push out	Human single rooted teeth, root canal obturated with gutta percha and AH-Plus sealer, then a post space was prepared and filled with a H3PO4 etched post.	Adaper Single Bond 2 + RelyX ARC® resin cement	FiberKor® post (glass fiber posts)	No change
Saraiva et al., (44)	Before bonding	Solution	-2 (during root canal shaping) -5.25 (after preparation of post space)	- 2	Root canals received no irrigation	Push-out	Human incisors, root canal obturated with gutta percha, then a post space was prepared and filled with a silanated post	Excite Dual-self-cure (2-step etch & rinse) Variolink II (dual-cure resin cement)	FRC Postec® Plus (fiber posts)	No change
Cecchin et al., (102)	After etching with 37% H3PO4 for 15s	Solution	5.25	5	Root canals irrigated with 0.9% saline	Push-out	Bovine incisors, root canal obturated with an etched (H3PO4) and resin covered post	Adaper Schotchbond Mutipurpose (total etch) + Rely X ARC (dual-cure resin cement)	Fiberglass post relined with Z250 composite resin	No change
Inoue et al., (103)	After etching with H3PO4 semi-gel for 15s	Gel	-	1	Root canals received no irrigation	Microtensile	Human molars, root canal obturated with gutta perch and zinc oxide eugnol sealer, then a post space was prepared and filled with an etched (H3PO4) and silanized (porcelain activator + Primer A & B of Clerfil Liner Bond II) indirect resin core	ED Primer + Panavia FluroCement	Indirect Clearfil DC resin core-build up	Increase
							Human maxillary central incisors, root canal	One Step Plus (lightly filled resin-based adhesive) + DUO LINK		

Mao et al., (104)	After etching with 32% H3PO4 semi-gel for 15s	Solution	10	1	Root canals irrigated with 0.9% saline	Push-out	obturated with gutta perch and AH 26 sealer, then a post space was prepared and filled with a post	(heavily filled dual-cure resin composite cements) One Step Plus (lightly filled resin-based adhesive) LuxaCore (heavily filled dual-cure resin composite cements)	Quartz fiber-reinforced double tapered posts	Increase
Varela et al., (105)	After etching with 37% ortho-H3PO4 for 60s	Solution	-10 (during root canal shaping)	-	Root canals received no irrigation	Tensile	Human single rooted teeth, root canal obturated with gutta percha and TopSeal sealer, then a post space was prepared and filled with a post	Panavia 21EX cement Dual Cement	Posts	No change
			-10 (after preparation of post space)	1				Panavia 21 Ex cement with ED Primer dentin adhesive Dual Cement with ED Primer dentin adhesive		Increase
Furuse et al., (106)	After etching	Solution	5.25v/v	10	Root canals irrigated with saline solution	Push-out	Bovine incisors, obturated with gutta percha and calcium hydroxide sealer (Sealer 26), root canal openings were sealed with glass ionomer, then a post space was prepared and filled with a post.	Schotbond Multipurpose (3-steps etch & rinse) + RelyX ARC (dual-cure resin cement)	Fiber reinforced posts	No change
	Before bonding							Xeno III (1-step self-etch) + RelyX ARC (dual-cure resin cement)		Decrease
da Cunba et al., (107)	Before bonding	Solution	5.25v/v	10	Root canal irrigated with 0.9% saline	Push-out	Bovin incisors, root canal obturated with gutta percha and CaOH sealer, root canal opening filled with glass ionoomer cement, then a post space was prepared and filled with post	Rely X U100 (self-adhesive cement)	Excato #3 (fiber posts)	Decrease
	After etching							Rely X ARC (dual-cure cement) with Single Bond 2 (2-step etch & rinse)		
	Before bonding							Rely X ARC (dual-cure cement) with Clearfil SE Bond (2-step self-etch)		

- NaOCl applied after etching (1st step of bonding) to coronal dentin
- NaOCl applied before boding to coronal dentin
- NaOCl applied before boding to pulp chamber dentin
- NaOCl applied before boding to radicular dentin (simulated root canals)
- NaOCl applied before boding to root canal dentin bonded to filling materials
- NaOCl applied before boding to root canal dentin bonded to posts
- NaOCl applied after etching to root canal dentin bonded to posts
- NaOCl applied before and after etching to root canal dentin bonded to posts

