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IMPACTO E NECESSIDADE DO USO DE SOLUÇÕES IRRIGADORAS E SOLVENTES EM ENDODONTIA: SÍNTESE DE CONHECIMENTO

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Dissertação apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade IMED, como requisito parcial à obtenção do título de Mestre em Odontologia.

Professor orientador: Prof. Dr. Ataís Bacchi

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Lara Dotto

Impacto e necessidade do uso de soluções irrigadoras e solventes em endodontia: síntese de conhecimento

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Notas Preliminares

O projeto de pesquisa relacionado à esta dissertação foi apresentado a banca de qualificação no dia 01 de abril de 2020 e aprovado pela Banca Examinadora composta pelos Professores Doutores Lilian Rigo e Rodrigo Alessandretti.

RESUMO

DOTTO, Lara., **Impacto e necessidade do uso de soluções irrigadoras e solventes em endodontia: síntese de conhecimento.** 2021, 151p. Dissertação Mestrado em Odontologia – Programa de Pós-Graduação em Odontologia. Faculdade Meridional, Passo Fundo, 2021.

O objetivo geral dessa dissertação foi verificar o impacto e necessidade das soluções irrigadoras e solventes no tratamento endodôntico através de diferentes métodos de síntese de conhecimento. Para isso, este trabalho foi dividido em 3 artigos com os objetivos descritos a seguir: (I) mapear, por meio de uma revisão de escopo, se os irrigantes do canal radicular influenciam as propriedades mecânicas dos dentes tratados endodonticamente (DTE) e quais propriedades podem ser afetadas; (II) mapear as evidências sobre o uso de solventes para dissolução e remoção de guta-percha durante retratamentos endodônticos, através de um revisão de escopo; (III) avaliar o efeito dos irrigantes de canal radicular na resistência de união entre os cimentos endodônticos e a dentina do canal radicular, por meio de uma revisão sistemática. Os principais achados são: (I) A maioria dos estudos comprovou um efeito negativo de todas as soluções nas propriedades mecânicas de DTE. Além disso, aumentos na concentração da solução e no tempo de exposição intensificaram os efeitos deletérios; (II) A maioria dos estudos sugere que o uso de solventes pode prejudicar a limpeza do canal radicular, independentemente do tipo de instrumentação utilizada, e facilitar a presença de resíduos de guta-percha na superfície radicular, devendo seu uso ser considerado apenas se o comprimento de trabalho anterior não for possível de acessar, e (III) O uso de substâncias irrigantes capazes de desmineralizar a superfície da dentina do canal radicular e/ou remover a camada de lama dentinária remanescente parece aumentar, ou, pelo menos, não comprometer a resistência de união do cimento à dentina radicular.

Palavras-chave: Revisão, Irrigantes do Canal Radicular, Retratamento, Solventes, Adesão, Guta-percha.

ABSTRACT

DOTTO, Lara., **Impact and necessity of the use of root canal irrigants and solvents in endodontic: knowledge synthesis.** 2021 p.151 Dissertation (Master degree in Dentistry). Graduate Program in Dentistry. Meridional Faculty, Passo Fundo, 2021.

The objective of this dissertation was to verify the impact and necessity of irrigating and solvent solutions in endodontic treatment through different methods of knowledge synthesis. For this, this work was divided into 3 articles with the objectives described below: (I) to map, through a scoping review, if the root canal irrigants influence the mechanical properties of endodontically treated teeth (ETT) and which properties can be affected; (II) to map the evidence about solvents' use for gutta-percha dissolution and removal during endodontic retreatments; and (III) to assess root canal irrigants' effect on the bond strength between endodontic sealers and root canal dentin, through a systematic review. The main findings are: (I) The majority of studies corroborated a negative effect of all solutions on the mechanical properties of ETT. Furthermore, increases in the concentration of the solution and in the time of exposure were found to intensify deleterious effects; (II) most studies suggested that solvents' use may complicate root canal cleanliness, regardless of the type of instrumentation used, and facilitate the presence of gutta-percha remnants in the root surface. Thus, the use of solvents should be avoided and its use should only be considered if the previous working length was not possible to access without it; and (III) The use of irrigant substances capable of demineralizing the surface of root canal dentin and/or removing the remnant smear layer seems to enhance, or, at least, does not compromise the push-out bond strength of the sealer to root dentin.

Key Words: Review, Root Canal Irrigants, Retreatment, Solvents, Adhesion Gitta-percha.

SUMÁRIO

1. INTRODUÇÃO

Dentre os desafios a serem enfrentados durante o tratamento endodôntico, destacam-se a limpeza, a modelagem e o desbridamento adequados do canal radicular para a eliminação da maior quantidade de bactérias, remoção de tecidos necróticos e qualquer reminiscência da camada de lama dentinária gerada pela preparação mecânica dos canais radiculares (1). Consequentemente, a ação da solução irrigante adequada durante a etapa química do tratamento endodôntico, pode culminar em uma melhor previsibilidade de sucesso e longevidade do tratamento. Isso é demonstrado a partir de estudos clínicos em que a recorrência da infecção é citada como o principal motivo de falha do tratamento (1, 2).

Soluções irrigadoras são também importantes, uma vez que além de auxiliarem na limpeza dos canais radiculares, podem influenciar e/ou afetar as propriedades mecânicas das estruturas dentais (3, 4). Muitos estudos tem identificado a relação entre defeitos mecânicos nessas estruturas, como a redução na microdureza na dentina radicular ou o aumento da incidência de fraturas verticais a partir do uso das soluções químicas (4, 5). Fatores como o aumento na concentração dos irrigantes, alta capacidade na remoção da lama dentinária e o tempo de exposição dessas soluções à dentina vem sendo discutidos como possíveis causas dessas falhas (4,6-10). Contudo, essa questão ainda é controversa e não está claro na literatura quais propriedades mecânicas poderiam ser afetadas por soluções irrigantes.

Nesse sentido e uma vez que as soluções irrigadoras são imprescindíveis durante o tratamento ou retratamento endodôntico, há estudos que mencionam alterações em dentina promovida pelo uso dessas substâncias modificando a superfície da dentina radicular e/ou promovendo alterações estruturais (11,12). Com base nisso, é lógico supor que qualquer alteração em dentina promovida pelo uso de diferentes soluções irrigantes também pode influenciar sua interação com o cimento utilizado durante a obturação do canal radicular (13). Tal situação, poderia interferir na adesão (força de união) entre tais substratos e também comprometer o selamento apical obtido, o que pode ser um fator predisponente para diminuir a longevidade do tratamento (13). Para isso, testes de resistência de união por *push-out* podem determinar a extensão da resistência ao deslocamento de um material de obturação aplicado à dentina tratada do canal radicular (14-19).

Ainda, é possível que o tratamento endodôntico não tenha sucesso na primeira tentativa, sendo que de maneira geral, essa falha irá ocorrer em função de uma infecção ou reinfecção (20). Assim, quando os métodos químicos e mecânicos falham na resolução de um tratamento endodôntico, é necessário partir para a próxima etapa de intervenção onde, se possível, a primeira opção não cirúrgica a ser considerada é o retratamento.

Para isso, é necessário que o material obturador seja removido do interior dos canais radiculares para que possam ser remodelados e limpos novamente (21). Existem diferentes técnicas e materiais possíveis de serem utilizados nessa etapa: instrumentação manual ou mecânica (rotatória ou reciprocante) usada comumente no tratamento endodôntico primário; limas rotatórias produzidas especificamente para retratamentos, pontas ultrassônicas, instrumentos aquecidos e lasers Nd: YAG (22,23). No entanto, uma das barreiras do retratamento é acessar o material obturador para que sua remoção seja eficaz, especialmente quando está bem condensado causando resistência à penetração do instrumento ou, em regiões mais críticas como as de curvatura da raiz onde há risco de perfuração (20,21,24-27). Nesses casos, recomenda-se o uso de solventes (20,21, 24-27).

Os solventes são soluções utilizadas no retratamento endodôntico para amolecer o material obturador, geralmente a guta-percha (GP) (28,29). Sua utilização destaca-se, especialmente, quando o material obturador se encontra bem condensado e em raízes curvas, e se realizado uma força excessiva poderia gerar transporte e até perfurações dos canais radiculares (29,30). Existem muitos tipos de solventes, como clorofórmio, eucaliptol, óleo de laranja, endossolv e xilol, mas nenhum deles atende aos requisitos de um solvente ideal, pois essas substâncias devem ser não-tóxicas e não-cancerígenas para tecidos adjacentes, pacientes e dentistas; "promover amolecimento eficiente da GP; e ser viável por um tempo adequado e econômico (22).

Diversos estudos (31-34) a respeito da influência dos solventes nas propriedades químicas e físicas da dentina radicular como modificações dos níveis de cálcio e fósforo da sua composição (31), microdureza e rugosidade demonstraram não ser significativas (32). Mesmo achado foi obtido, quando as amostras foram expostas por um tempo prolongado à superfície radicular ou quando foi promovido o aquecimento dos solventes, os resultados demonstraram que essas soluções não seriam capazes de alterar a composição histoquímica da dentina (33) bem como suas propriedades físicas. Dessa forma, parece estar claro na literatura que não há relação dos solventes na modificação estrutural da dentina radicular. Contudo, ainda é incerto a eficácia ou efetividade dessas substâncias na remoção da guta-percha durante o retratamento endodôntico.

Muitos estudos (21-24,27,28,35-69) testaram a efetividade ou eficácia de limas e solventes na remoção da guta-percha residual ou a quantidade de material remanescente após a utilização de diferentes limas e solventes. Também há vários estudos avaliando inúmeras soluções em diferentes concentrações (3-10, 70-126) e seus efeitos nas propriedades mecânicas dos dentes tratados endodonticamente, assim como usando teste de *push-out* para analisar o efeito de diferentes soluções irrigantes na resistência de união *push-out* de diferentes cimentos endodônticos (14-19).

No entanto, ainda não está claro na literatura (I) quais propriedades mecânicas poderiam ser afetadas por soluções irrigantes (II) qual é o solvente mais efetivo ou se realmente seria necessário o uso de solventes na remoção do material obturador e (III) qual é a influência de diferentes soluções na resistência de união *push-out* em diferentes cimentos endodônticos. Dessa forma, as revisões de escopo oferecem uma ferramenta importante que pode fornecer um mapa da variedade de evidências disponíveis (127) enquanto revisões sistemáticas fornecem respostas mais objetivas quando se tem perguntas específicas a respeito de alguma temática (128).

2. OBJETIVOS

Assim, o objetivo deste estudo será identificar através de diferentes metodologias de síntese de conhecimento: (I) se os irrigantes do canal radicular influenciam as propriedades mecânicas dos dentes tratados endodonticamente e quais propriedades podem ser afetadas, através de uma revisão de escopo; (II) mapear as evidências sobre o uso de solventes para dissolução / remoção de guta-percha durante os retratamentos endodônticos a partir de um revisão de escopo; e (III) avaliar os efeitos de irrigantes de canal radicular na resistência de união *push-out* de cimentos endodônticos usados para obturar dentes tratados endodônticos, por meio de uma revisão sistemática.

3. ARTIGO 1

Title page

Effect of root canal irrigants on the mechanical properties of endodontically treated teeth: a scoping review

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Effect of Root Canal Irrigants on the Mechanical Properties of Endodontically Treated Teeth: A Scoping Review

Abstract

Introduction: The aim of this study was to identify through a scoping review whether root canal irrigants influence the mechanical properties of endodontically treated teeth, and which properties could be affected. The protocol of this study, available online (https://osf.io/yc9nb/), followed the Joana Briggs Institute guidelines. Reporting was based on PRISMA Extension for Scoping Reviews.

Methods: We selected studies written in English that evaluated the effect of at least one irrigant on the mechanical properties of endodontically treated teeth. The search and study screening were performed in PubMed and Scopus databases by 2 independent researchers. A descriptive analysis was performed to consider the study design, the characteristics of the irrigants, and the properties tested.

Results: The initial Search yielded 608 citations, of which 66 were included. On the basis of the collected data, the most commonly used solutions were 17% EDTA, 2.5% or 5% sodium hypochlorite, and 2% chlorhexidine, and the most common tested properties were hardness and strength. Alterations in the modulus of elasticity, stress and strain concentration during preparation, and roughness were also assessed.

Conclusions: The majority of studies corroborated a negative effect of all solutions on the mechanical properties of endodontically treated teeth. Furthermore, increases in the concentration of the solution and in the time of exposure were found to intensify deleterious effects. However, disinfection of the canal is also a crucial factor in endodontic success. Thus, clinicians should consider these factors to mitigate the effects without interfering with antibacterial properties, customizing the choice of the solution to the case in hand.

Clinical significance: The unavoidable deleterious impact of irrigants on mechanical properties of endodontically treated teeth can be mitigated by reducing the concentration and time of exposure to the solutions, although they still had to guarantee root canal cleanness (antibacterial effects).

Keywords: dentistry; systematic reviews, reporting, PRISMA

INTRODUCTION

Adequate cleaning, shaping, and debridement of the root canal to eliminate bacteria, remove necrotic tissues, and any remainder of smear layer generated by mechanical preparation are among the clinical challenges faced on a daily basis during endodontic treatment[1]. Accordingly, the adequate action of any irrigant solution used in all of these considered factors can culminate in a predictability of success and longevity of the treatment. This is shown by clinical studies where the recurrence of infection is cited as a major reason for failure[1,2].

There are a number of irrigant solutions available for endodontic treatment, and many others are being tested; however, none meet all the requirements needed to be considered an ideal irrigant[2,3]. For example, the main requirements include a broad antibacterial spectrum, the dissolution of remnants of both vital and necrotic pulp tissue, and avoidance of the formation of smear layer during mechanical preparation (or dissolution when it is formed)[2]. However, each solution has unique properties. For example, sodium hypochlorite (NaOCl) and chlorhexidine (CHX) exhibit a broad antibacterial spectrum[1], but NaOCl is a potential irritant of periapical tissues[1]. Conversely, CHX does not dissolve the pulp tissue but is less cytotoxic to the periapical tissues than NaOCl[4]. Accordingly, it is sometimes necessary to use
the irrigant solution combinations or alternate with chelators to address some disadvantages[1,5,6].

Irrigant solutions are also important because they could influence the mechanical properties of the dental structure[7,8] as well as assist in the cleaning of the root canal. Some studies have identified a relationship between mechanical defects in dental structures such as a reduction in the microhardness of root dentin or an increase in the incidence of vertical fracture with auxiliary chemical solutions[8,9]. Factors such as increased concentrations of irrigant solutions, high capacity to remove smear layer, and time of dentin exposure to solutions are being discussed as possible causes of these faults[8,10–14]. However, this issue is still controversial, and it is unclear in the literature which mechanical properties could be affected by irrigant solutions. Accordingly, scoping reviews offer an important tool that can provide a map of the range of available evidence[15]. Thus, the aim of this study was to identify through a scoping review whether root canal irrigants influence the mechanical properties of endodontically treated teeth and which properties could be affected.

MATERIALS AND METHODS

The protocol of this study was based on the framework proposed by Peters et al[15] according to the Joana Briggs Institute and is available at the following link: (https://osf.io/yc9nb/). In addition, the reporting of this scoping review was based on PRISMA Extension for Scoping Reviews[16].

Inclusion Criteria

We selected studies in dentistry that considered the effect of irrigant solutions on the mechanical properties of endodontically treated teeth. This included studies that evaluated the study design and the effect of at least one irrigant solution on dentin, regardless of origin (human or animal), but only studies written in English were included.

Search

The search was performed by using 2 databases (PubMed and Scopus) without date restrictions (last executed on May 30, 2019). The following search strategy was drafted on the basis of MeSH terms of PubMed and adapted with specific terms for Scopus.

- PubMed: "Tooth, Nonvital"[Mesh] OR "Tooth, Nonvital" OR “Nonvital Tooth” OR “Tooth, Devitalized” OR “Devitalized Tooth” OR “Tooth, Pulpless” OR “Pulpless Tooth” OR “Teeth, Pulpless” OR “Pulpless Teeth” OR “Teeth, Devitalized” OR “Devitalized Teeth” OR “Teeth, Nonvital” OR “Nonvital Teeth” OR “Teeth, Endodontically-Treated” OR “Endodontically-Treated Teeth” OR “Teeth, Endodontically Treated” OR “Tooth, Endodontically-Treated” OR “Endodontically-Treated Tooth” OR “Tooth, Endodontically Treated” OR “dentin*” AND "Root Canal Irrigants"[Mesh] OR “Root Canal Irrigants" OR “Canal Irrigants, Root” OR “Irrigants, Root Canal” OR “Root Canal Medicaments” OR “Canal Medicaments, Root” OR “Medicaments, Root Canal” OR “Chlorhexidine” OR “EDTA” OR “Sodium hypochlorite” OR “chemical irrigant” OR “NaOCl” OR “CHX” OR “ethylenediamine tetraacetic acid” AND “fracture” OR “strength” OR “resistance” OR “fatigue” OR “mechanical properties” OR “flexural strength” OR “microhardness” OR “modulus of elasticity” NOT “bond”

- Scopus: "Tooth, Nonvital" OR "Nonvital Tooth" OR "Tooth, Devitalized" OR "Devitalized Tooth" OR "Tooth, Pulpless" OR "Pulpless Tooth" OR "Teeth, Pulpless" OR "Pulpless Teeth" OR "Teeth, Devitalized" OR "Devitalized Teeth" OR "Teeth, Nonvital" OR "Nonvital Teeth" OR "Teeth, Endodontically-Treated" OR "Endodontically-Treated Teeth" OR "Teeth, Endodontically Treated" OR "Tooth, Endodontically-Treated" OR "Endodontically-Treated Tooth" OR "Tooth, Endodontically Treated" AND "Root Canal Irrigants" OR "Canal Irrigants, Root" OR "Irrigants, Root Canal" OR "Root Canal Medicaments" OR "Canal Medicaments, Root" OR "Medicaments, Root Canal" OR "Chlorhexidine" OR "EDTA" OR "Sodium hypochlorite" AND "fracture" OR "strength" OR "resistance" OR "fatigue" OR "mechanical properties" OR "flexural strength" OR "microhardness" OR "modulus of elasticity" AND NOT bond AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (SUBJAREA, "DENT")).

Screening

Initially, the search was undertaken by using EndNote program (EndNote X9; Thomson Reuters, New York, NY). Two researchers (L.D., G.K.R.P.) independently identified articles by first analyzing titles and abstracts for relevance and presence of eligibility criteria. Retrieved records were classified as “include,” “exclude,” or “uncertain”. The full-text articles of the included and uncertain records were selected for further eligibility screening by the same researchers (acting independently). Discrepancies in screening of titles/abstracts and full-text articles were resolved through discussion. In case of disagreement, the opinion of a third reviewer (R.S.O.) was obtained.

Charting the Results

We created an Excel (Microsoft Excel, Redmond, WA) spreadsheet to record data according to the consensus of the 3 reviewers after testing. Then, one of the reviewers (L.D.) extracted the data, and another (G.K.R.P.) checked it. Data included the following information: study design; irrigation solutions tested; concentration of the solution; exposure time; final rinse; teeth type (human or animal); teeth conditions (split, filled, restored, using a dowel and if so the type of dowel); mechanical properties evaluated and the method used; and the main findings. In terms of identification of reviews (either systematic or not), the following data were collected: inclusion criteria, number of included articles, number of included articles grouped by mechanical test, main findings, level of evidence generated reported by authors, and conclusions.

Data Analysis

The synthesis focused on describing the irrigant solutions used, their characteristics, the properties tested, and whether solutions affected the mechanical properties of the teeth. A descriptive analysis was performed that considered the study design, the characteristics of the different irrigants, and the properties tested. Analysis was then presented in tables and graphs. Finally, we created a word cloud considering the substances tested by using the website https://www.wordclouds.com/ to illustrate the prevalence of using each solution graphically.

RESULTS

Search Findings

Figure 1 presents the flow chart for the study selection. The search initially yielded 608 potentially relevant citations (Scopus: n=395; PubMed: n=213). After removal of duplicates (31) and irrelevant articles (493), 84 citations met the eligibility criteria based on title and abstract. These were obtained and full-text screened, resulting in 66 remaining studies being included in the analysis (qualitative synthesis).