3.1. Bonding to Coronal Dentin

Looking at coronal dentin in particular, sodium hypochlorite has been used to pre-treat the coronal dentin surface upon which the adhesive is applied [Fig. 5 (a)] or after the application of acid etching, the first step in dentin bonding - [Fig. 5 (b)]. As observed in Fig. 5 (a), when applied before bonding to dentin, NaOCl was used as a solution at 0.5-6% concentration for 0.08 – 60 min. The time of NaOCl applications follows this order: 0.25 min > 0.5min = 10min > 1min = 60min = 0.08 min > 0.3 min = 20 min = 40 min = unknown. Human teeth (94%) represented the most common source of coronal dentin in these studies and microtensile or shear tests (44%) were also commonly employed to measure the bond strength to NaOCl-treated dentin. 50% of cases reported a reduction in bond strength; 31% reported no change but only 19% reported an increase in bond strength after application of NaOCl.



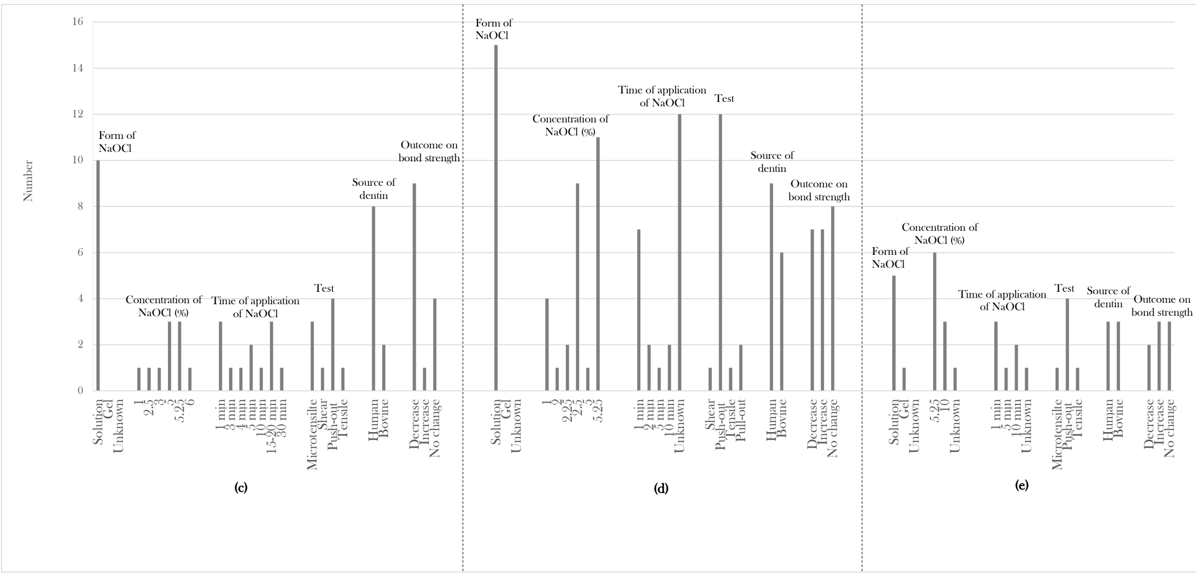


Fig. 5: Summary of studies dealt with the application of NaOCl before bonding (a) or after acid etching (b) of coronal dentin. Summary of studies dealt with the application of NaOCl before bonding to root canal dentin bonded to filling materials (c) or posts (d). Summary of studies dealt with the application of NaOCl after acid etching of root canal dentin bonded to posts (e).

When applied to etched dentin, NaOCl as a solution was used in 50% of cases at a concentration ranging from 0.5 – 10%. for 0.25-10 min (1 min was commonly used in 57% of cases). Still the microtensile or shear bond strength (47%) represents the most commonly used test. Human (79%) is also the common source of dentin for these studies. 40% of cases reported a reduction in bond strength; 40% reported no change but only 20% reported an increase in bond strength after NaOCl application.

Looking at the outcome of studies reported in Fig. 5 (a) and (b), the increase in bond strength after application of NaOCl to coronal dentin was only 20% in both cases (ie before bonding or after etching). The obvious outcome in both cases is the reduction in bond strength after application of NaOCl.

3.2. Bonding to Pulp Chamber Dentin

When sodium hypochlorite was applied before bonding to pulp chamber's dentin, only four studies were conducted using NaOCl solutions with concentration varies from 3-5.25%. for 1-30 min. Microtensile test was used in three studies, while the tensile was used in one study. A decrease in bond strength was reported in all studies (79-82).