Prior Published Review

Among the studies included in this scoping review, we found a systematic review[8] in which the authors explored the direct effect of NaOCl on the mechanical properties of root dentin. In general, considering only 9 studies published up to 2009, they concluded that there was strong evidence showing that NaOCl influences the mechanical properties of root dentin, and from a clinical perspective, it would be prudent to use a minimal concentration of NaOCl. However, discussion regarding which NaOCl concentration would be best advised was not possible (Supplemental Table S1).

Substances Assessed in Included

Studies Figure 2 summarizes the substances used in the included studies. The more a substance was used, the larger it appears in the word cloud. Accordingly, it can be noticed that the most commonly used solutions were 17% EDTA, 2.5% NaOCl, 5% NaOCl, saline as a control solution, and 2% CHX.

Effects of Root Canal Irrigants on the Mechanical Properties of Endodontically Treated Teeth (Results from Experimental Studies)

There were 2 additional experimental type of studies (one in vitro[17] and one in silico[1]) included in the present review, and their results are presented according to the properties evaluated. Figure 3 presents a correlation of the number of studies related to each of the properties assessed and the substance that was most widely reported being used. We can observe that hardness was the property most evaluated, and 17% EDTA was the substance most used (considering especially hardness and strength properties).

Hardness (Micro and Nano)

It was observed in in vitro studies that the irrigating solution usually demonstrates a deleterious effect on both micro and nano hardness (Supplemental Table S2). From a total of 36 studies, 21 showed a deleterious effect, regardless of the solution, as follows: a mixture of a bisbiguanide antimicrobial agent (CHX), a polyaminocarboxylic acid calciumchelating agent (EDTA), and a surfactant (cetrimide-cetyl-trimethyl-ammoniumbromide), known as QMiX; EDTA; ethyleneglycol-bis[b-aminoethylether]-N,N,N0,N0-tetraaceticacid (EGTA); EDTA plus Cetavlon (cationic agent with antiseptic properties) (EDTAC); ethylenediamine (EDA); EDTA-EDA mixture; cyclohexane-1,2-diaminetetraacetic acid (CDTA); hydroxyethylidene bisphosphonate (HEBP); citric acid (CA); peracetic acid (PA); maleic acid (MA); phytic acid (PhyA); phosphoric acid (PhA); NaOCl; sodium ascorbate (SA); 6% NaOCl with surface modifiers (Chlor-XTRA), chitosan; morinda citrifolia juice (MCJ); a mixture of doxycycline, citric acid, and a detergent (MTAD); 17% EDTA, cetrimide, and a specific surfactant (Smear Clear); cetrimide; tetracycline hydrochloride; hydrogen peroxide (HP); saline; deionized water and distilled water (DW) (Supplemental Table S2).

Another 14 studies showed a partially negative effect, with some solutions showing absence of effect, as follows: pomegranate; apple cider; grape vinegars; apple vinegar; EDTA; 17% EDTA solution with 0.84 g cetrimide (REDTA); EDTAC; acetic acid; MA; CA; glycolic acid (GA); NaOCl; Chlor-XTRA; sodium citrate; CHX; chlorhexidine with detergents (CHX-Plus); octenidine hydrochloride (OCT); chlorine dioxide (ClO2); chitosan; MCJ; MTAD; Smear Clear; HP; saline and DW (Supplemental Table S2). Only one study[18] demonstrated an absence of effect with the evaluated irrigants considered, as follows: EDTA; NaOCl; superoxidized water-Sterilox (Sx); and DW.

The most commonly used substance to evaluate this property was NaOCl (disregarding its concentration differences), with it not being used in only 5 studies[9,19–22]. Most commonly, it was found that the presence of the substance (no matter what concentration) had a deleterious effect on microhardness, but an increase in concentration had an increased effect. CHX
was considered in 9 studies, with 5 demonstrating absence of effect[23–27] and 4 demonstrating a negative effect[28–31]. All studies that tested acid solutions showed negative effects, irrespective of the acidic type (Supplemental Table S2); and only 2 studies considered vinegars, which, in general, demonstrated an absence of effect[7,23].

Regarding EDTA solution and similar compositional chelating agents (EDTAC, REDTA, CDTA, GDTA, and EDA), only 5 of the studies reviewed did not evaluate them[23,26,30,32,33]. It is well-known that there can be a deleterious effect with its use, regardless of concentration and time.

Finally, with regard to the use of commercially available cleansers (MTAD, QMix, and Smear Clear), solutions that present a component with antiseptic/antibacterial properties, an acidic component, and a surfactant, 7 studies considered such solutions and demonstrated a negative influence with at least one of these solutions (Supplemental Table S2). Only one study[34] demonstrated no influence using MTAD, and another study[35] demonstrated no influence using Smear Clear. Other solutions were also explored sporadically (for example, HEBP, Sx,SA, ClO2, OCT, HP, and MCJ); however, because very little information exists, no conclusive performance could be exemplified herein.

Strength Properties (Flexural Strength, Ultimate Tensile Strength, Vertical Root Fracture, or Fracture Resistance)

From 27 studies that considered strength properties, a large majority indicated harmful effects, where 5 demonstrated such effects for all considered solutions, as follows: EDTA; CA; NaOCl; alkalized or neutral NaOCl; saline; DW and deionized water[36–40]. Only 6 studies[12,30,41–43,17] demonstrated an absence of negative effect in any solution, as follows: EDTA; REDTA; lactic acid (LA); Pha; NaOCl; SA; CHX; QMix; MTAD; HP; saline; DW and deionized water, and 13 showed only partially harmful effects under specific solutions or protocols: EDTA; NaOCl and EDTA; CHX and EDTA; QMix and EDTA; grape seed extract (GSE) and EDTA; EDTA and cetrimide; CA, cetrimide, doxycycline hyclate, and polypropylene glycol; MA; HEBP; CHX; GSE; calcium hypochlorite (Ca(OCl)2); NaOCl; NaOCl with water; alkalized NaOCl; 2 mol/L NaOH with water; water; NaOCl and EDTA under 2 protocols; 1 mol/L NaOH; saline; DW and ultrapure water; and finally MTAD (Supplemental Table S3).

The most frequently used substance for this property was NaOCl (disregarding its concentration differences), which was not tested in 2 studies[12,44], although they used NaOCl solution during root canal preparation. Among these studies, no statistical differences were observed when NaOCl was tested with EDTA or MTAD[17], and they did not present deleterious effect on resistance to fracture in several studies (Supplemental Table S3). However, in other studies, the solution was found to alter the resistance to fracture, mainly when NaOCl concentration was increased and used under longer exposure periods (Supplemental Table S3). NaOCl has also been tested at higher pH[14,38,45] where the alkalized NaOCl solution deleteriously impacted the flexural strength of dentin.

Modulus of Elasticity

Those in vitro studies that evaluated the modulus of elasticity (Supplemental Table S4) indicated a completely heterogeneous performance. The most evaluated solution regarding this property was NaOCl (disregarding its concentration differences), where some studies corroborated a decrease in response to the use of NaOCl solutions and some discarded such effect

(Supplemental Table S4). Only 3 studies considered the use of EDTA under different protocols[13,46,47].

These studies used 17% EDTA; however, only one study[13] performed preparation and instrumentation of specimens that were exposed to the solution for 45 seconds, whereas the other studies used 2.5% NaOCl-associated EDTA using a 2-hour exposure protocol, which demonstrated a negative effect[46]. In one study[47], no effect under 3 minutes of exposure was demonstrated. Two studies showed that 17% EDTA significantly reduces the modulus of elasticity[13,46], and one study demonstrated that the solutions did not reduce the property evaluated, and there was no significant difference between the solutions in the group tested[47].

Stress and Strain Concentration

Five studies considered stress and strain concentration in response to the effect of different irrigant solutions used during mechanical preparation (Supplemental Table S5). Four studies used in vitro setups and strain gauge devices, where the tooth was maintained intact or only decoronated, with the root canal accessed and the solution positioned during mechanical preparation with the device glued to the cervical external portion of the root[48–51]. In general, it appeared that NaOCl increased tooth surface strain concentration. Meanwhile, a finite element analysis (in silico approach) was used in one study[52], and the findings also corroborated an increased stress and strain concentration in dentin with the use of the irrigant solutions.

Roughness

With regard to the studies that considered roughness (Supplemental Table S6), the irrigant solution demonstrated a potential roughening effect on dentin. The use of vinegars and acid solutions demonstrated a harmful effect in all cases, and the use of EDTA was almost universally harmful (absence of effect only in one study[53]). Data regarding NaOCl was very heterogeneous, where some studies suggested an absence of roughening effect, and some corroborated a deleterious effect (Supplemental Table S6).

DISCUSSION

This scoping review provides the first synthesis of information considering influence of various irrigant solutions on different mechanical properties of endodontically treated teeth. The importance of this scoping review lies in the extensive information on substances that can be used during the chemical-mechanical preparation of endodontic treatment. However, it is unclear whether these various substances could affect the mechanical properties of dental structures. Our results showed that concentrations and times of application significantly alter mechanical properties, and those increases in both variables lead to greater changes.

With regard to the studies included in our review, NaOCl was the most frequently used substance in tests (disregarding its concentration differences), because it is the longest established irrigant used by dentists[54,55]. This substance is recognized for its broad spectrum of antibacterial activity, large dissolution of vital and necrotic tissues, low cost, and easy availability[2]. However, such performance characteristics could result in a compromise of the dentin structures, as well as the already mentioned benefits. Accordingly, the systematic review that evaluated the direct effect of NaOCl (as an endodontic irrigant) on the mechanical properties of root dentin suggested strong evidence of NaOCl negatively altering the mechanical properties of root dentin and defended the use of the lowest possible concentrations. However, information concerning appropriate concentration levels was not available[8]. Those assumptions were corroborated when the data collected from all studies included in the present scoping review were considered.

The literature[10,39,56] demonstrated both concentration- and time-dependent effects of hypochlorite on organic dentin components, whereby with only a 1%concentration for up to 10 minutes, the alterations were at a minimum. However, time of exposure in which the properties were tested in most cases did not correspond to the clinical scenario, because this factor in particular could vary depending on the operator’s experience and different clinical situations. It would certainly be higher than 10 minutes, even though the main recommendation should be to reduce the exposure time to the minimum necessary for the case in hand[23,33,34]. On the basis of these observations, the data presented here greatly encourage the necessity for new studies to explore thematic efforts to define thresholds of time and concentration that guarantee root canal cleanliness without compromising the root dentin tissue mechanical properties.

With regard to the use of CHX, the mechanical properties of the dentin were not affected in one study only[57]. However, the majority of studies observed a deleterious effect (Supplemental Tables S1–S6). Despite that, the protocol of CHX application was very heterogeneous, sometimes as a single solution, sometimes associated with one or more other irrigants. Notwithstanding, the inherent substantivity of CHX must also be considered, because the substance could act over time. When laboratory tests were performed, there was a short period of action of irrigants; for instance, some studies left the solution in contact with the substrate for 1, 3, or 5 minutes (Supplemental Tables S1–S6). This exposure time does not represent what happens in a real clinical scenario. Thus, the clinical situation may lead to a greater effect on the mechanical properties of the teeth than those shown by these studies (Supplemental Tables S1–S6). Consequently, more studies are necessary to completely understand the effects of such solution.

Topographical/morphologic alterations are related to the presence of smear layer and opening of dentinal tubules[22,24,58–60]. Accordingly, chelating agents are decalcifying substances used to remove the smear layer[2]. This action is both necessary and important because it opens and exposes the dentinal tubules for penetration of irrigants and intracanal medicaments into the structure, and it improves the adhesion of the luting agent[61–63]. In general, regardless of whether specimens are instrumented, chelating agents have been demonstrated to be more likely to cause damage to the micro and nano hardness properties of the dental structure.

Regarding strength properties, specimens had a greater tendency to fracture when in contact with solutions in higher concentrations or for a longer exposure time because of greater removal of organic or inorganic matter from deeper layers, leading to a decrease in these properties. Until now, a chemical solution that shows perfect removal of smear layer and opening of dentinal tubules has not been available. Despite a discrete tendency in the literature to support the use of EDTA as the most adequate alternative, it has to be emphasized that the studies present completely heterogeneous data in this regard (Supplemental Table S3). However, its use for a short period seems to be less harmful to mechanical properties, especially strength. Therefore, when using EDTA at higher concentrations (15% or 17%), it should be used for short periods (up to 2 minutes) to try and minimize its impact[11,41,44,57]. Thus, if used after mechanical/chemical preparation as a final step to serve as a demineralizing agent, the benefits of this agent will be achieved without drastically influencing the mechanical properties of the teeth.

Beyond the effect of solutions on mechanical properties, the disinfection of the canal is a crucial factor for endodontic success[1,2]. Therefore, the extent to which it is possible to reduce the concentration and the time of exposure of the solution without affecting the antibacterial properties of substances should be taken into account, because the mechanical properties become irrelevant if no success is achieved in the endodontic treatment. This scoping review showed that the lowest NaOCl concentrations capable of altering the mechanical properties were 1% for microhardness, 0.5% for flexural strength, and 0.6% for elastic modulus.

However, previous studies have shown that 0.5% NaOCl for bacterial removal is effective only for the dentin surface layer, suggesting that to achieve greater effectiveness in removing bacteria, it is necessary to use NaOCl with other agents[4] or under higher concentration, especially in cases of pulp necrosis, where cleaning of the deepest layers of dentin is required. This aspect is different from a vital pulp treatment, where the number of pathogens is lower than in a necrotic tooth. Thus, the concentration of the solution that would be used in a necrotic tooth is traditionally higher than the concentration that would be used in vital pulp[4]; more studies should address these different scenarios of pulp vitality/presence of pathogens. Accordingly, 10 studies corroborate minimum effect of NaOCl on strength properties with concentrations of up to 2% (Supplemental Table S3). However, a decrease in time of exposure to a minimum should still be considered on the basis of the findings presented herein.

It is evident that the present scoping review presents some limitations. First, the included studies tested different mechanical properties and various substances. Moreover, different methods were also used; specimens were analyzed under different conditions (sectioned, whole, and filled) and different storage conditions until the moment of the test was considered. All these factors lead to heterogeneity, which limits exact comparison between studies. Second, because this was a scoping review, we did not conduct a risk of bias assessment of the included studies; this could be undertaken in the future during a full systematic review. Finally, our scoping review identified that future studies should focus on establishing which solution concentration and application time are required for viable and safe exposure, without compromising the mechanical properties of the teeth, but to guarantee adequate root canal cleanness.

CONCLUSION

Regardless of the considered irrigation solution, most existing cases corroborate the occurrence of some damage to the mechanical properties of endodontically treated teeth. Thus, the available literature seems to determine that factors such as concentration and exposure time should be considered to mitigate deleterious effects, without interfering with antibacterial properties. In addition, it is necessary to know the characteristics of each solution to decide which is the more suitable, ensuring the success of endodontic treatment and causing minimal mechanical damage to the case in hand.

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Table Captions

Table 1 – Description of data obtained on included review studies.

Table 2 – Description of data obtained on included in vitro studies that evaluated micro and nanohardness properties.

Table 3 – Description of data obtained on included in vitro studies that evaluated strength properties (flexural strength, ultimate tensile strength – UTS, vertical root fracture, or fracture resistance – compression at 45°).

Table 4 – Description of data obtained on included in vitro studies that evaluated modulus of elasticity properties.

Table 5 – Description of data obtained on included studies (in vitro and in silico) that evaluated stress and strain concentration during mechanical preparation using the irrigant solutions.

Table 6 – Description of data obtained on included in vitro studies that evaluated roughness properties.

Figure Captions

Figure 1 – Flowchart of study selection.

Figure 2 – Word cloud representing the substances used. The more a substance was used, the bigger it appears in the word cloud.

Figure 3 – Relation between properties tested and the most substance used. CHX, chlorhexidine.

Table Captions

Table 1. Description of data obtained on included review studies.

Author	Type of study	Data base considered	Eligibility criteria	Characteristic of included studies	Main result	Reported quality of evidence	Conclusions (Main findings)
Pascon *et al*., 2009	Systematic review	Cochrane Library, Embase, PubMed and Web of Science (from 1984 to 2008)	Papers that studied the direct effect of NaOCl (as endodontic irrigant) on the mechanical properties of root dentine	9 (5 considering flexural strength; 4 microhardness; 1 tensile strength; and 2 modulus of elasticity)	Decrease on flexural and tensile strength, modulus of elasticity, and microhardness when NaOCl was used as an irrigant solution during canal preparation	Strong	Authors suggest that NaOCl adversely alters the mechanical properties of root dentine, when used as an endodontic irrigant. From a clinical point of view, they emphasize that it would be prudent to select a suitable NaOCl concentration, which had minimal effects on the mechanical properties of the tooth while achieving the desired debridement effect. However, this optimum NaOCl concentration has not yet been determined.

Legends: Sodium hypochlorite (NaOCl)

Table 2. Description of data obtained on included *in vitro* studies that evaluated micro and nanohardness properties.

Author	Irrigate solutions tested	Moment of usage of the solution	Concentration	Time	Volume	Wash-out	Type of tooth	Tooth condition during analysis	Storage conditions	Standard moisture condition	Conclusions (Main findings)
Akbulut *et al.,* 2019	DW; pomegranate; apple cider; grape vinegars; NaOCl; CHX; OCT	Not prepared, the root dentin was exposed to the irrigant solution	2.5% NaOCl, 2% CHX.	15 or 30 min	NR	NR	Human, mandibular incisor teeth	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	DW up to 3 months	NR	There was no statistically significant difference on microhardness between irrigant groups. The increase on time of exposure (15 to 30min) with all solutions lead to a harmful effect.
Akbulut and Terlemez, 2019	NaOCl; CHX; EDTA	During preparation: DW between files; After (final) it was used the evaluated solutions	2.5% NaOCl; 17% EDTA; and 2% CHX.	1 min	6mL	DW	Human, single rooted mandibular premolars	Sectioned: longitudinally sliced	DW up to 3 months	Yes	Among the irrigant groups, NaOCl and CHX did not alter microhardness. EDTA statistically decreased such outcome.
Akcay *et al.,* 2013	7.5% EDTA + 2.5% NaOCl; 7.5% EGTA + 2.5% NaOCl; 7.5% CDTA + 2.5% NaOCl; 7.5% EDTA + 2.5% EDA; EDTA-EDA mixture + EDTA-EDA mixture.	Not prepared, the root dentin was only exposed to the irrigant solution	7.5% EDTA, 2.5% NaOCl, 7.5%CDTA, 7.5%EGTA.	1 min	50mL	DW	Human, canine teeth	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	0.01% thymol solution	NR	All tested solutions reduced the microhardness. EDTA-EDA single mixture has led to least change on the microhardness.
Akcay and Sen, 2012	5% EDTA; 5% EDTA + 0.25% cetrimide; 5% EDTA + 0.50% cetrimide; 0.25%	Not prepared, the root dentin was only	5% EDTA; 0.25% cetrimide; 0.50% cetrimide.	1 min	50mL	DW	Human, canine teeth	Sectioned: longitudinally sliced, polished	0.1% thymol solution	Yes	All tested solutions reduced the microhardness. The use of surfactants higher than 0.25% in

	cetrimide; 0.50% cetrimide.	exposed to the irrigant solution						and embedded in acrylic resin			concentration is questionable for clinical conditions.
Aranda-Garcia *et al*., 2013	DW; EDTA; MTAD; Smear-Clear; QMiX.	During preparation: DW; After (final) it was used the evaluated solutions + 2.5% or 1.3% NaOCl	17% EDTA.	EDTA (3min); MTAD (5min); Smear-Clear(1min); QMiX (2min)	Unclear	2.5% NaOCl for all, except to BioPure MTAD where 1.3% NaOCl was used	Human, upper canines	Sectioned: coronal removal for preparation; longitudinally sliced, polished, embedded in acrylic resin, tested, submitted to the solution and tested again	0.1% thymol solution	NR	All protocols reduced equally the microhardness.
Ari *et al.*, 2004	DW; NaOCl; HP; EDTA; CHX	Not prepared, the root dentin was only exposed to the irrigant solution	5.25% NaOCl; 2.5% NaOCl; 3% HP; 17% EDTA; 0.2% CHX	15min	5mL	DW	Human, mandibular anterior teeth	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	Buffered saline	NR	Only CHX did not significantly decreased microhardness.
Aslantas *et al.,* 2014	EDTA; REDTA; CHX; CHX-Plus; NaOCl; Chlor-XTRA	Not prepared, the root dentin was only exposed to the irrigant solution	17% EDTA; 2% CHX; 6% NaOCl.	5min	5mL	Not executed	Human, third molars	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	0.5% chloramine-T	NR	EDTA and NaOCl significantly decreased microhardness, regardless of the presence of surfactant. EDTA was most harmful than NaOCl and CHX.
Baldasso *et al.,* 2017	DW; QMix + NaOCl; EDTA + NaOCl; CA + NaOCl; PA + NaOCl; NaOCl	During preparation: DW between files; After (final) it was used the evaluated solutions	17% EDTA; 10% CA; 1% PA; 2.5% NaOCl.	Qmix for 2 min + NaOCl for 5 min; EDTA for 5min + NaOCl for 5min; CA for 5min + NaOCl for 5min; PA for 5min + NaOCl for 5min; NaOCl for 5min	2 ml/ min	DW	Human, mandibular incisors	Sectioned: Coronal and apice removal, submitted to the preparation and solutions and tested.	DW	NR	All solutions decreased microhardness. QMiX and 17% EDTA reduced at a greater depth when compared to 10% CA and 1% PA.
Ballal *et al.,* 2015	Saline; ClO_2; EDTA; MA; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	13.8% ClO_2; 17% EDTA; 7% MA; 2.5% NaOCl	1min	5mL	DW	Human, maxillary central incisors	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	0.2% sodium azide	NR	13.8% ClO_2 and 2.5% NaOCl reduced microhardness more than 17% EDTA. There was no signifi cant difference between other experimental groups.
Ballal *et al.,* 2010a	Saline; EDTA; MA	Not prepared, the root dentin was only exposed to the irrigant solution	17% EDTA; 7% MA	1min	1mL	NR	Human, maxillary central incisors	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	0.2% sodium azide	NR	Maleic acid reduced the microhardness of root dentin similar to EDTA.
Bello *et al.,* 2019	DW; EDTA; CA; GA	Not prepared, the root dentin was only exposed to the irrigant solution	17% EDTA; 10% CA; 5% GA; 10% GA; 17% GA	1min	50mL	DW	Human, mandibular teeth	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	Saline	NR	CA 10% and GA 17% significantly reduced microhardness.

Cruz-Filho *et al.*, 2002	EGTA	Not prepared, the root dentin was only exposed to the irrigant solution	1% EGTA; 3% EGTA; 5% EGTA.	5min	50uL	NR	Human, maxillary incisors	Sectioned: horizontally and longitudinally sliced, embedded in acrylic resin, exposed to the solutions and tested	NR	NR	All EGTA solutions significantly reduced dentin microhardness in a concentration-dependent relation (1%<3%<5%).
Cruz-Filho *et al.*, 2011	EDTA; CA; MA; AA; apple vinegar; sodium citrate	During preparation: 1% NaOCl between files; After (final) it was used the evaluated solutions	15%EDTA; 10% CA; 5% MA; 5% AA; 10% sodium citrate	5min	50uL	1% NaOCl	Human, single rooted maxillary central incisors	Sectioned: coronal removal for preparation; longitudinally sliced, submitted to the solutions and tested	0.1% thymol solution	NR	Except for sodium citrate, all tested chelating solutions reduced microhardness.
Das *et al.*, 2014	DW; NaOCl +EDTA + CHX; MCJ + EDTA; NaOCl + QMix	Not prepared, the root dentin was only exposed to the irrigant solution	5% NaOCl+ 17% EDTA + 2% CHX; 6% MCJ+17% EDTA; 5% NaOCl + QMix	5min (each)	5mL (each)	DW	Human, maxillary central incisors	Sectioned: longitudinally sliced, polished and embedded in acrylic resin	0.1% Thymol	NR	All irrigating solutions, except for DW, decreased dentin microhardness.
De-Deus *et al.*, 2006	EDTA; EDTAC; CA	Not prepared, the root dentin was only exposed to the irrigant solution	EDTA 17%; EDTAC 17%; CA10%.	1;3;5min	50uL	DW	Human, canine teeth	Sectioned: horizontally sliced into 4 mm thick, polished, exposed to the solutions and tested	10% neutral formalin	NR	Microhardness decreased with increasing time of application of chelating solutions. There were no significant differences between initial microhardness for the three groups as well as after 1 min of application of the substances.
Dineshkumar *et al.*, 2012	DW; NaOCl + EDTA; NaOCl + MTAD; NaOCl + HEBP	Not prepared, the root dentin was only exposed to the irrigant solution	1.3%NaOCl+17% EDTA; 1.3% NaOCl+ MTAD; 1.3% NaOCl+18% HEBP.	20min NaOCl + 1min EDTA; 20min NaOCl + 5min MTAD; 20min NaOCl + 5min HEBP	NR	NR	Human, single-rooted mandibular premolars	Sectioned: longitudinally sliced, polished, embebeed in acrylic resin, exposed to the solutions and tested	NR	NR	All solutions decreased microhardness.
Eldeniz *et al.*, 2005	DW; CA + NaOCl; EDTA + NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	19% CA + 5.25% NaOCl; 17% EDTA + 5.25% NaOCl	150s (each solution)	NR	Not reported	Human, mandibular anterior teeth	Sectioned: longitudinally sliced, polished, embebeed in acrylic resin, exposed to the solutions and tested	Phosphate buffered saline	NR	Significant differences were observed in microhardness among the test groups, citric acid group being the least harmful.

Garcia *et al.*, 2013	NaOCl; Chlor-XTRA	During preparation: DW between files; After (final) it was used the evaluated solutions	2.5% NaOCl solution and gel	15min	NR	DW	Human, upper canines	Sectioned: coronal removal for preparation; longitudinally sliced, submitted to the solutions and tested considering two regions apical and cervical	0.1% thymol	NR	All substances reduced equally dentin microhardness.
Ghisi *et al.*, 2014	DW; 2% NaOCl; 5% NaOCl; Sx; 17% EDTA	During preparation	2% NaOCl; 5% NaOCl; Sx + 17% EDTA; 2% NaOCl + 17% EDTA; 5% NaOCl + 17% EDTA; Sx+17% EDTA; 17% EDTA	30min; when using EDTA it was added 5 min extra	10mL (2mL for each instrument); when using EDTA it was added 2mL extra	NaOCl or Sx	Bovine incisors	Sectioned: coronal removal for preparation; longitudinally sliced and tested	DW	NR	None solution presented statistical difference from DW.
Kalluru *et al.*, 2014	EDTA; EDTAC; NaOCl; MTAD	Not prepared, the root dentin was only exposed to the irrigant solution	17% EDTA; 17% EDTAC; 3% NaOCl.	0; 2 and 5 min	NR	Unclear	Human, single rooted mandibul ar premolar	Sectioned: coronal removal, exposed to the solutions and tested	10% neutral buffere d formalin for two weeks; than DW until use	NR	EDTA, EDTAC drastically reduced the microhardness with the increase on time of exposure (2 min already statistically signifcant reduction). NaOCl and MTAD did not altered the microhardness significantly.
Kara Tuncer *et al.*, 2015	EDTA + NaOCl; EDTA + CHX; QMix; MA.	During preparation: 2.5% NAOCl; After (final) it was used the evaluated solutions	17% EDTA + 2.5% NaOCl; 17% EDTA + 2% CHX.	1min (each)	5mL (each)	Deionized water and DW	Human, maxillary canine teeth	Sectioned: coronal removal for preparation; longitudinally sliced, embedded in acrylic resin, polished and tested at apical, middle and cervical regions	0.1% thymol solution	NR	Maleic acid decreased the microhardness significantly more than QMix, 17% EDTA + 2% CHX and 17% EDTA + 2.5% NaOCl. QMix and 17% EDTA + 2% CHX caused the same reduction in the microhardness of root canal dentine in all three regions.
Marcelino *et al.*, 2014	Deionized water; NaOCl; NaOCl + SA; SA; CHX; PhA; PhA + CHX; PhA + NaOCl.	During preparation: 2.5% NaOCl between files followed by 17% EDTA for 5 min and washed for 1	5.25% NaOCl; 5.25% NaOCl + 10% SA; 10%SA; 2%CHXgel; 37%PhA; 37%PhA+2%CHX ;	10 min for Deionized water; and 10% SA; 5 min for 5.25% NaOCl; and 2% CHX; 15seg for 37%PA	10 mL for Deionized water; 5.25% NaOCl; and 10% SA	Deionized water	Human, canines	Mixed: whole (only root canal access) during preparation and exposure to the solutions; but before testing	0.1% thymol solution	NR	The use of deionized water only lead to the highest microhardness. All other solutions impacted deleteriously and did not differ among each other.

		min with DW. After that it was used the evaluated solutions	37%PhA+5.25%NaOCl.					each root was shaped into bars			
Nikhil *et al.,* 2016	PhyA; EDTA; chitosan.	Not prepared, the root dentin was only exposed to the irrigant solution	1% PhyA; 17%EDTA; 0.2% chitosan	3min	50uL	DW	Human, canine teeth	Sectioned: coronal removal; longitudinally sliced, embedded in acrylic resin, polished and tested prior and after exposure to the solution	NR	NR	All tested chelators reduced microhardness. 17% EDTA reduced more significantly than 1% phytic acid and 0.2% chitosan (where the latter were similar).
Oliveira *et al.,* 2007	Saline; NaOCl; CHX.	Final (5 mL of saline solution).	1%NaOCl; 2%CHX.	15min	1mL	NR	Human, single rooted premolars	Sectioned: coronal removal for preparation; horizontally sliced in three thirds (cervical, midle, and apical), embedded in acrylic resin, polished, exposed to solutions and tested	Saline	NR	2% chlorhexidine and 1%NaOCl solutions significantly reduced the microhardness.
Patil and Uppin, 2011	DW; NaOCl; HP; EDTA; CHX.	Not prepared, the root dentin was only exposed to the irrigant solution	5%NaOCl; 2.5%NaOCl; 3% HP; 17%EDTA; 0.2%CHX.	15min	5mL	Distilled water	Human, intact permanent maxillary and mandibular incisor teeth	Sectioned: longitudinally sliced, polished, embedded in acrylic resin, exposed to the solutions and tested	Buffered saline	NR	CHX did not harm microhardness. NaOCl shown the most deleterious impact, regardless of concentration. HP and EDTA show intermediary effect.

Pimenta *et al.,* 2012	DW; EDTA; CA; chitosan.	Not prepared, the root dentin was only exposed to the irrigant solution	15% EDTA; 10% CA; 0.2% chitosan.	5min	50uL	1% NaOCl	Human, maxillary central incisors	Sectioned: coronal removal for preparation; horizontally sliced and divided in 4 quadrants, each one was embedded in acrylic resin, polished, exposed to solutions and tested	0.1% thymol	NR	All solutions tested reduced the microhardness in a way that was statistically similar to each other.
Saghiri *et al.,* 2009	NaOCl; EDTA; MTAD; CHX; Saline	During preparation, saline solution (0.9% NaCl). After that (final) the evaluated solution	2.6% NaOCl; 17% EDTA + 2.6%NaOCl; MTAD clinical Protocol (1.3% NaOCl +MTAD); 2%CHX	5min 2.6% NaOCl; 17% EDTA + 2.6%NaOCl for 1 or 5 min each; MTAD clinical Protocol (20 min 1.3% NaOCl + 5min MTAD); 2min 2% CHX	NR	DW	Human, maxillary and mandibular premolar teeth.	Sectioned: horizontally sliced with 4mm thickness	0.5% chloram in T up to 1 week	NR	At a depth of 100 µm, all solutions except 2% CHX and saline solutions decreased microhardness significantly. At a 500 µm depth, only NaOCl and MTAD considerably reduced.
Saha *et al.,* 2017	NaOCl; EDTA; chitosan; MCJ	Not prepared, the root dentin was only exposed to the irrigant solution	3% NaOCl; 17% EDTA; 0.2% chitosan; 6% MCJ	15min	NR	DW	Human, premolars	Sectioned: coronal removal; longitudinally sliced, embedded in acrylic resin, polished and tested prior and after exposure to the solution	0.1% thymol	NR	A 6% MCJ and 3% NaOCl showed negligible effect on the microhardness.
Saleh and Ettman, 1999	Saline; HP; NaOCl; EDTA.	During preparation: Saline between files; After (final) it was used the evaluated solutions.	3% HP + 5% NaOCl; 17%EDTA.	60seg	1mL (each)	Only the EDTA-irrigated canals were rinsed thoroughly with copious amounts of purified water.	Human, intact maxillary incisor teeth	Sectioned: coronal removal for preparation; horizontally sliced in three thirds (cervical, midle, and apical), embedded in acrylic resin, polished, exposed to	Phosphate buffered saline	NR	Both H_2O_2/NaOCl and EDTA irrigating solutions significantly reduced the microhardness.

								solutions and tested			
Sayin *et al.*, 2007	NaOCl; EDTA; EDTAC; EGTA; tetracycline hydrochloride	Not prepared, the root dentin was only exposed to the irrigant solution	2.5% NaOCl; 17% EDTA; 15% EDTAC; 17% EGTA; 1% tetracycline hydrochloride; 17% EDTA + NaOCl; 15% EDTAC + NaOCl; 17% EGTA + NaOCl; 1% tetracycline hydrochloride + NaOCl.	5min	10mL	DW	Human, maxillary incisor and mandibular premolar	Sectioned: coronal removal; longitudinally sliced, embedded in acrylic resin, polished and tested prior and after exposure to the solution	DW up to 2 months	NR	All treatment regimens except distilled water significantly decreased the microhardness of the root canal dentin.
Slutzky-Goldberg *et al.,* 2004	Saline; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	2.5% or 6% NaOCl.	5;10;20min (changed every minute)	NR	NR	Young, bovine, lower central incisors.	Sectioned: exposure of the root canal, preparation using the testing solutions between files; After that longitudinally sliced; embedded in acrylic resin and tested	Saline	NR	There was a difference in dentin microhardness between treated samples and controls in all groups tested, at the different depths considered (500, 1000 and 1500μm) depicting a time-dependent relation (5<10<20min).
Taneja *et al.,* 2014	DW; NaOCl; EDTA; PA; QMix	Not prepared, the root dentin was only exposed to the irrigant solution	5% NaOCl+DW; 5% NaOCl +17% EDTA; 5% NaOCl +2.25% PA; 5% NaOCl +QMix.	5min (each)	NR	NR	Human, single rooted premolars.	Sectioned: horizontally sliced and divided in 4 quadrants, each one was embedded in acrylic resin, polished, exposed to solutions and tested	Formalin for 1 week; then saline until use	NR	Irrigation with NaOCl + DW and NaOCl + QMix were less harmfull than others. NaOCl + PA was the most harmfull. NaOCl + EDTA presented intermediary performance.
Tartari *et al.,* 2013	Saline; NaOCl; EDTA; CA; HEBP	Not prepared, the root dentin was only exposed to the irrigant solution	5% NaOCl + 18% HEBP; 2.5% NaOCl; 2.5% NaOCl + 17% EDTA + 2.5% NaOCl; 2.5% NaOCl + 10% CA + 2.5% NaOCl; 2.5% NaOCl + 9%	Mixture 5% NaOCl and 18% HEBP (30 min); 2.5% NaOCl (30 min); 2.5% NaOCl (30 min) + 17% EDTA (3 min); 2.5% NaOCl (30 min)	40mL	DW	Human, single-rooted teeth	Sectioned: coronal and apical removal; longitudinally sliced and divided in thirds (cervical, middle and apical), after	0.1% thymol	NR	All tested irrigation regimens significantly reduced the microhardness.

			HEBP + 2.5% NaOCl	+ 10% CA (3 min); 2.5% NaOCl (30 min) + 9% HEBP (5 min); 2.5% NaOCl (30 min) + 17% EDTA (3 min) + 2.5% NaOCl (3 min); 2.5% NaOCl (30 min) + 10% CA (3 min) + 2.5% NaOCl (3 min); 2.5% NaOCl (30 min) + 9% HEBP (5 min) + 2.5% NaOCl (3 min).				embedded in acrylic resin, polished, tested, exposed to the solutions and tested again			
Ulusoy and Görgül, 2013	Saline; EDTA; NaOCl; MA; MTAD; Smear-Clear	During preparation: saline solution between files; After (final) it was used the evaluated solutions	17% EDTA + 2.5% NaOCl; 7% MA + 2.5% NaOCl; 1.3% NaOCl+ BioPure MTAD; Smear-Clear + 2.5% NaOCl; 5% NaOCl.	17% EDTA (5 min) + 2.5% NaOCl (5 min); 7% maleic acid(5 min) + 2.5% NaOCl (5 min); 1.3% NaOCl (20 min) + BioPure MTAD(5 min); Smear Clear (5 min) + 2.5% NaOCl (5 min); 5% NaOCl (5min);	1mL (each)	Group 1.3% NaOCl+ BioPure MTAD: finally flushed with 3 mL distilled water after irrigant application.	Human, single rooted teeth.	Sectioned: coronal removal for preparation; horizontally sliced and longitudinally divided in 4 quadrants, each one was embedded in acrylic resin, polished, exposed to solutions and tested	DW	NR	EDTA, maleic acid and MTAD showed a significant reduction in microhardness. Smear Clear, NaOCl and saline did not.
Wang *et al.*, 2017a	Saline; MA; NaOCl; EDTA	During preparation: 2.5% NaOCl between files; after that it was used the evaluated solutions	2.5% NaOCl; 7%MA +2.5% NaOCl; 17%EDTA +2.5% NaOCl	7%MA for 30s or 45s or 1 min or 3 min + 1 min (2.5% NaOCl); 45 seg (17%EDTA) +1 min (2.5% NaOCl); 1min 2.5% NaOCl only	5mL (each)	Distilled water	Human, single rooted premolars	Sectioned: coronal removal; longitudinally sliced, embedded in acrylic resin, polished and tested prior and after exposure to the solution	0.2% sodium azide until use	NR	All of the protocols reduced the micro and nanohardness after irrigation compared with the pre-treatment values. MA solutions were more aggressive, specially after 1min.
Zaparolli *et al.,* 2012	DW; NaOCl; EDTA.	Not prepared, the root dentin was only exposed to the irrigant solution	1% NaOCl; 17% EDTA; 1% NaOCl + 17% EDTA	10min	0.5mL (each)	DW	Human, mandibular molars	Roots shaped into blocks considering the coronal substrate	Saline	NR	All irrigating solutions, except for DW reduced microhardness

Legends: Sodium hypochlorite (NaOCl); chlorine dioxide (ClO_2); Ethylenediamine tetraacetic acid (EDTA); EDTA + 0.84 g cetyltrimethylammonium bromide (REDTA); ethyleneglycol-bis[b-aminoethylether]-N,N,N0,N0-tetraaceticacid (EGTA); trans1,2diaminocyclohexane NNN',N'tetraaceticacid (CDTA); Ethylenediamine (EDA); EDTA plus Cetavlon (EDTAC); hydroxyethylidene bisphosphonate (HEBP); Hydrogen peroxide (HP); Citric acid (CA); Maleic acid (MA); Peracetic acid (PA); Phosphoric acid (PhA); phytic acid (PhyA); glycolic acid (GA); acetic acid (AA); Chlorhexidine gluconate (CHX); Chlorhexidine gluconate with surface modifier by Vista Dental (CHX Plus); 6% NaOCl with surface modifiers by Vista Dental (Chlor-Xtra); octenidine-hydrochloride (OCT); root canal cleanser developed by SybronEndo (Smear Clear); Solution with antimicrobial activity used for the smear layer removal in final irrigation manufactured by Dentistry (QMix); Antibacterial root canal cleanser manufactured by Dentsply (MTAD); super-oxidized water - 400 ppm Sterilox (Sx); sodium ascorbate (SA); Morinda Citrifolia Juice (MCJ); Distilled Water (DW); Not Reported (NR).

Table 3. Description of data obtained on included *in vitro* studies that evaluated strength properties (flexural strength, ultimate tensile strength – UTS, vertical root fracture, or fracture resistance – compression at 45°).