3.3. Bonding to Radicular Dentin

When sodium hypochlorite was applied before bonding to radicular dentin (ie, when simulated root canals were used for testing), only one study has been carried out (83). In this study, NaOCl solution (1.3%) was used for 1 min. Micropush-out test was used to test the bond strength of human dentin to RealSeal SE. There was an increase in bond strength.

3.4. Bonding to Root Canal Dentin

Generally, when NaOCl was used for root canal irrigation, it was always used as a solution except in just one case where gel was used (103). In most cases, it was used before the application of bonding agents; the treated root canal dentin was filled with filling materials [Fig. 5 (c)] or posts [Fig. 5 (d)]. In some cases, where posts were used, NaOCl application was also carried out after acid etching of dentin [Fig. 5 (e)]. Human dentin was used in 65% of cases; the rest used bovine dentin. Push-out was the most common test used for measuring the bond strength of treated dentin.

When dentin bonded to filling materials, the concentration of NaOCl varied from 1-6% and the time of application ranged from 1-30 min. The outcome of NaOCl application was a reduction in bond strength in 64% of cases, no change in 29% and an increase in only 7%.

When dentin bonded to posts and NaOCl applied before bonding, the concentration of NaOCl varied from 1-5.25% and the time of application ranged from 1-10 min. The outcome of NaOCl application was no change in 36% of cases, a reduction in bond strength in 32% of cases and an increase in only 32%.

When dentin bonded to posts and NaOCl applied after etching, the concentration of NaOCl was mostly 5.25% and 10% and the time of application ranged from 1-10 min. The outcome of NaOCl application was no change in 37.5% of cases, an increase in 37.5% of cases while a redcution in 25% of cases.

3.5. Risk of Bias Assessment

The results of risk of bias assesement is give in Table 3. Only 11 articles showed high risk of bias (ie 15.9%); 47 articles have medium risk of bias (68.1%). The remaining 11 articles have low risk of bias (15.9%); most of studies were carried out on root canal dentin irrigated with sodium hypochlorite before bonding to posts. As a standardization of technique, one operator performed the procedures in only 8/69 studies (11.6%). Only 23/69 studies (33.3%) carried the randomization of samples. No blinding was performed in the data analysis; only one study out of 69 (1.4%) performed blinding. 14 studies out of 69 (20.3%) did not follow the manufacturer instructions during preparation of materials used.

Summary of outcome of all included articles has been presented in Table 4 (a). Considering the outcome of articles with high risk of bias (low methodological quality), there is a strong evidence to support that 2.5-10% sodium hypochlorite has no effect on bond strength of coronal or root canal dentin with various materials. Similar outcome was obtained with articles having low risk of bias (high methodological quality). On the other hand, considering the outcome of articles with medium risk of bias (low methodological quality), there is a strong evidence to support that 2.5-10% sodium hypochlorite reduces the bond strength of coronal or root canal dentin with various materials - Table 4 (b & c).

Table 3: Risk of bias assessment for studies included in this review.