Author	Irrigate solutions tested	Moment of usage of the solution	Concentration	Time	Volume	Wash-out	Type of tooth	Tooth condition during analysis	Storage condition	Standard moisture condition	Filling	Restoration	Propriety considered	Conclusions (Main findings)
Al-Kahtani *et al.*, 2010	EDTA + NaOCl; MTAD + NaOCl	Final (Irrigation during preparation with NaOCl)	17% EDTA; 5.25% NaOCl	Not reported	10 mL (each)	NaOCL	Human, single canal teeth	Sectioned (only coronal removal)	Saline + 0.2% CHX	NR	Lateral condensation technique with RealSeal	NR	Vertical root fracture	No statistical difference among conditions.
Ayad *et al.*, 2011	HP; NaOCl; HP + NaOCl; EDTA; LA	During preparation	5% HP; 5% NaOCl; 15% EDTA; 10% and 20% LA	Not reported	3 mL at each file change	NR	Human, maxillary central incisors	Sectioned (only coronal removal)	DW with 0.1% thymol	NR	Lateral condensation technique with Ketac-Endo Aplicap root	Post + resin cement (Panavia 21) + resin composite core + metal crown	Fracture resistance	The only difference was observed with the use of 10% and 20% LA and 15% EDTA, which significantly increased fracture resistance.
Ayranci *et al.*, 2018	NaOCl; EDTA	Final (Irrigation during preparation with NaOCl)	5% NaOCl; 15%EDTA	120seg (NaOCl); EDTA (agitated for 40 s)	2mL (NaOCl); 1mL (EDTA)	DW	Human, maxillary anterior teeth	Sectioned (coronal and apical removal)	DW	NR	Lateral condensation technique with Endo Plus sealer	NR	Vertical root fracture	The different canal irrigation techniques altered resistance to fracture.
Bhandary *et al.*, 2017	DW; EDTA + NaOCl	Final (Irrigation during preparation with NaOCl)	17% EDTA + 1% NaOCl; 8% EDTA + 1% NaOCl; 17% EDTA + 1% NaOCl; 8% EDTA + 1% NaOCl.	1 min NaOCl; 10min for DW; 17% and 8% EDTA varied from 1 to 10 min	10 mL (each)	NR	Human, single rooted teeth	Sectioned (only coronal removal)	Saline	NR	Single cone technique with AH Plus sealer	Coltosol F (sealing)	Vertical root fracture	No deleterious impact on resistance to fracture. Recommended protocol: EDTA higher concentration with shorter exposure, or lower concentration

														at a longer exposure time.
Cecchin *et al.,* 2015	DW; NaOCl + EDTA; CHX + EDTA; Qmix + EDTA; GSE + EDTA	Not prepared, the root dentin was only exposed to the irrigant solution	2.5% NaOCl; 2% CHX; 6.5% GSE	40min	2mL	Rinsed with DW, immersed in 17% EDTA for 3 min; rerinsed with DW	Human, molars for flexural strength, single rooted teeth for UTS	Sectioned (roots were shaped into bars for flexural strength and hourglass for UTS)	Frozen for up to 3 months	NR	Not applica ble	Not applicable	Flexura l strengt h; UTS	The use of GSE and CHX does not interfere in the mechanical properties of dentine. Furthermore, NaOCl and Qmix harm dentine mechanical properties.
Cecchin *et al.,* 2017	NaOCl; $Ca(OCl)_2$; GSE	Two scenarios: root dentin bars and hourglass was only exposed to the solution; or as a final solution after teeth preparation (DW between files)	6% NaOCl; 6% $Ca(OCl)_2$; 6.5% GSE	30min	2mL	Rinsed with DW, immersed in 17% EDTA for 3 min and thoroughly rinsed with DW again	Human, molars for flexural strength, single rooted teeth for UTS and fracture resistance	Sectioned (roots were shaped into bars, hourglass, or only decoronate d)	Frozen for up to 3 months	NR	Not applica ble	Not applicable	Flexura l strengt h; UTS and Vertical root fractur e	Different than NaOCl, GSE and Ca(OCl)2 are promising irrigation solutions that do not negatively affect the in vitro dentin mechanical properties.
Cullen *et al.,* 2015	Saline; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	0.5; 2; 4.125; 6.0; and 8.25% NaOCl	60min (changed every 6min)	2mL	NR	Human, permanent mandibular molars	Sectioned (roots were shaped into bars)	0.5% chlorami ne-T	NR	Not applica ble	Not applicable	Flexura l strengt h	Only a trend toward decreasing flexural strength with increasing NaOCl concentration.
Gu *et al.,* 2017	Deionized water; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	2%; 4%; 6%; 8% NaOCl	Up to 240 min (refreshed every 10 min)	20mL	Deionized water	Human, third molars	Sectioned (roots were shaped into bars)	Saline + 0.02 % sodium azide for up to 1 month	NR	Not applica ble	Not applicable	Flexura l strengt h	All experimental groups had decreased flexural strength; Factors 'time of exposure 'and 'concentration of the solution' directly affect the flexural strength.
Grigorat os *et al.,*2001	Saline; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	3 and 5% NaOCl	2h (changed every 15min)	50mL	DW	Human, unclear which kind	Sectioned (roots were shaped into bars)	4% formal-saline	NR	Not applica ble	Not applicable	Flexura l strengt h	NaOCl solutions reduced the flexural strength of dentine.

Jungbluth *et al.*, 2011	Saline; 1mol/L NaOH; NaOCl with water; alkalized NaOCl; 2 mol/L NaOH with water.	Not prepared, the root dentin was only exposed to the irrigant solution	10% NaOCl with water; 10% NaOCl with 2mol/L NaOH	30min	5mL	Ultrapure water	Human, maxillary third molars	Sectioned (roots were shaped into bars)	0.2% thymol solution for up to 1 year	Yes	Not applicable	Not applicable	Flexural strength	The alkalized NaOCl solution deleteriously impacted flexural strenght of dentin. Other solutions were similar to saline.
Khoroushi *et al.*, 2017	Saline; NaOCl; CA; EDTA; NaOCl+DW+CA	During preparation	2.5% NaOCl; 10% CA; 17% EDTA	1-3 minutes (each)	5mL (each)	NR	Human, premolars	Whole (only root canal access)	0.1% thymol solution	NR	Lateral condensation technique with AH26 sealer	Composite resin	Fracture Resistance	The irrigation protocols used during endodontic treatment decreased the coronal fracture resistance of teeth.
Khoroushi *et al.*, 2018	NaOCl; CHX; NaOCl+CHX; NaOCl + EDTA; NaOCl+EDTA+CHX	During preparation	2.5% NaOCl; and 2% CHX always for 1 minute; 17% EDTA always for 3 minutes;	1-3 minutes (each)	5mL (each)	NR	Human, premolars	Whole (only root canal access)	0.1% thymol solution	NR	Lateral condensation technique with AH26 sealer	Composite resin	Fracture Resistance	The use of CHX shown the higher fracture resistance, followed by NaOCL + CHX; other solutions shown the most deleterious impact.
Lantigua Domínguez *et al.*, 2018	Saline; NaOCl; HEBP; EDTA; CHX.	During preparation	2.5% NaOCl + 17% EDTA; 2% CHX + 17% EDTA; mixture 5% NaOCl + 18% HEBP.	25min total for all (22 min 1st solution + 3 min 2nd solution)	12mL (each)	DW	Human, premolars	Sectioned (only coronal removal)	Saline solution for up to 30 days	NR	Not reported	Not reported	Vertical root fracture	The combined solution of 5% NaOCl and 18% HEBP decreased root fracture resistance.
Machnick *et al.*, 2003	Saline; NaOCl; EDTA; MTAD	Not prepared, the root dentin was only exposed to the irrigant solution	0.66% 1.31% 2.63% and 5.25% NaOCl; 17% EDTA; MTAD (2h) or MTAD clinical protocol (20 min 1.3% NaOCl +5 min MTAD).	2h (changed every 15 min); except for MTAD clinical protocol	30mL, except for MTAD clinical protocol	Deionized water	Human, molars	Sectioned (roots were shaped into bars)	0.1% chloramine T	NR	Not applicable	Not applicable	Flexural Strength	A reduction in flexural strength was observed only at 2-h MTAD and EDTA groups.
Mai *et al.*, 2010	Water; NaOCl + EDTA under two protocols	Not prepared, the root dentin was only exposed to the irrigant solution	5.25% NaOCl + 17% EDTA.	10 or 60min NaOCl + 2min EDTA	NR	Deionized water	Human, third molars	Sectioned (roots were shaped into bars)	NR	NR	Not applicable	Not applicable	Flexural strength	Only under longer exposure periods NaOCl solution potentiates EDTA effects and lead to decrease on flexural strength.

Marcelino *et al.,* 2014	Deionized water; NaOCl; NaOCl+SA; SA; CHX; PA; PA+CHX; PA+NaOCl.	Final (During preparation root canals were irrigated with NaOCl between each file followed by 17% EDTA).	5.25% NaOCl; 5.25% NaOCl + 10% SA; 10% SA; 2%CHX; 37%PA; 37%PA+2%CHX; 37%PA+5.25%NaOCl.	10 min for Deionized water; and 10% SA; 5 min for 5.25% NaOCl; and 2% CHX; 15seg for 37%PA	10 mL for Deionized water; 5.25% NaOCl; and 10% SA	DW	Human, canines	Mixed. Root canal access during preparation and exposure to solutions; shaped into bars for testing	0.1% thymol solution	NR	Not applicable	Not applicable	Flexural strength	Flexural strength was not affected by the chemical agents.
Marending *et al.,* 2007a	Ultrapure water; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	1; 5; and 9% NaOCl.	1h	5mL	Ultrapure water	Human, maxillary third molars	Sectioned (roots were shaped into bars)	0.1% thymol solution for up to 1 year	NR	Not applicable	Not applicable	Flexural strength	NaOCl caused a concentration-dependent reduction of flexural strength (except to 1%).
Marending *et al.,* 2007b	DW; NaOCl; EDTA; NaOCl + EDTA (two protocols)	Not prepared, the root dentin was only exposed to the irrigant solution	2.5% NaOCl; 17% EDTA	30 min total (21 min at the first solution followed by 3 min in each of the following)	5mL (each)	Distilled water	Human, maxillary third molars	Sectioned (roots were shaped into bars)	0.2% thymol solution for up to 1 year	NR	Not applicable	Not applicable	Flexural strength	All protocols involving the use of NaOCl deleteriously impacted the flexural strength.
Sim *et al.,* 2001	Saline; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	Saline; 0.5; and 5.25% NaOCl	2h (changed every 10 min)	200mL	Water	Human, unclear which kind	Sectioned (roots were shaped into bars)	4% formal-saline	NR	Not applicable	Not applicable	Flexural strength	5.25% NaOCl significantly reduces the flexural strength.
Souza *et al.,* 2014	Distilled water; NaOCl; alkalized or neutral NaOCl	During preparation	Neutral NaOCl (pH of 7.2); alkalized NaOCl (ph 12.8)	26min	30mL	Distilled water	Bovine, anterior incisors.	Sectioned (only coronal removal)	Saline	NR	NR	NR	Fracture resistance	Both testing solutions lead to a decrease on fracture strength.
Souza *et al.,* 2019	Alkalized NaOCl	During preparation	5.25% alkalized NaOCl	11.5 min or 19min	15 mL or 30mL for 11.5min or 19min	Distilled water	Bovine, anterior incisors.	Sectioned (coronal and apical removal)	Saline	NR	NR	NR	Fracture resistance	Raising the volume and/or time of alkalized NaOCl solution reduces the fracture resistance.
Tiwari *et al.,* 2016	Saline; EDTA; EDTA + cetrimide; CA +cetrimide+ doxycycline hyclate + polypropylene glycol	Final (2% NaOCl was used during preparation)	10%; 15% or 17% EDTA; 0.2% or 0.75% cetrimide; 10.5% CA; 1% doxycycline hyclate; polypropylene glycol	NR	10mL	NR	Human, maxillary premolars.	Sectioned (only coronal removal)	Saline	NR	NR	NR	Vertical root fracture	10% EDTA provided the highest fracture resistance compared with other irrigants, been statistically

														similar to saline.
Uzunoglu *et al.*, 2012	Distilled water; NaOCl; EDTA	Final (During preparation, between each file, 2 mL of 1% NaOCl was used).	17% EDTA +1% NaOCl; 5% EDTA+1% NaOCl	1min or 10 min (17% or 5% EDTA) + 1min (1% NaOCl)	10mL (each)	Saline	Human, mandibular incisors	Sectioned (only coronal removal)	0.5% chloramine-T	NR	Single cone technique and AH 26 sealer	NR	Vertical root fracture	Only 17% EDTA for 10 min decreased the fracture resistance in comparison to DW
Uzunoglu *et al.*, 2016	Saline; EDTA; REDTA; CHX; Qmix; MTAD.	Final (During preparation using 1 mL 2.5% NaOCl between each file).	17% EDTA; 2% CHX.	1 minute except for MTAD that was applied for 5 minutes	5mL (each)	Distilled water	Human, mandibular incisor	Sectioned (only coronal removal)	0.2% sodium azide	NR	Single cone technique and AH 26 sealer	Coltosol F (sealing)	Vertical root fracture	No statistical difference among conditions in comparison to saline.
Wang *et al.*, 2017a	Saline; MA; NaOCl; EDTA.	Final (Between each file, the root canals were irrigated with 2mL of 2.5% NaOCl).	7%MA +2.5% NaOCl; 17%EDTA +2.5% NaOCl.	MA for 30s up to 3 min; EDTA for 45 seg; NaOCl for 1 min	5mL (each)	Distilled water	Human, single rooted premolars	Sectioned (only coronal removal)	0.2% sodium azide	NR	Lateral condensation technique with AH Plus sealer	NR	Vertical root fracture	Only the use of 7% MA for 3 min impacted deleteriously the fracture resistance.
Wang *et al.*, 2017b	DW; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	1%; 5% and 10% NaOCl	Up to 60min	2mL	NR	Human, premolars	Sectioned (roots were shaped into bars)	0.5% thymol	NR	Not applicable	Not applicable	Flexural strength	All NaOCl concentrations decrease the flexural strength, especially longer exposure periods.
Zhang *et al.*, 2010	NaOCl; EDTA	Not prepared, the root dentin was only exposed to the irrigant solution	5.25%NaOCl + 17%EDTA/2min; 1.3% NaOCl + 17%EDTA/2min; only 17% EDTA for 2 min	Up to 240 min	5mL	Deionized water (3 times)	Human, third molars	Sectioned (roots were shaped into bars)	Saline + 0.02% sodium azide for up to 1 month	NR	Not applicable	Not applicable	Flexural strength	NaOCL at 5.25% for time exposures longer than 60min promote deleterious impact on flexural strengh.

Legends: Sodium hypochlorite (NaOCl); Sodium hydroxide (NaOH); mixture of 2-mol/L NaOH with 10% NaOCl (alkalized NaOCl); mixture of 10% NaOCl with 1% sodium bicarbonate - $NaHCO_3$ (neutral NaOCl); Ethylenediamine tetraacetic acid (EDTA); EDTA + 0.84 g cetyltrimethylammonium bromide (REDTA); hydroxyethylidene bisphosphonate (HEBP); Hydrogen peroxide (H_2O_2 - HP); Lactic acid (LA); Citric acid (CA); Maleic acid (MA); Phosphoric acid (PA); Grape seed extract (GSE); Chlorhexidine gluconate (CHX); Solution with antimicrobial activity used for the smear layer removal in final irrigation manufactured by Dentistry (Qmix); Antibacterial root canal cleanser manufactured by Dentsply (MTAD); Calcium hypochlorite ($Ca(OCl)_2$); Distilled Water (DW); sodium ascorbate (SA); Not Reported (NR); Ultimate tensile strength (UTS).

Table 4. Description of data obtained on included *in vitro* studies that evaluated modulus of elasticity properties.

Author	Irrigate solutions tested	Moment of usage of the solution	Concentration	Time	Volume	Wash-out	Type of tooth	Tooth condition during analysis	Storage conditions	Standard moisture condition	Conclusions (Main findings)
Cullen *et al.*, 2015	Saline; NaOCl	Not prepared, the root dentin was only exposed to the irrigant solution	0.5; 2; 4.125; 6.0; and 8.25% NaOCl	60min (changed every 6min)	2 mL	NR	Human, mandibular molars	Sectioned (roots were shaped into bars)	0.5% chloramine-T, than saline at 4°C until test	NR	No statistical difference in modulus of elasticity between groups (NaOCl and Saline).
Grigoratos *et al.*,2001	Saline; NaOCl		3 and 5% NaOCl	2h (changed every 15min)	50 mL	Distilled water	Human, unclear which type		4% formal-saline	NR	NaOCl (3 and 5%) reduced the modulus of elasticity of dentine.
John *et al.*, 2013	Saline; NaOCl		5% NaOCl	36min	12 mL (2 mL/min, maintained for 10 min after each 4 ml)	NR	Human, maxillary central incisors		NR	Yes	NaOCl did not impacted the modulus of elasticity on flexural testing, however on ultrasonic measurements a reduction was observed.
Jungbluth *et al.*, 2011	Saline; NaOH; NaOCl + water; NaOCl + NaOH; NaOH + water		10% NaOCl with water; 10% NaOCl with 2mol/L NaOH; 1mol/L NaOH	30min	5 mL	Ultrapure water	Human, maxillary third molars		0.2% thymol solution at 5°C up to 1 year	Yes	No statistical difference in modulus of elasticity.
Machnick *et al.*, 2003	Saline; NaOCl; EDTA; MTAD		5.25%; 2.63%; 1.3%; and 0.66% NaOCl; 17% EDTA; MTAD; MTAD clinical protocol (20 min 1.3% NaOCl + 5 min MTAD)	2h (changed every 15 min); except for MTAD clinical protocol	30 mL	Deionized water	Human, molars		4°C in 100% humidity containing 0.1% chloramine T	NR	A significant reduction of modulus of elasticity was observed with 2h-MTAD, EDTA, and 0.6% NaOCl.
Marending *et al.*, 2007a	Ultrapure water; NaOCl		1; 5; and 9% NaOCl	1h	5 mL	Ultrapure water	Human, maxillary third molars		0.1% thymol solution after extraction for up to 1 year	NR	NaOCl caused a concentration dependent reduction of modulus of elasticity (5 and 9%).
Marending *et al.*, 2007b	DW; NaOCl; EDTA		2.5% NaOCl + 17% EDTA + 2.5% NaOCl + DW; 2.5% NaOCl + DW + 2.5% NaOCl + 17% EDTA; 2.5% NaOCl + DW + 2.5% NaOCl + DW; DW + 17% EDTA + DW + DW; DW	30 min total (21 min first solution followed by 3 min in each of the following)	5 mL (each)	Distilled water	Human, maxillary third molars		0.2% thymol solution at 5°C for a maximum of 1 year	NR	No statistical difference in modulus of elasticity between groups
Sim *et al.*, 2001	Saline; NaOCl		0.5 and 5.25% NaOCl	2h (changed every 10 min)	200 mL	Water	Human, unclear which type		4% formal-saline	NR	Only 5.25% NaOCl reduces the elastic modulus of dentine.
Wang *et al.*, 2017a	Saline; MA; NaOCl; EDTA	During preparation: 2.5% NaOCl	2.5% NaOCl; 7% MA +2.5% NaOCl; 17% EDTA +2.5% NaOCl	7% MA for 30s, 45s, 1min or 3min + 1 min	5 mL (each)	DW	Human, single rooted	Sectioned: coronal removal; longitudinally	0.2% sodium azide until use	NR	All protocols reduced the modulus of elasticity

		between files; after, it was used the evaluated solutions		NaOCl; 45 seg for 17% EDTA +1min NaOCl; 1min NaOCl			premolars	sliced, embedded in acrylic resin, polished and tested			after irrigation. MA solutions were more aggressive, specially after 1min.

Legends: Sodium hypochlorite (NaOCl); Ethylenediamine tetraacetic acid (EDTA); Antibacterial root canal cleanser manufactured by Dentsply (MTAD); Maleic acid (MA) Distilled water (DW); Not reported (NR)

Table 5. Description of data obtained on included studies (*in vitro* and *in silico*) that evaluated stress and strain concentration during mechanical preparation using the irrigant solutions.

Author	Type of study	Irrigate solutions tested	Moment of usage of the solution	Concentration	Time	Volume	Wash-out	Type of tooth	Storage conditions	Propriety considered	Conclusions (Main findings)
Belli *et al.*, 2014	*in silico*	NaOCl; EDTA; MTAD	Not applicable	5.25% NaOCl; 17% EDTA	A three-dimensional finite element model of maxillary central incisor (human) with complete filling and bonding simulation with the restorative sets					Stress (Finite Element Analysis)	NaOCl, EDTA and MTAD increased the stresses at root dentine.
Goldsmith et al., 2002	*in vitro*	Saline and NaOCl	During mechanical testing, the solution was inserted and the TSS monitored	7.3%; 5.1%; and 3% NaOCl	30 min (each)	NR	Saline	Human, premolars	4% formal saline	TSS	3.0%, 5.1%, and 7.3% NaOCl had no statistically significant effect.
Rajasingham *et al.*, 2010	*in vitro*	Saline; NaOCl; EDTA	During preparation, before mechanical stimuli	3 and 5% NaOCl; 17% EDTA; 3% NaOCl + 17% EDTA; 5% NaOCl + 17% EDTA	30 min (each)	NR	Saline	Human, premolars	4% formal-saline	TSS	5% NaOCl alone, and when alternated with 17% EDTA for sufficient duration may significantly increase TSS.
Sim *et al.*, 2001	*In vitro*	Saline; NaOCl	During mechanical testing, the solution was inserted and the TSS monitored	Scenarios altering from saline only; to different combinations using saline, 0.5% and 5.25% NaOCl	2h (changed every 30 min)	Unclear	Water	Human, second premolars (decoronated)	4% formal saline	TSS	The use of 5.25% NaOCl increased TSS concentration during mechanical loading.
Sobhani *et al.*, 2010	*in vitro*	Saline; NaOCl; EDTA	Final, before mechanical stimuli	5% NaOCl; 5%NaOCl + 17% EDTA	10 min	3mL	Saline	Human, premolars	10 mL of 4% formal saline	TSS	5% NaOCl alone, and when alternated with 17% EDTA for sufficient duration may significantly increase TSS.

Legends: Sodium hypochlorite (NaOCl); Ethylenediamine tetraacetic acid (EDTA); antibacterial root canal cleanser manufactured by Dentsply (MTAD); Tooth surface strain (TSS); Not Reported (NR)

Table 6. Description of data obtained on included *in vitro* studies that evaluated roughness properties.

Author	Irrigate solutions tested	Moment of usage of the solution	Concentration	Time	Volume	Wash-out	Type of tooth	Tooth condition during analysis	Storage conditions	Standard moisture condition	Conclusions (Main findings)
Akbulut *et al.*, 2019	DW; Vinegars (pomegranate; apple cider; grape); NaOCl; CHX; OCT	The root dentin was only exposed to the irrigant solution priot to test	2.5% NaOCl, 2% CHX	15/ 30 min	NR	NR	Human mandibular incisor teeth	All studies used sectioned roots	Distilled water for <3 months until further processing	NR	Only vinegar solutions shown a softening effect on the root canal dentin over time, and increased roughness.
Ari *et al.*, 2004	DW; NaOCl; H_2O_2; EDTA; CHX		5.25% NaOCl; 2.5% NaOCl; 3% H_2O_2; 17% EDTA; 0.2% CHX	15 min	5mL	Distilled water	Human mandibular anterior teeth		Immediately stored in buffered saline and submitted to the study	NR	Only CHX and H_2O_2 solutions did not lead to higher roughness than distilled water.
Ballal *et al.*, 2015	Saline; ClO_2; EDTA; MA; NaOCl		13.8% ClO_2; 17% EDTA; 7% MA; 2.5% NaOCl	1 min	5mL	Distilled water	Human maxillary central incisors		0.2% sodium azide at 4°C until further processing	NR	All solutions lead to higher roughness than saline, MA the highest, followed by NaOCl and EDTA, and than by ClO_2.
Ballal *et al.*, 2010	Saline; EDTA; MA		17% EDTA; 7% MA	1 min	1mL	NR	Human maxillary central incisors		0.2% sodium azide until further processing	NR	All solutions lead to higher roughness than saline, MA the highest, followed by EDTA.
Bello *et al.*, 2019	DW; EDTA; CA; GA		17% EDTA; 10% CA; 5% GA; 10% GA; 17% GA	1 min	50mL	5-mL distilled water.	Human mandibular teeth		Saline solution at 4 °C until further tests	NR	All solutions lead to higher roughness than DW.
Eldeniz *et al.*, 2005	DW; CA + NaOCl; EDTA + NaOCl		19% CA + 5.25% NaOCl; 17% EDTA + 5.25% NaOCl	150 s (each)	NR	Not reported	Human mandibular anterior teeth		Phosphate buffered saline at 4°C until used	NR	Only the protocol using CA significantly increased surface roughness in comparison to DW.
Patil and Uppin, 2011	DW; NaOCl; H_2O_2; EDTA; CHX.		5% NaOCl; 2.5% NaOCl; 3% H_2O_2; 17% EDTA; 0.2% CHX	15 min	5mL	Distilled water	Human maxillary and mandibular incisor teeth		37°C in buffered saline until used	NR	Only the protocol using chlorhexidine gluconate did not increase the surface roughness of root canal dentin in comparison to DW.

Legends: Sodium hypochlorite (NaOCl); Octenidine-hydrochloride (OCT); Chlorhexidine gluconate (CHX); Chlorine dioxide (ClO_2); Ethylenediamine tetraacetic acid (EDTA); Hydrogen peroxide (H_2O_2 - HP); citric acid (CA); glycolic acid (GA); maleic acid (MA); Distilled Water (DW); Not Reported (NR)

Figure 1- Flowchart of study selection.

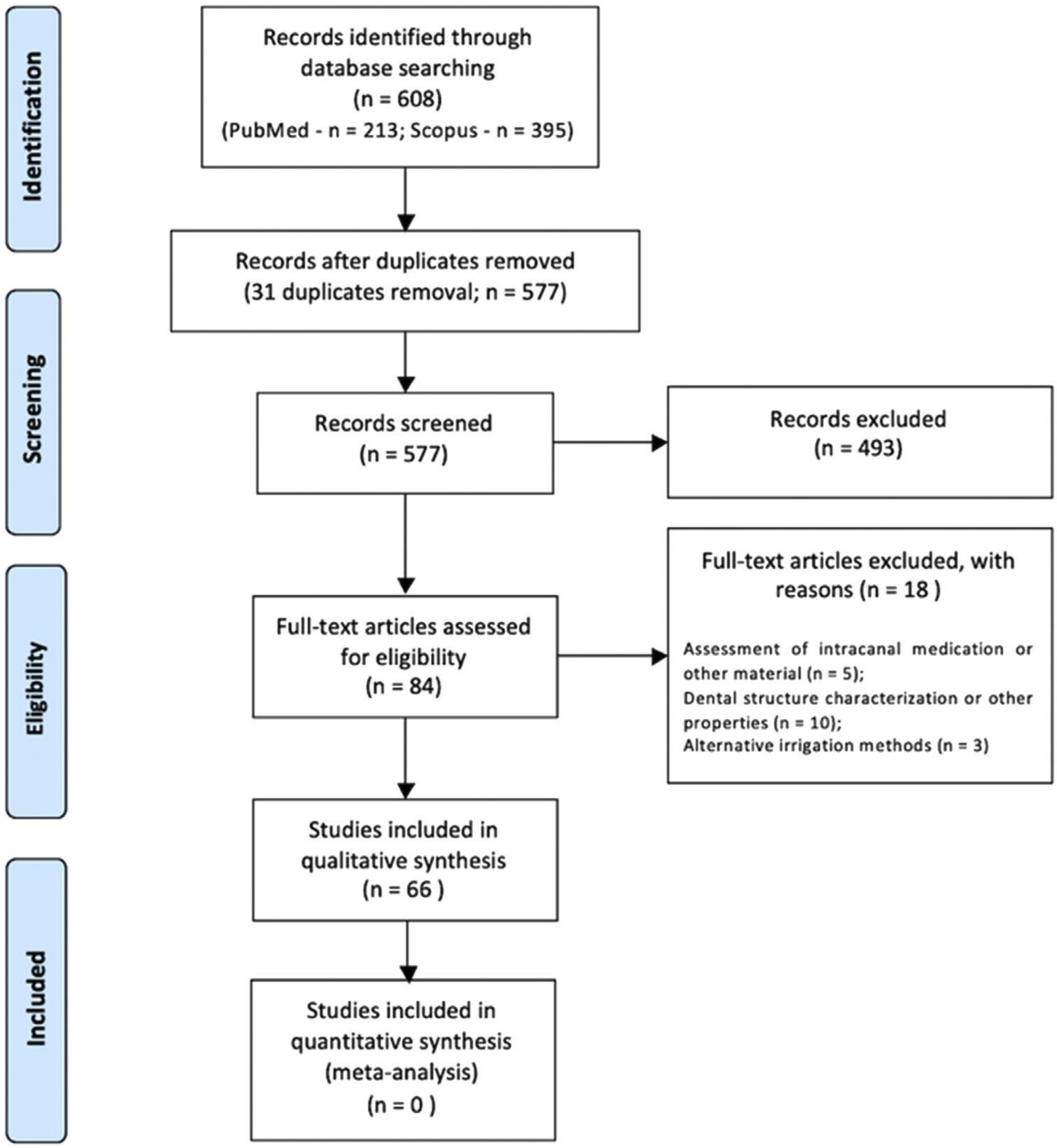
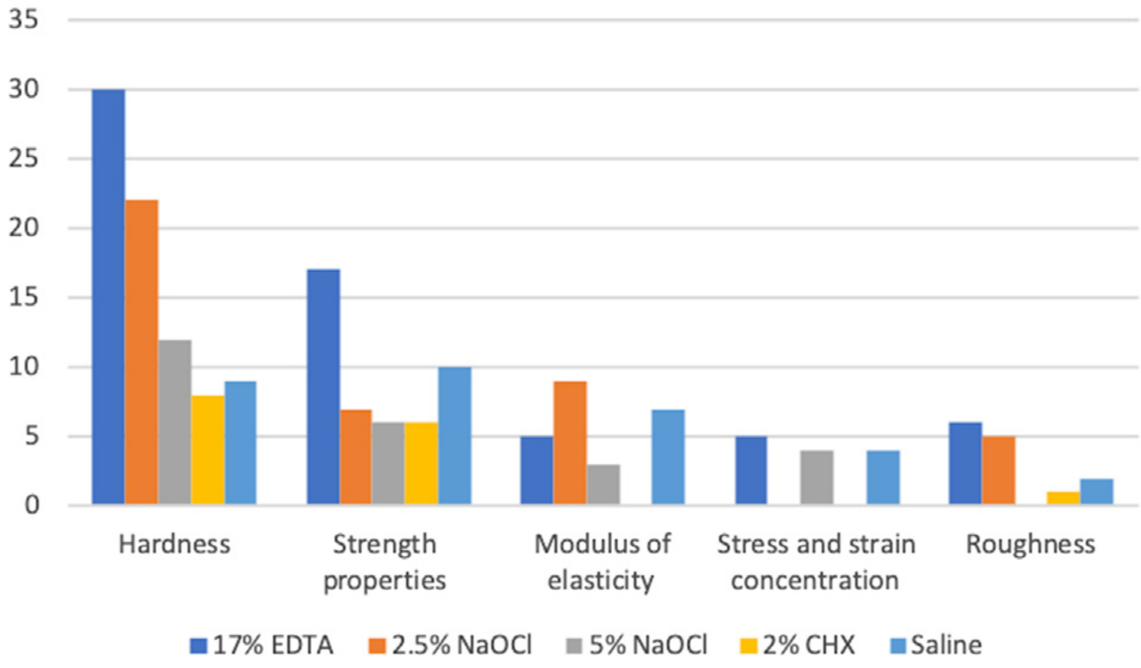


Figure 2 – Word cloud representing the substances used. The more a substance was used, the bigger it appears in the word cloud.

Figure 3 – Relation between properties tested and the most substance used. CHX, chlorhexidine.



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4. ARTIGO 2

Title page

The use of solvents for gutta-percha dissolution/removal during endodontic retreatments: A scoping review

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ABSTRACT

This scoping review study aimed to map the evidence about solvents' use for gutta percha dissolution and removal during endodontic retreatments. The study protocol followed the Joanna Briggs Institute guidelines, available online (https://osf.io/5vy8n/). Reporting was based on PRISMA Extension for Scoping Reviews. We selected dentistry studies that considered the effectiveness of solvents in gutta percha dissolution in endodontic retreatments and compared their performance to the use of instrumentation techniques without solvents. The search and study screening were performed in PubMed and Scopus databases by two independent researchers. A descriptive analysis considered the study design, method/technique used for obturation, method/technique used for instrumentation during retreatment, solvent solutions tested, exposure time, and main findings. A total of 41 studies were included. Despite that, most studies suggested that solvents' use may complicate root canal cleanliness, regardless of the type of instrumentation used, and facilitate the presence of gutta-percha remnants in the root surface. Thus, the use of solvents should be avoided and its use should only be considered if the previous working length was not possible to access without it. Despite that, high heterogeneity was observed, further studies are still encouraged comparing the performance and effects of different solvents in different clinical scenarios.

KEYWORDS
chloroform, gutta-percha, root canal retreatment, scoping review, solventes

1 INTRODUCTION

Failure to resolve root canal infection is among the main causes of unsuccessful endodontic treatment.[1] This failure follows signs or symptoms of apical periodontitis, such as, persistent apical lesion and pain.[2] Overall, the endodontic causes of failure essentially involve existing infection or re-infection.[3] If possible, the first nonsurgical option considered for a failed primary endodontic treatment is retreatment. It requires the removal of the filling root material so that the root canals can be shaped and cleaned.[1] Different techniques and materials allow this: hand or mechanical (rotatory or reciprocation) instrumentation used commonly on the primary endodontic treatment, rotary files designed explicitly for retreatments, ultrasonic tips and files, heat pluggers, and Nd:YAG lasers.[4,5] However, a barrier to retreatment is access to the obturator material for its removal to be effective, especially when it is well condensed and resistant to instrument penetration or, most critically, in curvature regions of the root where perforation is a risk.[1,3,6-9] In these cases, the use of solvents is commonly advocated.[1,3,6-9]

Solvents are solutions used in endodontic therapy to soften the root filling material, usually the gutta-percha (GP).[2,10] Many types of solvents are available, such as, chloroform, eucalyptol, orange oil, tetrachloroethylene (Endosolv), and xylene, but none meet all the requirements of an ideal solvent, which should be nontoxic and noncarcinogenic to adjacent tissues, patient, and clinicians; deliver efficient GP softening; be viable for an adequate time and cost-effective.[4] For example, chloroform has long been the solvent of choice because of its high volatility, but it is the most cytotoxic to periapical tissues, it could be even hepatotoxic and has been classified as a Class 2B carcinogenic material.[11,12] Therefore, new substances have been tested,[3,4,13-15] but none have been shown to have sufficient properties to justify their use. Thus, to choose a solvent is still a challenge.

Many studies[1,4-7,9,10,14-47] have tested the efficacy of files and solvents in removing residual GP during retreatment, or the amount of material remaining after using different files and solvents. However, which methods are more effective and whether solvents are essential for root material filling removal are still unclear. Additionally, scoping reviews offer an important tool that can provide a map of the range of available evidence.[48] Thus, this scoping review study aimed to map the evidence about the use of solvents for GP dissolution and removal during endodontic retreatments, and discuss the necessity of using such a solution.

2 MATERIALS AND METHODS

The protocol of this study was developed prospectively based on the framework proposed by Peters et al., 201548 according to the Joanna Briggs Institute guidelines, and is available online (https://osf.io/5vy8n/). Additionally, the reporting of this scoping review was based on the PRISMA Extension for Scoping Reviews.[49]

2.1 Inclusion criteria

We selected dentistry studies that considered the effectiveness of solvents in dissolving GP in endodontic retreatment, comparing their performance to the use of instrumentation techniques without solvents. It included studies that evaluated the effect of at least one solvent solution on GP, regardless of the teeth type (human, bovine, or other animal) and regardless of how the outcome was measured. In relation to study design, we included reviews that discussed GP removal and dissolution in endodontic retreatment, clinical trials, and in vitro laboratory tests. We classified the study design based on the author report. Studies testing other root filling materials than GP were not considered.

2.2 Search

The search was performed in two databases, MEDLINE (PubMed) and Scopus, limited to articles written in English, without time restriction. The search strategy was based on MeSH terms for PubMed and specific terms for Scopus using keywords (Table 1). The last search was conducted in September 2019.

2.3 Screening

Initially, the search was undertaken using the EndNote software (EndNote X9, Thomson Reuters, New York, NY). Two researchers (LD and GKRP) independently identified articles by first analyzing titles and abstracts for relevance and the eligibility criteria. Retrieved records were classified as either "include," "exclude," or "uncertain". The full-text articles of the included and uncertain records were selected for further eligibility screening by the same two reviewers, acting independently. Discrepancies in screening of titles and abstracts or full-text articles were resolved through discussion. In case of disagreement, the opinion of a third reviewer was sought.

2.4 Charting the results

We created a form using the Excel software (Office, Microsoft, Redmond, Washington, EUA), which three reviewers tested to reach a consensus for data collection. Then, one reviewer extracted the data and another checked it. The data collected were study design, method or technique used for obturation, method or technique used for instrumentation during retreatment (manual or rotary), solvent solutions tested, exposure time, moment of use of the solvent (final rinse or during instrumentation), method to access GP, characteristics of the teeth (human, bovine, or other animals; straight or curved roots; other details), and main findings. In case of identification of systematic or other reviews, data collected were inclusion criteria, number of included articles, main findings, level of evidence generated reported by authors, and conclusions.

2.5 Data analysis

The data synthesis focused on describing the solvent solutions used, their characteristics, and which solvents were necessary and effective for GP dissolution and removal during endodontic retreatment. A descriptive analysis was performed that considered the study design and different solvents tested using tables. A word cloud was created using the website https://www.worditout.com/ to illustrate graphically the prevalence of use of each solution.

3 RESULTS

3.1 Search findings

Figure 1 presents the flow chart for the study selection. The search initially yielded 501 potentially relevant citations (Scopus: n = 239; PubMed: n = 262). After removing duplicates (98) and irrelevant papers (345), 58 citations met the eligibility criteria based on title and abstract. These were obtained and full text screened, resulting in 41 remaining studies being included in the qualitative synthesis analysis.

3.2 Prior published reviews

Among the studies included in this scoping review, we found a systematic review[5] and a literature review.[4] The systematic review investigated the effectiveness of different procedures in removing root canal filling materials using micro-computed tomography imaging assessment only. In general, considering 22 studies published up to 2008, it corroborated the use of solvents to enhance penetration of files, but not to improve cleaning of the root canal. However, it emphasized that not all protocols fully removed the root canal filling materials and suggested larger preparation sizes and hybrid techniques to reduce the remaining material. The eligibility criteria and the quality or level of evidence were not reported by the authors. The literature review suggested that the use of solvents in the coronal and middle thirds of root canals should be done with caution to avoid potential toxicity (Table 2).

3.3 Solvents assessed in included studies

Figure 2 summarizes the substances used in the included studies. The more a substance was used, the larger it appears in the word cloud. Notably, the most commonly used solvents were chloroform, eucalyptol, Endosolv R, and xylol.