No.	Author	Presence of control	Description of sample size	Randomization of samples	Procedures carried by one operator	Blinding of operator	Materials used according to manufacturers' instruction	Risk of bias
1.	Francescantonio et al., (45)	Y	Y	N	N	N	Y	Medium
2.	Prati et al., (30)	Y	N	N	N	N	Y	High
3.	Uceda-Gomez et al., (46)	Y	Y	N	N	N	Y	Medium
4.	Osorio et al., (47)	Y	Y	Y	N	N	Y	Medium
5.	Yiu et al.,(48)	Y	Y	N	N	N	Y	Medium
6.	Saboia et al., (49)	Y	Y	Y	N	N	Y	Medium
7.	Baseggio et al., (50)	Y	Y	Y	N	N	N	Medium
8.	dos Santos et al., (51)	Y	Y	Y	N	N	N	Medium
9.	Perdigão et al., (52)	Y	Y	Y	N	N	Y	Medium
10.	Uceda-Gomez et al., (53)	Y	Y	Y	Y	N	Y	Low
11.	Manjunath & Vinutha (54)	Y	Y	Y	N	N	N	Medium
12.	Correr et al., (55)	Y	Y	Y	N	N	Y	Medium
13.	Montagner et al., (56)	Y	Y	Y	Y	N	Y	Low
14.	Lisboa et al., (57)	Y	Y	N	N	N	N	High
15.	Aguilera et al., (58)	Y	Y	Y	N	N	Y	Medium
16.	de-Souza et al., (59)	Y	Y	Y	N	N	Y	Medium
17.	Sauro et al., (60)	Y	Y	N	N	N	N	High
18.	Goncalves et al., (61)	Y	Y	Y	N	N	Y	Medium
19.	Arias et al., (62)	Y	Y	Y	N	N	N	Medium
20.	Taniguchi et al., (63)	Y	Y	N	N	N	Y	Medium
21.	Stevens et al., (64)	Y	Y	N	N	N	Y	High
22.	Cecchin et al., (65)	Y	Y	Y	N	N	Y	Medium
23.	Hassan et al., (66)	Y	Y	N	N	N	N	High
24.	Ebrahimi-Chaharom et al., (67)	Y	Y	Y	N	N	Y	Medium
25.	Gönülol et al., (68)	Y	Y	Y	N	N	Y	Medium
26.	Farina et al., (69)	Y	Y	Y	N	N	Y	Medium
27.	Nassar et al., (70)	Y	Y	Y	N	N	N	Medium
28.	Abo et al., (71)	Y	Y	Y	N	N	Y	Medium
29.	Saber & El-Askary (72)	Y	Y	N	N	N	Y	Medium
30.	Kunawarote et al., (73)	Y	Y	Y	N	N	Y	Medium
31.	Kambara et al., (74)	Y	Y	Y	N	N	N	Medium
32.	Ayad & Garcia-Godoy (75)	Y	Y	Y	Y	N	N	Medium
33.	Kasraei et al., (76)	Y	Y	Y	Y	N	Y	Low
34.	Sasafuchi et al., (77)	Y	Y	N	N	N	Y	Medium
35.	Prasansuttiporn et al., (78)	Y	Y	N	N	N	Y	Medium
36.	Vongphan et al., (79)	Y	Y	N	N	N	Y	Medium
37.	Bhat Gorwish et al., (80)	Y	Y	Y	N	N	Y	Medium
38.	Ozturk & Ozer (81)	Y	Y	N	N	N	Y	Medium
39.	Santos et al., (82)	Y	Y	N	N	N	Y	Medium
40.	Shretha et al., (83)	Y	Y	Y	N	N	Y	Medium
41.	Morris et al., (84)	Y	Y	Y	N	N	Y	Medium
42.	Manimaran et al., (85)	Y	Y	Y	N	N	Y	Medium

43.	Erdemire et al., (21)	Y	Y	Y	N	N	Y	Medium
44.	Gu et al., (43)	Y	Y	Y	N	Y	Y	Low
45.	Ari et al., (86)	Y	Y	Y	N	N	Y	Medium
46.	Stelzer et al., (87)	Y	Y	N	N	N	N	High
47.	Haragushiku et al., (88)	Y	Y	Y	N	N	Y	Medium
48.	Ishizuka et al., (89)	N	Y	N	N	N	Y	High
49.	Rocha et al., (42)	Y	Y	Y	N	N	Y	Medium
50.	Weston et al., (31)	Y	Y	Y	N	N	Y	Medium
51.	Bournziniat et al., (90)	Y	Y	Y	N	N	Y	Medium
52.	Lacerda et al., (91)	Y	Y	N	N	N	Y	Medium
53.	Khoroushi et al., (92)	Y	Y	Y	N	N	Y	Medium
54.	Arisu et al., (93)	Y	Y	Y	N	N	Y	Medium
55.	Alkhudhairy & Bin-Shuwaish (94)	Y	Y	Y	N	N	Y	Medium
56.	Faria-e-Silva et al., (95)	Y	Y	N	N	N	N	High
57.	Bueno et al., (96)	Y	Y	Y	Y	N	Y	Low
58.	Bitter et al., (97)	Y	Y	Y	Y	N	Y	Low
59.	Ertas et al., (98)	Y	Y	N	N	N	Y	Medium
60.	Pelegrine et al., (99)	Y	Y	Y	Y	N	Y	Low
61.	Haragushiku et al., (100)	Y	Y	N	N	N	Y	Medium
62.	Kaif and Raj (101)	Y	Y	N	N	N	N	High
63.	Saraiva et al., (44)	Y	Y	Y	Y	N	Y	Low
64.	Cecchin et al., (102)	Y	Y	Y	Y	N	Y	Low
65.	Inoue et al., (103)	Y	N	N	N	N	N	High
66.	Mao et al., (104)	Y	Y	Y	N	N	Y	Medium
67.	Varela et al., (105)	Y	Y	Y	Y	N	Y	Low
68.	Furuse et al., (106)	Y	Y	N	N	N	Y	High
69.	da Cunba et al., (107)	Y	Y	Y	Y	N	Y	Low