3.4 Effectiveness of solvents for GP dissolution and removal during endodontic retreatment (experimental results)

The present review included 36 in vitro studies (Table 3) and three ex vivo studies.[6,10,30] In general, most studies found that the use of solvents, regardless of composition, does not present benefits to GP removal. Other studies encouraged consideration of solvents when the GP is difficult to remove because it is closely adhered to the walls or in the apical portion, making it impossible to reach the previous working length,[16,39] or when mechanical methods fail to retrieve of GP in retreatment.[41]

3.4.1 Chloroform

Chloroform was the most-used solvent,[1,7,9,16-19,21,24-26,28-31,33,34,41,43] along with an ethyl ether–chloroform mixture.[6] In general, the studies did not reveal any beneficial effect of chloroform, with the main findings agreeing that using chloroform to remove GP made the process more difficult compared with the control group without any solvent,[7,9,17,19,25,26,28,30,31,33] or did not produce differences compared with the control group.[1,18,29,43]

A few studies showed advantages with chloroform, including much greater efficacy of GP removal with mechanical files,[21] benefits when mechanical methods failed to retrieve GP[41] or when the removal of filling material was difficult,[16] and shortened time of retreatment.[34]

3.4.2 Eucalyptol

Of the studies using eucalyptol as the solvent,[22,23,28,39,45,46] only one did not consider its use a disadvantage.[23] However, the study found no significant difference to the other tested methods, such as, mechanical instrumentation with FlexMaster GT Rotary and ProTaper or manual instrumentation with Hedstroem files, without solvent. Horvath et al., 2009[28] and Boarium et al., 2015[39] concluded that the use of eucalyptol led to more GP and sealer remnants on root canal walls and inside dentinal tubules than in control groups that tested Gates-Glidden drill plus Hedstroem[28] and ProTaper Universal, K3 Endo rotary nickel–titanium system or Gates-Glidden plus K-type file.[39] One study assessed the effectiveness in GP removal of Nd:YAG laser plus eucalyptol or dimethylformamide, finding that the Nd:YAG laser was capable of softening GP in vitro, but the addition of solvents did not improve its removal.[22]

3.4.3 Endosolv R

All studies that evaluated this solvent concluded that the use of Endosolv R did not present beneficial effects.[9,14,35,44] One study tested the final irrigation with passive ultrasonic irrigation (PUI) associated with Endosolv R or distilled water; where both strategies were ineffective in removing filling debris from root canal walls.[35]

3.4.4 Xylol

Four studies assessed xylol.[10,20,27,38] Two found benefits when xylol was associated with manual instrumentation.[20,27] Rached-Júnior et al., 2014[38] evaluated the removal of filling material under different operatory vision (direct or operating microscope) and methods (ProTaper retreatment with or without solvent and ultrasound with or without solvent), concluding that, independent of the operatory vision, the use of xylol was associated with greater removal of filling material in both evaluated methods. The difference was found under an operating microscope, where the use of ultrasound and xylol provided better results than the mechanical files and xylol, but none of the protocols tested was associated with complete removal of the filling material.[38] Only one study did not find benefits using xylol.[10]

3.4.5 Orange oil

Barreto et al., 2016[42] and Salgado et al., 2019[47] evaluated orange oil and concluded no benefit to its use. However, Barreto et al., 2016[42] tested the effect of this substance after using ProTaper retreatment in both groups and performed the final irrigation with PUI and orange oil compared with PUI and sodium hypochlorite (NaOCl), and conventional irrigation with NaOCl. Kumar et al., 2012[32] and Das et al., 2017[15] used RC Solve (an orange oil derivative with the basic ingredient D-limonene) and did not find benefits compared to ProTaper Universal retreatment files or Mtwo retreatment files,[15] or ProTaper Universal Retreatment or Gates-Glidden drill plus Hedstroem,[32] without RC Solve.

3.4.6 Xylene

Two studies that evaluated xylene with mechanical or manual instrumentation agreed that, when using manual instrumentation, solvents' use yields better root canal cleanliness.[36,40]

3.4.7 Tetrachloroethylene

Mittal et al., 2014[37] found that no technique evaluated was 100% effective in removing filling material, but the use of Gates-Glidden drill plus ProTaper retreatment system with tetrachloroethylene solvent was better than Gates-Glidden drill plus Mtwo or Gates-Glidden drill plus H file, both with and without solvent.

4 DISCUSSION

This scoping review provides the first synthesis of information on the use of different solvents during endodontic retreatment on GP dissolution and removal. This scoping review's importance lies in the wide use of these substances during endodontic retreatment.[4,5] However, the literature was unclear on whether these solvents were really effective in GP removal. Based on present data, it was shown that regardless of the instrumentation technique (manual or mechanical) chosen by the clinician, the use of solvents during the process of desobturation may bring disadvantages in root canal cleanliness, and it should only be considered if the previous working length was not possible to access without it.[16,39]

Some studies showed that solvents might make root filling material removal more difficult, as it could make the structure of the material viscous and highly adhesive, resulting in the formation of films of softened GP on the root canal surface, even penetrating into root canal irregularities or dentinal tubules.[14,19,28,31,44] The alteration of material properties in response to the use of solvents may even make the retreatment procedure longer or more difficult. Barreto et al., (2016)[42] corroborated this effect when the solvent (orange oil) was used to associate with PUI. These changes to the filling material's characteristics may reduce the instrumentation effectivity,[42] and the obliteration of root dentinal tubules may also impair the action of intracanal medicaments and the adaptation of the subsequent new filling material on the root canal walls.[10,21,24,27,28] Most studies showed persistence of intracanal GP remnants, regardless of the root third evaluated.[10,14,15,20,27,28,30,40,47,50] However, it was more common and the GP more abundant in the root apical third.[1,6,39,44,47,50,51]

Regarding the type of instrumentation, mechanical systems, even with solvent association, were more ineffective for complete removal of root canal filling[6,10,27,51] than manual files.[20] It may also be due to the effect of the prior mentioned film of softened GP material present at the root canal wall surface[14,19,28,31,44] associated with the files' mechanical motion and the temperature increase generated, reducing the performance of these systems.[10] Besides, mechanical files for retreatment were designed to be used alone, without association with any substance. Thus, it seems that there is no beneficial effect of the use of solvents with such retreatment files.[7,9,14,15,29,30,32-35,42,44,46,47] Manual instrumentation may also have been the most effective because these files could be more easily manipulated against the walls, removing the debris[10,20] in the cervical third, and the apical third due to the enlargement of the apical foramen.[20,39,52] Further, our review showed that when the performance between manual and mechanical techniques was similar, the studies failed to notice completely cleaned canals, that is, remnants of GP were always present. [6,29] Thus, these contradicting findings might be attributed to differences in specimen assembly, instruments, materials, and methodological procedures.[47]

The literature suggests that there may be no one best system to remove the root filling material entirely.[47,50] Studies have encouraged the combination of methods (manual and mechanical files[6,10,40];) to achieve cleaner root canals without debris and remnants of material filling.[1,6,31] It is also true when the presence of GP and sealer is seen in deep grooves and depressions on dentin walls in the apical third,[1,28,44] or in dentinal tubules with the increasing dissolution of the root filling material, regions that could require additional instrumentation to remove such material. Or perhaps, this could be the only scenario where the use of solvents can be considered.[7,42]

Retreatment in straight canals is a relatively simple task compared with curved ones.[6,44,50] Furthermore, curved canals may cause instrument distortion or separation and breakage.[6,44] The isthmus region and flattened roots also usually show more residual GP, because the penetration of GP and sealer into the spaces makes the removal of the material more critical.[42] This corroborates the fact that in such scenarios, it is necessary to use different types of instrumentation (manual and mechanical), as well as auxiliary irrigating solutions other than solvents (e.g., NaOCl, chlorhexidine, sterile saline, or distilled water) to optimize the removal of remnant material from the root canals.[1,6,10,17,20,28,41,47,50] However, data in other literature[24] disputes that the material removal technique (e.g., using solvent) is a determining factor in cleaning the root canal walls, defending the obturator material (cement and/or filling material) as an influencing factor. We cannot forget that all of these inconsistent data are based on the high heterogeneity of existing studies and still encourage well-designed studies evaluating this topic.

Studies of solvents' effectiveness in root material filling removal rarely compare the performance of different solvents with each other.[1,9,19,21,23,33,47,51] It is made it difficult, or perhaps erroneous, any conclusion about a solvent's effectiveness and whether it is better than others. Therefore, we suggest studies comparing the performance and effects of different solvents on the effective removal of GP, to make possible recommendations of the situations for its real need, the most suitable solvent for complete material removal (without any detrimental effect such as change in the state of GP and obliteration of the dentinal tubes), and which instrumentation is most indicated in cases where the use of solvent is indispensable.

Despite its strengths, our scoping review has some limitations. The included studies tested various solvents and different instrumentation systems, but they rarely compared such different factors among each other. Moreover, different obturation methods with different sealers were also used; specimens were analyzed under different sizes and shapes and under different assessment methods. All of these factors lead to increased heterogeneity, which limits the quality of the evidence obtained.

5 CONCLUSION

No unanimous solvent exists for the effective removal of filling material. In fact, most studies suggested that solvents may even complicate root canal cleanliness and facilitate the presence of GP remnants in the root surface. Thus, the use of solvents should be avoided and its use should only be considered if the previous working length was not possible to access without it. Despite that, high heterogeneity was observed, and further studies are still encouraged comparing the performance and effects of different solvents in different clinical scenarios.

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Table Captions

Table 1 – Search strategy.

Table 2 – Summary of findings of included reviews.

Table 3 – Summary of findings of included experimental studies (in vitro and ex vivo).

Figure Captions

Figure 1 – Flowchart of study selection.

Figure 2 – Word cloud representing the solvents used. The more a substance was used, the bigger it appears in the word cloud.

Table Captions

Table 1 – Search strategy.

- PubMed: “Solvent” OR “Solvents” OR “Gutta-percha Solvent” OR “Chloroform” OR “Eucalyptol” OR “Orange Oil” OR “Endosolv E” OR “Xylene” AND "Gutta-Percha"[Mesh] OR "Gutta-Percha removal" NOT “Sealing” NOT “Bond”.
- Scopus: "Solvent" OR "Solvents" OR "Gutta-percha Solvent" OR "Chloroform" OR "Eucalyptol" OR "Orange Oil" OR "Endosolv E" OR "Xylene" AND "Gutta-Percha" [mesh] OR "Gutta-Percha removal" AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re")) AND (LIMIT-TO (LANGUAGE , "English")).

Table 2 – Summary of findings of included reviews.

Author	Type of study	Data base considered	Eligibility criteria	Number of included articles	Quality/Level of evidence reported by authors	Main findings
Rossi-Fedele et al. 2017	*Systematic Review*	PubMed and major endodontic journals (Australian Endodontic Journal; Dental Traumatology (previously named Endodontics and Dental Traumatology); International Endodontic Journal; Journal of Endodontics; and Oral Surgery, Oral Medicine, Oral Pathology (previously published as Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics)	Not reported	22	Not reported	Corroborate the use of solvents to enhance penetration of files, but not to improve cleaning of the root canal. However, it emphasizes that all protocols considered not fully remove the root canal filling materials. Thus, larger preparation sizes and hybrid techniques were

						recommended to reduce the remaining material.
Good et al. 2012	Literature Review	Not reported	Not reported	Not reported	Not reported	Corroborate the use of solvents in coronal and middle thirds of root canals cautiously to avoid its toxic potential.

Table 3 – Summary of findings of included experimental studies (in vitro and ex vivo).

Author	Study design	Obturation			Retreatment				Control condition	Final Irrigation	Analysis		Main findings
		Method/technique	Cement type used	Restoration	Instrumentation technique	Solvents used	Time of exposure	Moment of using			Method to access GP presence	Type and characteristics of the substrate	
Akhavan et al. 2012	In vitro	Lateral condensation technique (main and secondary GP cones)	AH26 - root canal sealer resin-based, non-acrylic, eugenol-free cement (Dentsply)	Sealed with temporary material (NR)	Mechanical instrumentation (Gates Glidden #3 + Mtwo or Gates Glidden #3 + D-RaCe)	Chloroform	NR	Prior and after each instrument (1x)	Absence of solvent (only instrument)	5.25% NaOCl	Visual inspection at stereomicroscope	Human molars, sectioned vertically, before analysis	The use of solvent difficulted GP removal on coronal and middle sections. No effect on apical. Thus, there was no beneficial use of solvents.
Aydin et al. 2009	Ex vivo	Lateral condensation technique (main and secondary GP cones)	Diaket - polyketone-based root canal sealer (3M Espe)	NR	Mechanical instrumentation (HERO 642) or Manual instrumentation (Hedstroem + H-files)	Ethyl ether–chloroform mixture	NR	Between instruments, until achieving the working length	Absence of solvent (only instrument)	NR	Analyzing digitally photographs of each section. The percentage of the residual canal filling was determined for each root third of each canal.	Human molars, sectioned horizontally	Canal filling remnants were least in the H-files + solvent group, but there was no statistically significant difference between two hand file groups. There was significantly less canal filling in the hand file groups than in the HERO 642 groups.

Barreto et al. 2016	In vitro	Single cone technique (main cone only)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (ProTaper Retreatment + Pro Taper Next)	Orange Oil	1min	Between instruments	Absence of solvent (only instrument)	2.5% NaOCl.	CT scan	Human molars	Passive ultrasonic irrigation with solvent did not improve the removal of filling material from mesial roots of mandibular molars when compared to conventional irrigation with NaOCl. Thus, there was no beneficial use of solvents.
Betti et al. 2001	In vitro	Lateral condensation technique (main and secondary GP cones)	Zinc oxide eugenol based root canal sealer (SS White)	Sealed with temporary material (Cimpat, Septodont)	Mechanical instrumentation (Quantec SC rotary instruments) or manual instrumentation (K-type file + Hedstroem)	Xylol	NR	Prior retreatment	Absence of solvent (only instrument)	NR	Quantitative analysis of teeth halves using a scanner and evaluated using Sigma Scan software. Qualitative analysis of radiographs taken after the removal of the filling, and each third of the canal was evaluated. The radiographs were digitized using a scanner and each half evaluated for quantitative analysis	Human central incisors	Hand instruments and solvent cleaned canals more effectively.
Betti et al. 2009	In vitro	Lateral condensation technique (main and secondary GP cones)	Zinc oxide eugenol based root canal sealer (Septodont)	Sealed with temporary material (Coltosol, Coltene)	Manual instrumentation (K-type file + Hedstroem)	Xylol	NR	Prior retreatment	Absence of solvent (only instrument)	NR	Radiographs were taken and the teeth were grooved longitudinally and split. Each half of the root and each radiograph were digitized using a scanner. The area of residual debris was measured using computer software.	Human central incisors, sectioned vertically	Hand instruments yielded better root canal cleanliness. Hand files performed significantly better than Profile series 29 instruments in the radiographic analysis; however, there were no statistical differences in the teeth

													halves analysis.
Betti et al. 2010	Ex vivo	Lateral condensation technique (main and secondary GP cones)	Zinc oxide eugenol based root canal sealer (Septodont)	Sealed with temporary material (Coltosol, Coltene)	Mechanical instrumentation (GPX instruments) or manual instrumentation (K-type file + Hedstroem)	Xylol	NR	Prior retreatment	Absence of solvent (only instrument)	NR	Radiographs were taken, and the teeth were grooved longitudinally and split. The area of residual debris was measured using a software.	Human central incisors, sectioned vertically	In general, the hand files group performed significantly better, but there were no statistical differences among the GPX groups. The use of xylol as solvent in GPX groups neither shortened the time for filling removal nor improved the filling materials removal. Thus, there was no beneficial use of solvents.
Bhagavaldas et al. 2017	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (MtwoR or D-RaCe)	Endosolv R	NR	Before each file	Absence of solvent (only instrument)	NR	Visual inspection at stereomicroscope	Human first premolars, sectioned vertically	Root canals retreated with D-RaCe with or without the use of solvent showed significantly less filling material at all levels compared to Mtwo R with or without the solvent. The use of solvent, had a negative impact on the removal of the filing material, even though statistically not significant. Thus, there was no beneficial use of solvents.
Boariu et al. 2015	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal	NR	Mechanical instrumentation (ProTaper Universal or K3 Endo rotary	Eucalyptol	NR	At each third of the working length	Absence of solvent (only instrument)	NaOCl 5.25%	Radiographic analysis and, after the teeth were longitudinally	Human single rooted teeth, sectioned vertically	K3 and Gates Glidden systems alone or associated with

			sealer (Dentsply)		nickel-titanium system) or manual instrumentation (Gates Glidden + K-type file)						sectioned, each half of the teeth was examined under the dental operating microscope		Eucalyptol demonstrated that there is no significant difference between their efficiency in removal of endodontic materials. The dental microscope analysis showed that the use of organic solvents leads to an increase in the residues of GP and sealer on root canal walls and inside the dentinal tubules. Thus, there was no beneficial use of solvents.
Bodrumlu et al. 2008	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Manual instrumentation (Gates Glidden drill + K-type file + Hedstroem)	Chloroform	NR	After use of Gates glidden drill	Absence of solvent (only instrument)	NR	Visual inspection at stereomicroscope	Human anterior teeth and molars, sectioned vertically	There was no statistical difference in degree of removal of material among all removal techniques. Thus, there was no beneficial use of solvents.
Campello et al. 2019	In vitro	Single cone technique (main cone only)	Sealer 26 - calcium hydroxide based root canal sealer (Denstply)	NR	Mechanical instrumentation (Gates Glidden drill + MtwoR + Supplementary cleaning step with XP-endo Finisher R)	Eucalyptol	3 min	After use of Gates glidden drill and before use XP-endo Finisher R	Absence of solvent (only instrument)	2.5% NaOCl.	Micro-CT	Human molars	The use of a solvent did not improve filling material removal. Thus, there was no beneficial use of solvents.
Colaco et al. 2015	In vitro	Lateral condensation technique (main and secondary GP cones)	Zinc oxide eugenol based root canal sealer (Dentsply)	NR	Manual instrumentation (H-files)	Xylene	NR	Prior retreatment	Absence of solvent (only instrument)	NR	Microscope	Single-rooted human teeth, sectioned vertically	Rotary techniques (control mechanical group) significantly left lesser GP remnants than manual technique

													(experimental group). In manual techniques, Hand files + Xylene significantly left lesser GP remnants than control manual group.
Colombo et al. 2016	In vitro	Tagger's hybrid technique (Vertically condensed gutta-percha)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavit G, 3M ESPE)	Mechanical instrumentation (ProTaper D NiTi rotary instruments or WaveOne)	Chloroform	NR	ProTaper group: after first instrument; WO group: prior retreatment.	Absence of solvent (only instrument)	NR	Operating microscope	Human premolars, sectioned vertically	There was no significant difference between groups regarding the amount of residual filling material. Thus, there was no beneficial use of solvents.
Das et al. 2017	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (NR)	Mechanical instrumentation (ProTaper Universal Retreatment files or Mtwo retreatment files or R-Endo)	RC solve (Prime Dental)	5 min	Prior retreatment	Absence of solvent (only instrument)	NR	Visual inspection at stereomicroscope	Single-rooted human mandibular premolars, sectioned vertically	While ProTaper Universal was found to be equally effective with/without the use of solvent, Mtwo retreatment rotary instrumentation system showed increased effectiveness in removal of gutta-percha without the use of solvent. Thus, there was no beneficial use of solvents.
Dadresanfar et al. 2011	Ex vivo	Lateral condensation technique (main and secondary GP cones)	AH26 - root canal sealer resin-based, non acrylic, eugenol-free cement (Dentsply)	Sealed with temporary material (Coltosol, Coltene)	Mechanical instrumentation (Mtwo Retreatment or ProTaper)	Chloroform	NR	Before each instrument	Absence of solvent (only instrument)	NR	Visual inspection at stereomicroscope and scanning electron microscopy	Human, single-canalled distal roots of mandibular molars, sectioned vertically	Mtwo R left fewer filling remnants in all locations of the canal compared to ProTaper Universal, however the solvent adversely effected gutta-percha

													removal in coronal and middle thirds by Mtwo R. Chloroform as a solvent adversely affects the efficiencies of Mtwo R instruments. Thus, there was no beneficial use of solvents.
Ezzie et al. 2006	In vitro	Continuous wave compaction and back-fill technique	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Glass ionomer restorative material (Fuji IX GP, GC America)	Mechanical instrumentation (ProFile 0.06 rotary files)	Chloroform	NR	During the retreatmen t	Absence of solvent (only instrumen t)	17% EDTA + 5.25% NaOCl	Visual inspection at stereomicroscop e and electron microscopy	Human, single-canal teeth, sectioned vertically	The material removal technique was not a significant factor in determining the cleanliness of the canal walls. Thus, there was no beneficial use of solvents.
Fariniuk et al. 2017	In vitro	Hybrid thermomechanical compaction technique	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Glass ionomer restorative cement (Vidrion R, SS White)	Manual instrumentation (Gates Glidden drill + Hedstroem)	Eucalyptol	NR	Between instrument s	Absence of solvent (only instrumen t)	NR	The half of roots were scanned and analysis was perfomed with software.	Human, mandibular premolars, sectioned vertically	Hand files group showed the highest quantity of GP remnant and amount of filling material, being statistically different in all thirds. There was no beneficial use of solvents.
Ferreira et al. 2001	In vitro	Tagger's hybrid technique (Vertically condensed gutta-percha)	Pulp Canal sealer - zinc oxide eugenol based root canal sealer (Sybron Endo)	NR	Mechanical instrumentation (Gates Glidden drill + ProFiles 0.04) or manual instrumentation (Gates Glidden drill + K-Flexofiles or Gates Glidden drill + Hedstroem)	Chloroform	NR	After use of Gates glidden drill (all groups) and during the process once (just K-Flexofiles group)	Absence of solvent (only instrumen t)	Water	Microfocal macroradiograph ic technique	Human, molars and premolars with curved roots	The results indicated that ProFiles or hand files with chloroform produced similarly clean canals. The efficacy of gutta-percha removal with ProFiles is much greater when chloroform is used. There was no

													statistically significant difference in canal cleanliness between K-Flexofiles and ProFiles.
Gu et al. 2008	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mixed instrumentation (Glidden drill + Hedstroem + ProTaper Universal or Gates Glidden drill + Hedstroem + K-Flexofiles)	Chloroform	NR	After use of Gates glidden drill	Absence of solvent (only instrumen t)	5.25% NaOCl + 17% EDTA	Visual inspection at stereomicroscop e	Human, maxillary anterior teeth.	The canal wall cleanliness was less satisfactory in groups which chloroform had been used. Thus, there was no beneficial use of solvents.
Hassanloo et al. 2007	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (Gates Glidden drill + K3 rotatory)	Chloroform	NR	After use of Gates glidden drill	Absence of solvent (only instrumen t)	2.5% NaOCl + sterile saline	Dissecting microscope	Human, maxillary incisors, sectioned vertically	The use of chloroform decreased residue in both groups.
Horvath et al. 2009	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Coltosol, Coltene)	Manual instrumentation (Gates Glidden drill+ Hedstroem)	Eucalyptol or Chloroform	NR	During the retreatmen t	Absence of solvent (only instrumen t)	17% EDTA + 3% NaOCl	Scanning electron microscopic	Human, maxillary incisor and canine, sectioned vertically	Solvents led to more gutta-percha and sealer remnants on root canal walls and inside dentinal tubules. Thus, there was no beneficial use of solvents.
Hulsmann et al. 1997	In vitro	Lateral condensation technique (main and secondary GP cones)	AH26 - root canal sealer resin-based, non acrylic, eugenol-free cement (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Manual instrumentation (Hedstroem)	Chloroform	NR	During the retreatmen t	Absence of solvent (only instrumen t)	NR	The slices were photographed under a light microscope and the specimens were evaluated	Human, single-rooted anterior and premolar, sectioned vertically	The best root canal cleanliness was achieved with Hedstrom files alone. Thus, there was no beneficial use of solvents.
Hulsmann et al. 2004	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (FlexMaster or GT Rotary or ProTaper) or manual instrumentation (Hedstroem)	Eucalyptol	NR	During the retreatmen t	Absence of solvent (only instrumen t)	NR	The slices were photographed under a light microscope and the specimens were evaluated	Human, single-rooted anterior teeth, sectioned vertically	The use of eucalyptol as a solvent shortened the time to reach the working length and to remove the gutta-percha, but this was

												not significant. Nevertheless, completely cleaned root canal walls could not be achieved with any of the techniques under investigation.
Jain et al. 2015	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (Cavity, 3M ESPE)	Manual instrumentation (Gates Glidden drills + Hedstroem + H files)	Chloroform	15 sec	After use of Gates glidden drill	Absence of solvent (only instrument)	3% NaOCl	Scanning electron microscopic	Human, mandibular premolar, sectioned vertically	The chloroform should be utilized only when mechanical methods fail to achieve retrieval of gutta percha in retreatment cases.
Kfir et al. 2012	In vitro	Lateral condensation technique (main and secondary GP cones)	AH26 - root canal sealer resin-based, non acrylic, eugenol-free cement (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (SafeSider or ProTaper Universal Retreatment) or manual instrumentation (Hedstroem)	Chloroform	NR	Prior retreatment	Absence of solvent (only instrument)	2.5% NaOCl	The roots were assessed with radiographic evaluation using a software and the half of roots were evaluated using endodontic operating microscope	Human, maxillary anterior single-rooted, sectioned vertically	Radiographic evaluation of root filling material left in the canal revealed no difference between the groups. Microscopic evaluation revealed substantial amounts of root filling residues in all groups with no difference amongst them. The use of chloroform in combination with mechanized instruments failed to reduce retreatment time. Thus, there was no beneficial use of solvents.
Khalilah et al. 2013	In vitro	Lateral condensation technique (main and secondary GP cones)	AH26 - root canal sealer resin-based,	Sealed with temporary material	Mechanical instrumentation (ProTaper Universal Retreatment) or	Chloroform	2 min (H file group) or until soften the	After use of Gates glidden drill (group H Files);	Absence of solvent (only instrument)	2.5% NaOCl	Visual inspection at stereomicroscope	Human, mandibular premolars with one canal,	In all groups, no significant difference was found in remaining

			non acrylic, eugenol-free cement (Dentsply)	(Coltosol, Coltene)	manual instrumentation (Gates glidden drill + H files)		gutta (PTUR group)	after the use of first PTU file and refreshed between files (1x).				sectioned vertically	gutta-percha and sealer with or without using chloroform, but chloroform shortened the time of retreatment.
Kumar et al. 2012	In vitro	Lateral condensation technique (main and secondary GP cones)	Zinc oxide eugenol-based root canal sealer (NR)	NR	Mechanical instrumentation (ProTaper Universal Retreatment) or manual instrumentation (Gates glidden drill + Hedstroem)	RC Solve (Prime Dental)	NR	After use of Gates glidden drill (group Hedstroem Files); after the use of first PTUR file	Absence of solvent (only instrumen t)	NR	Visual inspection at stereomicroscop e	Human, mandibular premolars, sectioned vertically	There was no statistical significant differences regarding the amount of filling remnants between groups. Thus, there was no beneficial use of solvents.
Latheef et al. 2016	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Sealed with temporary material (NR)	Mechanical instrumentation (ProTaper Retreatment + manual irrigation or ProTaper Universal Retreatment + PUI)	Endosolv R (Septodont)	NR	Before PTUR	Absence of solvent (only instrumen t)	Saline solution	Scanning electron microscopic	Maxillary molars 1st and 2nd molars, sectioned vertically	Endodontic retreatment without using any solvent showed more cleanliness of dentinal tubules when compared with the groups using Endosolv R solvent. The use of Endosolv R led to more gutta-percha and sealer on root canal walls and inside dentinal tubules. Thus, there was no beneficial use of solvents.
Ma et al. 2012	In vitro	Continuous wave of condensation or Lateral condensation technique (main and secondary GP cones)	iRoot SP - bioceramic root canal sealer (Innovativ e BioCerami x Inc)	Sealed with temporary material (Caviton, GC Europe)	Mechanical instrumentation (ProTaper Universal Retreatment)	Chloroform	NR	Prior retreatmen t	Absence of solvent (only instrumen t)	5% NaOCl	Micro-CT, after and before de retreatment	Human, mandibular incisor teeth	It was impossible to remove root canal filling material completely in the oval canals regardless of retreatment by using PTUR with or without a solvent.

													Thus, there was no beneficial use of solvents.
Mittal et al. 2014	In vitro	NR	Zinc oxide eugenol based root canal sealer (NR)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (Gates glidden drill + ProTaper Universal Retreatment or Gates glidden drill + Mtwo) or manual instrumentation (Gates glidden drill + H file);	Tetrachloroethylene (Amdent)	1 min	After use of Gates glidden drill	Absence of solvent (only instrument)	NR	CT scan, after and before de retreatment	Human, mandibular molar	None of the technique was 100% effective in removing the filling materials, but the ProTaper retreatment system with solvent was better.
Muller et al. 2013	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	Glass ionomer restorative cement (Vermeer, 3M ESPE)	Mechanical instrumentation (ProTaper Universal Retreatment + PUI with solvent)	Endosolv R (Sepodont)	NR	At the end with PUI (solvent or DW)	Absence of solvent (only instrument)	DW	Scanning electron microscopic	Human, premolar teeth, sectioned vertically	PUI with Endosolv R or distilled water was not effective in filling debris removal from root canal walls. Thus, there was no beneficial use of solvents.
Rached-Junior et al. 2014	In vitro	Tagger's hybrid technique (Vertically condensed gutta-percha)	Endofill - zinc oxide eugenol based root canal sealer (Denstply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (ProTaper Retreatment or ultrasound)	Xylol	NR	Between instruments	Absence of solvent (only instrument)	DW	Confocal microscopy	Human, root canals of incisors	The use of ultrasound/xylol under an operating microscope (OM) provided better results. The use of xylol was associated with greater removal of filling material in both ProTaper retreatment and ultrasound groups, regardless of the vision (directly or through surgical microscope).
Reddy et al. 2013	In vitro	Lateral condensation technique (main and secondary GP cones)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	NR	Mechanical instrumentation (ProTaper Retreatment) or manual instrumentation (Hedstroem)	Xylene	NR	NR	Absence of solvent (only instrument)	NR	Visual inspection at stereomicroscope	Human, single rooted anterior teeth, sectioned vertically	The use of xylene resulted in better root canal cleanliness, first with

													mechanical instrumentation, after using manual instrumentation.
Sae-Lim et al. 2000	In vitro	Lateral condensation technique (main and secondary GP cones)	Roth's Sealer - zinc oxide eugenol based root canal sealer	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (Profile NiTi rotatory) or manual instrumentation (Hedstroem + K-Flex)	Chloroform	NR	Prior retreatment	Absence of solvent (only instrument)	1% NaOCl	Visual inspection at light microscopes	Human, single-rooted anterior teeth, sectioned vertically	There was no beneficial use of solvents.
Saglam et al. 2014	In vitro	Lateral condensation technique (main and secondary GP cones)	AH26 - root canal sealer resin-based, non acrylic, eugenol-free cement (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (ProTaper Universal Retreatment)	Chloroform or Endosolv R	2 min	After the first PTUR file	Absence of solvent (only instrument)	1% NaOCl	Micro-CT, after and before de retreatment	Human, molar teeth	The use of chloroform or Endosolv R did not result in less root canal filling material remnants when compared with retreatment without solvent. Thus, there was no beneficial use of solvents.
Salgado et al. 2019	In vitro	Tagger's hybrid technique (Vertically condensed gutta-percha)	AH Plus - epoxy resin-based root canal sealer (Dentsply)	NR	Mechanical instrumentation (ProTaper Universal Retreatment)	Orange Oil	2 min	Prior retreatment (1min) and after the first file (1min)	Absence of solvent (only instrument)	2% CHX gel with an orange oil solvent or 5% NaOCl with an orange oil solvent	Scanning electron microscopic	Human, maxillary premolars, sectioned vertically	Groups in which a solvent was used showed a less effective cleaning ability. The use of orange oil with NaOCl or CHX does not improve the removal of residual root canal filling materials. Thus, there was no beneficial use of solvents.
Takahashi et al. 2009	In vitro	Thermomechanical compaction with a hybrid technique	Zinc oxide eugenol based root canal sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Mechanical instrumentation (ProTaper Universal Retreatment) or manual instrumentation (Gates glidden drill + K-files)	Chloroform	NR	After use of Gates glidden drill (K files group); after using first PTUR file (PTUR group)	Absence of solvent (only instrument)	2.5%NaOCl	Operating microscope	Human, maxillary anterior teeth, sectioned vertically	All of the techniques proved helpful for the removal of endodontic filling material, and they were similar in material

													remaining after retreatment, but the ProTaper Universal rotary retreatment system without chloroform was faster. Thus, there was no beneficial use of solvents.
Vidučić et al. 2003	In vitro	Lateral condensation technique (main and secondary GP cones)	Diaket - polyketone -based root canal sealer (3M Espe)	Sealed with temporary material (Cavit, 3M ESPE)	Nd:YAG laser with Eucalyptol or Nd:YAG laser with dimethylformamide	Eucalyptol or DMF	18 sec for eucalyptol; 16 sec for DMF	Prior retreatment	Absence of solvent (only Nd:YAG laser)	NR	The specimens were examined under binocular loupe and with photographs with the aid of a computer program	Human, permanent maxillary central incisors, sectioned vertically	The Nd:YAG laser is capable of softening gutta-percha in vitro, but the addition of solvents did not improve its removal. Thus, there was no beneficial use of solvents.
Wilcox 1993	In vitro	Lateral condensation technique (main and secondary GP cones)	Roth's Sealer - zinc oxide eugenol based root canal sealer	Sealed with temporary material (Cavit, 3M ESPE)	Manual instrumentation (Hand file size 20)	Chloroform	NR	During the retreatment	Absence of solvent (only instrument)	NR	Photographed and projected onto white paper and the remaining gutta-percha and canal outlines were traced.	Human, single canal teeth, sectioned vertically	The cleanest canals were those treated without chloroform and in which the carrier was easy to remove. The use of solvent should be considered only if GP is removed with difficulty.
Wolcott et al. 1999	In vitro	NR	Thermaseal - epoxy-based resin sealer (Dentsply)	Sealed with temporary material (Cavit, 3M ESPE)	Manual instrumentation (NiTi hand files)	Chloroform	NR	Prior retreatment and was replenished as needed until the files penetrated to within 5 mm of the working length.	Absence of solvent (only instrument)	NR	Visual inspection at stereomicroscope	Human, mandibular premolars, sectioned horizontally	The difference between the two groups in the amount of filling material removed was not significant. Thus, there was no beneficial use of solvents.

Legends: Gutta-percha (GP); Not reported (NR); Sodium hypochlorite (NaOCl); Computed tomography scan (CT scan); Gutta Percha Removers (GPX); Micro computed tomography (Micro-CT); WaveOne (WO); Ethylenediamine tetraacetic acid (EDTA); ProTaper Universal Retreatment (PTUR); Distilled water (DW); dimethylformamide (DMF); RC Solve (orange oil derivative with the basic ingredient D-Limonene); Endosolv (6.5% formamide and 33.5% phenylethelic acid)

Figure Captions

Figure 1 – Flowchart of study selection.

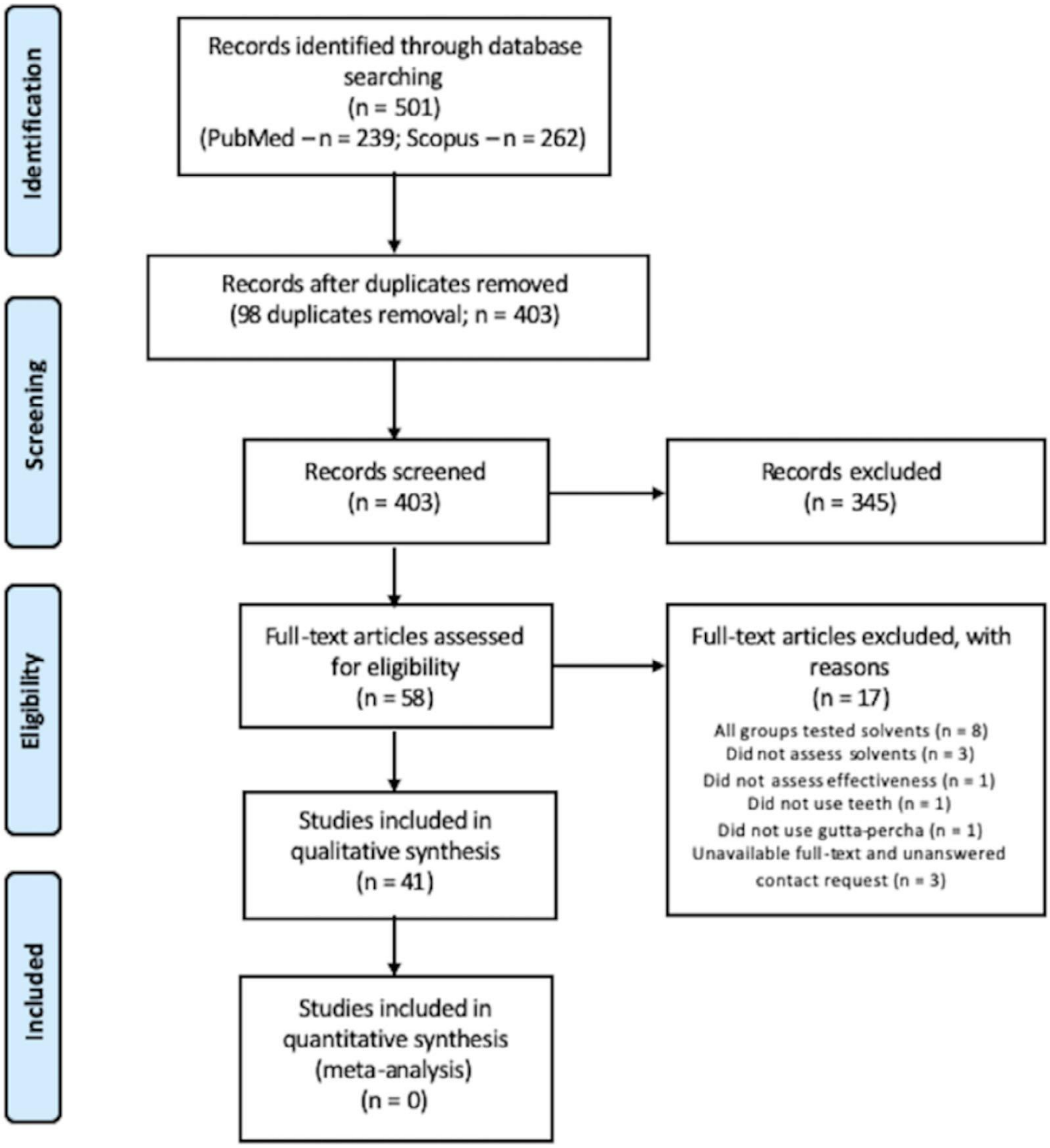

Figure 2 – Word cloud representing the solvents used. The more a substance was used, the bigger it appears in the word cloud.

5. ARTIGO 3

Title page

Effect of root canal irrigants on push-out bond strength of endodontic sealers: a systematic review

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ABSTRACT

This study aimed to assess root canal irrigants' effect on the bond strength between endodontic sealers and root canal dentin, through a systematic review. The study protocol is available online (https://osf.io/x9tw4/). We selected studies considering the effects of root canal irrigants on sealer bond strength and comparing the influence of such agents used during the endodontic treatment and/or at final irrigation. The search was performed in the PubMed and Scopus databases. The screening was performed by two independent researchers. Data were extracted by one researcher and verified by another. A descriptive analysis was performed. A total of 39 studies were included. The majority demonstrated that using some irrigant substances such as ethylenediaminetetraacetic acid, maleic acid, phosphoric acid, and peracetic acid could improve, or at least not damage, the pushout bond strength. In opposition, a decrease in this outcome was observed when using only sodium hypochlorite or saline solution. The use of irrigant substances capable of demineralizing the surface of root canal dentin and/or removing the remnant smear layer seems to enhance, or, at least, does not compromise the push-out bond strength of the sealer to root dentin.

KEYWORDS

Adhesion; AHPlus; bioceramic; gutta-percha; root canal solutions

1. Introduction

During endodontic treatment, it is necessary to prepare the root canals for adequate cleanness and debridement [1]. This process can result in the presence of a smear layer, debris, and necrotic tissues [1]. Thus, it is crucial to use irrigant solutions to remove such undesirable remnants. For which, there are different solutions, presenting distinct compositions and concentrations. Alternative presence of surfactants and association with chelating agents have also been tested [1].