NaOCl applied after etching (1st step of bonding) to coronal dentin

NaOCl applied before boding to coronal dentin

NaOCl applied before boding to pulp chamber dentin

NaOCl applied before boding to radicular dentin (simulated root canals)

NaOCl applied before boding to root canal dentin bonded to filling materials

NaOCl applied before boding to root canal dentin bonded to posts

NaOCl applied after etching to root canal dentin bonded to posts

NaOCl applied before and after etching to root canal dentin bonded to posts

Additional article for antioxidants to reverse the action of NaOCl

Table 4: (a) Detailed summary of outocme from all included (whether low, medium or high risk of bias) studies to NaOCl application on dentin bond strength. CD: coronal dentin. RCD: root canal dentin. F: filling materials. P: posts.

Step of NaOCl Application	Outcome to NaOCl Application		
	Decrease (%)	Increase (%)	No Change (%)
Before bonding to CD	50	19	31
After etching to CD	40	20	40
Before bonding to RCD bonded to F	64	7	29
Before bonding to RCD bonded to P	32	32	36
After bonding to RCD bonded to P	25	37.5	37.5

(b) Summary of outcome to NaOCl application on coronal dentin bond strength.

Type of articles (No.)	Outcome to NaOCl Application		
	Decrease (%)	Increase (%)	No Change (%)
Low risk of bias articles (3)	-	-	100
Medium risk of bias articles (27)	54.5	18.2	27.3
High risk of bias articles (5)	27.3	27.3	45.5

(c) Summary of outcome to NaOCl application on root canal dentin bond strength.

Type of articles (No.)	Outcome to NaOCl Application		
	Decrease (%)	Increase (%)	No Change (%)
Low risk of bias articles (8)	27.3	18.2	54.5
Medium risk or bias articles (20)	63.6	22.7	13.6
High risk of bias articles (6)	33.3	22.2	44.4

4. Discussion

Main Findings: Within the limitation of this review, the evidence from articles with high (low quality) or low risk of bias (high quality) indicates that 2.5-10% sodium hypochlorite has no effect on bond strength of dentin (coronal or root canal) with various materials. The evidence from articles with medium risk of bias (low quality) indicates that 2.5-10% sodium hypochlorite reduced the bond strength of dentin (coronal or root canal) with various materials.

Strength and Limitations: To the best of authors knowledge, this is the first study to systematically review and assess a wide range of experimental-based articles considering the effect of sodium hypochlorite on bond strength of dentin to various restorative materials. This review was based on comprehesive search strategies using PubMed, Google Scholar, Cochrane Library and OpenThesis database. A manual search was also conducted for references of identified articles. Risk of bias assessment showed that 11 articles out of 69 have low risk of bias (15.9%); 8 articles used root canal dentin to study the effect of sodium hypochlorite (ie more relevant to endodontic use).

The limitations with review however include: (1) there was a significant heterogeneity in testing methodologies used to study the effect of sodium hypochlorite on bond strength to dentin. Regardless of heterogeneity in methodology, the outocme obtained from articles with low risk of bias are highly correlated for both coronal and root canal dentin. The same was also observed with the outcome obtained from articles with medium risk of bias. (2) Although *in vitro* studies attempt to simulate the clinical situations, the clinical trials are the best way to provide a relevant evidence on the effectiveness of any material. However, there is no clinical trials have been conducted on sodium hypochlorite and its effect on dentin bonding to various materials. Therefore, correlating the clinical data with *in vitro* studies was not feasible. (3) Because of heterogeneity of the studies, it was not feasible to conduct a meta-analysis.

Clinical Significance: This review suggest the need for the development of a standaridized method to get relevant data from the patients receiving sodium hypochlorite as an irrigant during endodontic treatment to reflect its action on adhesion of dentin to various materials.

Conflict of Interest

"The author(s) report no conflict of interest for this study."

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