Some studies have already investigated the effect of these solutions on the mechanical properties of endodontically treated teeth. They stated that factors such as solution concentration, exposure time, and its association with other agents (such as surfactants or chelating agents) might be capable of modifying the root dentin surface, promoting structural alterations (decrease the Ca/P ratio), altering surface roughness and hardness, among other characteristics [1]. Based on this, it is logical to assume that any dentin alteration promoted by using different irrigant solutions could also influence its interaction with the sealer used during root canal obturation. This might interfere in the adhesion (bond strength) between such substrates and also compromise the obtained apical sealing, which could be a predisposing factor to decrease the treatment longevity [2].

Push-out bond strength tests may determine the extent of resistance to a filling material's dislodgement applied to the treated root canal dentine. Many studies have been carried out using such test to assess the effect of different irrigant solutions on the push-out bond strength of different endodontic sealers [3–8]. However, there is no consensus in the literature about the influence of different solutions on the push-out bond strength of the different endodontic sealers tested [9]. Thus, this study aimed to assess the effects of root canal irrigants on the push-out bond strength of endodontic sealers used to obturate endodontic treated teeth, through a systematic review.

2. Materials and methods

This study was not registered in a registry database (e.g. PROSPERO) due to the inclusion criteria' nature (in vitro studies). However, the study protocol is available online (https://osf.io/x9tw4/). The reporting of this study is based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [10].

2.1. Inclusion criteria

We selected studies in dentistry written in the English language which considered the effects of root canal irrigants on push-out bond strength of endodontic sealers and compared the influence of such agents during the endodontic treatment and/or in final irrigation. Studies were included regardless if chelating agents or surfactants were used, irrespective of the teeth type (human or animal), regardless if the use of irrigants were associated with passive or active methods, and regardless of the instrumentation type or obturation method. The outcome (bond strength) should be measured by the pushout test. Only in vitro studies were included concerning the adopted study designs. Study groups testing other root filling materials (not gutta-percha) were not considered.

2.2. Search

The search was performed in two databases: MEDLINE (PubMed) and Scopus, limited to articles written in the English language and without time restriction. The search strategy is presented in Table 1 and was based on PubMed Mesh terms and specific terms of Scopus. The last search was conducted in February 2020.

2.3. Screening

The search was initially undertaken using the EndNote program (EndNote X9, Thomson Reuters, New York, NY). Two researchers identified articles by first analyzing titles and abstracts for relevance and the eligibility criteria' presence. Retrieved records were classified as include, exclude, or uncertain. The full-text articles of the included and uncertain documents were selected for further eligibility screening by the same two reviewers. Discrepancies in the screening of titles/abstracts and full-text articles were resolved through a discussion. In case of disagreement, the opinion of a third reviewer was consulted.

2.4. Data extraction

We created a form using the Excel program, which three reviewers tested to reach consensus for the data collections. Then, one of the reviewers extracted the data, and another checked it. The following data were collected: author, year, irrigant solution protocol used during and/or in the final endodontic treatment (including concentration, the amount used, and whether surfactants were used with irrigant solutions); chelating agents used during the treatment; method/technique used for instrumentation during retreatment (manual or rotary); method/technique used for obturation; sealer used for obturation (calcium silicate-based, epoxy resin-based, silicone-based and methacrylate-based sealers); control groups used; type of the teeth (human or animal); the time between obturation and push-out test; and the main study findings with a focus on the push-out test results.

2.5. Risk of bias

The risk of bias of included studies was assessed based on previous studies [11,12]. The following parameters were considered: teeth randomization, materials used according to the manufacturer's instruction, permanent storage of teeth in hydric solution, the blindness of outcome assessment. The parameters used were discussed by all researchers involved; the judgment was carried out by one researcher and verified by another. Assessment of risk of bias was conducted using Review Manager 5.3 software.

2.6. Data analysis

We performed a descriptive analysis considering the characteristics of included studies and identifying the effects of root canal irrigants on push-out bond strength of endodontic sealers contemplating different substances used.

3. Results

3.1. Search

Figure 1 shows a flow chart of the study selection. A total of 39 studies fulfilled the selection criteria and were included in the qualitative analysis (See supplemental material).

3.2. Characteristics of included studies

The ProTaper rotary system (Dentsply Maillefer, Ballaigues, Switzerland) was the method most used for instrumentation of specimens. The most tested irrigant solution was sodium hypochlorite (NaOCl), regardless of its concentration. However, when considering a specific substance with a standardized concentration, the substance most tested was 17% ethylenediaminetetraacetic acid (EDTA). The most used type of sealer was resin-based (the majority used the AH Plus – Dentsply DeTrey, Konstaz, Germany), whereas the single-cone technique was the most used method for obturation. The type of teeth most evaluated was human.

3.3. Descriptive analysis

Table 1 shows the characteristics of the included studies and the results related to the influence of irrigant solutions tested on push-out bond strength (POBS) of endodontic sealers. Most studies (21) [3–7,13–27], regardless of the irrigant solutions tested, generally found that at least one substance positively affected (increased) the POBS.

3.3.1. Sodium hypochlorite

One study demonstrated that NaOCl as the final irrigant decreases the POBS of Tricalcium silicate-based sealer (Endosequence BC sealer), whereas cetrimide-cetyl-trimethyl- ammonium-bromide (QMix) provided the highest POBS [7]. Other studies also found that NaOCl significantly decreased the resin-based sealer's bond strength (AH Plus) to dentin [6,28].

Association and variations between 5.25% NaOCl and 2% CHX were studied by Gupta et al. [29]. In that study, the authors concluded that the highest bond strength is noted in the resin-based sealer group without precipitate, i.e. the group irrigated with saline solution plus 2% CHX without association with NaOCl. Another association tested was 2.6% NaOCl plus a mixture of tetracycline, citric acid, and detergent (MTAD), resulting in significantly lower mean POBS for a resin-based sealer [19].

3.3.2. Chlorhexidine

The use of 2% CHX as the final rinse, following 17% EDTA, improved the POBS of GP and the resin-based sealer [17]. When 2% CHX gel was used during chemomechanical preparation, 17% EDTA enabled better bond strength values [14]. However, when the bond strength of GP and a resin-based sealer were tested after using an MTAD or MTAD þ 2%CHX, the resin-based sealer was adversely affected by these substances [30]. Still, Razmi et al. [31] tested the effect of the 2% CHX and 5.25% NaOCl on POBS, resin-based sealer, and Endosequence BC sealer and concluded that although the bond strength of the resin-based sealer was not affected by the irrigant type, CHX reduced the bond strength of bioceramic sealer with calcium silicate-based composition [31].

3.3.3. Peracetic acid

The influence of the Peracetic Acid (PAA) on POBS was controversial. Gaddala et al. [5] assessed the use of this substance as a final irrigant compared with Smear Clear (irrigant solution containing EDTA, detergent, and cetrimide) and found that the PAA improved the bond strength of root canal sealers compared to the control group (distilled water), but was not statistically significant compared to Smear Clear. Keine et al. [26] found no difference between the use of PAA and NaOCl-EDTA-NaOCl groups, but the root canal sealer showed higher values for bond strength in both groups than in the groups treated with NaOCl and saline groups.

3.3.4. Chelating agents

In relation to EDTA, the use of this substance after irrigant solutions (like 2.5% NaOCl) increased the POBS [6,13,14,17,18,20,26,27] as well as the EDTA plus Cetavlon (EDTAC) [22] or REDTA (17% EDTA þ 0.84 g cetyltrimethylammonium bromide) and EDTA-T (17% EDTA þ 1.25% sodium lauryl ether sulfate) [24].

On the other hand, Mozayeni et al. [16] found that the mean bond strength of resin-based sealer (AH26 - Dentsply Caulk, Germany) to dentin walls was significantly greater using MTAD compared with a combination of EDTA and NaOCl or saline groups. The same was concluded by Uzunoglu et al. [21], showing that the samples irrigated with QMix had higher POBS values than the samples irrigated with 17% EDTA. Similarly, other authors concluded that EDTA's use reduces the POBS on resin-based sealers [32] or on calcium silicate-based sealers [25].

The use of 7% maleic acid [19] and 37% phosphoric acid [14] increases the POBS on resin-based sealer when used after NaOCl.

3.3.5. Surfactant agents

Two studies [4,23] assessed the effect of surfactants on POBS of resin-based sealer. Fahmy et al. [4] compared the Tween 80 (T80) surfactant with different concentrations (1%, 0.9%, 0.6%) with 17% EDTA and 2.5% NaOCl with different substances combinations. The addition of T80 to the demineralizing irrigants improved the bond strength value of GP and resin-based sealer on dentin, whereas its addition to NaOCl demonstrated lower results. Guneser et al. [23] tested 5% NaOCl with various surfactants: 0.1% Benzalkonium chloride (BAK), 0.1% Tween 80; 0.1% Triton X-100 (TRX), and concluded that the POBS in the NaOClþTRX group was higher than in the control group (NaOCl without surfactants), NaOClþBAK, and NaOClþT80 groups, whereas the bond strength of the last two groups was similar to the control group.

3.3.6. Natural irrigants

The effect of proanthocyanidin (from grape seed extract capsules) and bamboo salt on the POBS of a resin-based sealer was tested after 5.25% NaOCl [33], and it was observed that the use of these natural substances eliminated the harmful effect on bond strength generated by NaOCl. Trindade et al. [8] concluded that the 2% CHX or 15% proanthocyanidin enhanced long-term POBS of methacrylate resin-based sealers (EndoREZ - Ultradent, South Jordan, USA).

3.4. Risk of bias

Figure 2 presents the risk of bias judgment. The majority of studies were judged as ‘low risk’ considering the domains ‘teeth randomization’ and ‘storage of teeth permanently in hydric solution’. All studies were judged as ‘unclear’ considering the blindness of outcome assessment. The majority of studies were judged as ‘unclear’ related to the ‘materials used according to the manufacturer’s instruction’ domain.

4. Discussion

This systematic review provides the first synthesis of information considering root canal irrigants' effect on push-out bond strength (POBS) of different endodontic sealers to root canal dentin. Our results showed that chelating agents or other substances with similar capacity to remove the smear layer after using irrigant solutions seem to increase the POBS of the endodontic sealer.

The use of substances that promote smear layer removal seemed to increase the POBS, regardless of the type of endodontic sealer used and the irrigant solution used before applying the demineralizing agent and. These findings could be related to the alteration on the treated dentin surface since EDTA, maleic acid or phosphoric acid (chelating agents), and peracetic acid (used as the final rinse solution) are used for removing the smear layer and consequently decalcification of the root canal surface [13,14,19,26]. These properties of the cited substances may improve the contact between the endodontic sealer and dentin, facilitating molecular attraction and adhesion or chemical penetration for the micromechanical interlocking of the sealer [30].

Furthermore, the addition of surfactants to irrigants may reduce fluid tension and enhance these substances' wettability properties, influencing the adaptation of sealers and root canal dentin [4]. For this reason, Fahmy et al. [4] showed that T80 (Polysorbate 80) addition to the demineralizing irrigants improved the POBS using a resin-based sealer. Guneser et al. [23] found that the addition of Benzalkonium chloride (BAK) or T80 to NaOCl solution did not cause a POBS reduction, and irrigation with NaOCl plus Triton X-100 (TRX) increased the POBS values, most likely because the TRX has a higher surface tension-reduction ability than the other two surfactants.

NaOCl was the most frequently used substance in tests (disregarding different concentrations), probably because it is the most used irrigant solution by dentists [7]. The importance of NaOCl especially consists in the broad spectrum of antibacterial activity, but in relation to POBS, the use of NaOCl as a unique irrigant used during the endodontic treatment showed to decrease the push-out, regardless of the sealer used [6,7,19,28,29,33].

Additionally, POBS between resin-based sealers and root canal dentin was adversely affected by using 2% CHX, particularly after MTAD31, or by bioceramic sealer with calcium silicate-based composition [31]. However, the

POBS increased when EDTA was used after CHX [14,17]. The use of CHX plus MTAD or only MTAD adversely affected the POBS on a hydrophobic resin-based sealer. A possible explanation is that MTAD contains T80 detergent, which could increase dentin permeability, as well as penetration and diffusion into the dentinal tissues (and the intertubular fluid), affecting the interaction of hydrophobic sealer to the surface of root canal dentin [30].

Resin-based sealers were the most tested, especially AH Plus (Dentsply DeTrey, Konstaz, Germany), probably because this root canal sealer presents satisfactory physicochemical properties, long-term dimensional stability, low solubility and disintegration, good apical sealability and adhesion [8,18,31]. In relation to the effect of different irrigant solutions on POBS with this sealer, most studies showed that irrigants could not cause damage to POBS, and demineralizing irrigants such as peracetic acid or chelating agents could improve such outcomes [5,6,13,14,17–20,22,24,26,27]. This fact corroborates a previous study that showed that the epoxy resin-based sealers present good retention to root canal dentin with higher POBS values in relation to other endodontic sealers.

This systematic review presents some limitations. First, data extraction was not performed duplicated; however, one author reviewed any possible data inconsistencies. Second, the studies assessed the effect of different irrigant solutions on different endodontic sealers and the methods/techniques for instrumentation and obturations. All these factors lead to heterogeneity, which limits the exact comparison among studies. Third, a high proportion of included studies presented an 'unclear' risk of bias considering the domains 'blind outcome assessment' and 'materials used according to the manufacturer's instruction', which could be related to the poor reporting quality of some of the included studies.

Finally, our results are clinically relevant since the use of demineralizing agents and substances capable of removing the smear layer were shown to improve or at least not to cause damage to the bond strength between the endodontic sealer and root dentin, potentially providing better longevity and prognosis to endodontic treatment. In using these substances, clinicians will be combining the excellent effect of cleanness and disinfection without harming the bond strength of the sealer to the surface of the root canal dentin. In relation to new endodontic sealers such as bioceramics, few studies tested the effect of irrigant solutions on POBS; therefore, based on this review, more studies considering such systems are still encouraged.

5. Conclusion

Although the limitations of included studies, the use of irrigant substances capable of demineralizing the surface of root canal dentin and/or removing the remnant smear layer seem to enhance push-out bond strength, or at least does not reduce it.

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Table Captions

Table 1 – Search strategy.

Table 2 – Characteristics of included studies.

Table 3 – Effects of irrigant solutions on POBS of sealers.

Figure Captions

Figure 1 – Flow diagram of study selection.

Figure 2 – Review authors' judgements about each risk of bias item presented as percentages across all included studies and about each risk of bias item for each included study.

Table 1 – Search strategy

PUBMED
("Root Canal Irrigants"[Mesh] OR “Root Canal Irrigants" OR “Canal Irrigants, Root” OR “Irrigants, Root Canal” OR “Root Canal Medicaments” OR “Canal Medicaments, Root” OR “Medicaments, Root Canal” OR “Chlorhexidine” OR “EDTA” OR “Sodium hypochlorite” OR “chemical irrigant” OR “NaOCl” OR “CHX” OR “ethylenediamine tetraacetic acid")) AND ("sealer" OR "canals sealer" OR "Root Canal Sealer")) AND push out bond strength)
SCOPUS
"Root Canal Irrigants" OR "Canal Irrigants, Root" OR "Irrigants, Root Canal" OR "Root Canal Medicaments" OR "Canal Medicaments, Root" OR "Medicaments, Root Canal" OR "Chlorhexidine" OR "EDTA" OR "Sodium hypochlorite" OR "chemical irrigant" OR "NaOCl" OR "CHX" OR "ethylenediamine tetraacetic acid" AND "sealer" OR "canals sealer" OR "Root Canal Sealer" AND push AND out AND bond AND strength AND (LIMIT-TO (SUBJAREA , "DENT")) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re"))

Table 2 – Characteristics of included studies.

Author	Method/technique used for instrumentation	Method/technique used for obturation	Type of the teeth (human or animal)	Time between obturation and push-out test
Albino Souza, M., et al. (2017).	ProTaper rotary system	Lateral condensation technique	Human	37°C and 95% humidity for 20 days.
Antunes, P.V.S., et al (2020).	Reciproc	Unclear	Human	100% relative humidity and 37°C for 72 hours
Aranda-Garcia, A. J., et al. (2013).	ProTaper rotary system	Single-cone technique	Human	37°C and 100% humidity for 7 days
Cecchin, D., et al. (2017).	ProTaper rotary system	Cold lateral compaction technique	Human	2 weeks
Dalbem, F., et al. (2015).	K-files (manual)	Lateral condensation technique	Animal	37°C and 100% humidity for 7 days
Dinesh, K., et al. (2014).	K3 nickel-titanium rotary instruments	Thermoplasticized obturation technique	Human	100% humidity for 48 hours
Donnermeyer, D., et al. (2019).	NiTi F360 rotatory files	Single-cone technique	Human	7°C and 100% humidity for 2 months

El-Ma'aita, A. M., et al. (2013).	ProTaper rotary system	Thermoplastic injection technique	Human	37°C in synthetic tissue fluid (STF) for 7 days
Ertas, H. and B. Sagsen (2015).	ProTaper rotary system	Cold lateral compaction technique	Human	37°C for 3 days
Fahmy, S. H., et al. (2015).	ProTaper rotary system	Lateral condensation technique	Human	NR
Forough Reyhani, M., et al. (2014).	RaCe rotary system	Lateral condensation technique	Human	5% relative humidity and 37ºC
Franceschini, K. A., et al. (2016).	K3 rotary system	Lateral condensation technique	Human	37ºC and 100% relative humidity for 24 hours
Gaddala, N., et al. (2015).	ProTaper rotary system	Single-cone technique	Human	37°C, 100% humidity for three days
Gandhi, B., et al. (2016).	ProTaper rotary system	Single-cone technique	Human	37°C and 100% humidity for one week
Graziele Magro, M., et al. (2014).	ProTaper rotary system	Single-cone technique	Human	37°C and 100% humidity for 7 days
Gundogar, M., et al. (2018).	Protaper Next	Single-cone technique	Human	37°C and 100% relative humidity for seven days
Guneser, M. B., et al. (2017).	ProTaper rotary system	Single-cone technique	Human	37 °C and 100 % humidity for 2 weeks
Gupta, H., et al. (2013).	0.06 profile nickel titanium instruments	Unclear	Human	DW at 37°C for 24 hours
Güzel, C., et al. (2018).	ProTaper rotary system	Single-cone technique	Human	37ºC and 100% humidity for 2 weeks.
Hashem, A. A., et al. (2009).	K3 0.06 taper nickel-titanium rotary instruments	Single-cone technique	Human	100% humidity for 48 hours
Kamalasanan, R. R., et al. (2017).	ProTaper rotary system	Single-cone technique	Human	100% humidity for 48 hours and incubated for two weeks at 37°C
Keine, K. C., et al. (2019).	ProTaper rotary system	Single-cone technique	Human	37°C and 100% relative humidity for 7 days
Kumar, P., et al. (2019).	ProTaper rotary system	Single-cone technique	Human	DW for 7 days
Leal, F., et al. (2015).	ProTaper rotary system	Unclear	Human	37°C and 100% relative humidity for 1 week
Magro, M. G., et al. (2015).	ProTaper rotary system	Single-cone technique	Human	37°C and 100% humidity for 7 days
Mozayeni, M. A., et al. (2013).	FlexMaster nickel titanium rotary files + K-files	Cold lateral compaction technique	Human	100% humidity at 37°C for 24 h.
Ok, E., et al. (2013).	ProTaper rotary system	Lateral condensation technique	Human	37 °C and 95% humidity for 1 week

Pheenithicharoenkul, S. and A. Panichuttra (2016).	ProTaper rotary system	Lateral condensation technique	Human	37°C and 100% humidity for 48 h
Prado, M., et al. (2013).	Mtwo nickel-titanium rotary system	Gutta-percha cones	Human	37°C and 100% relative humidity for 2 weeks
Ravikumar, J., et al. (2014).	ProTaper rotary system	Single-cone technique	Human	100% humidity for 48 hours
Razmi, H., et al. (2016).	ProTaper rotary system	Lateral condensation technique	Human	37°C temperature and 90% humidity for one week.
Rocha, A. W., et al. (2012).	K-files (manual)	Cold lateral compaction; Vertical compaction	Animal	37°C and 100% humidity for 7 days
Shokouhinejad, N., et al. (2010).	Mtwo nickel-titanium rotary instruments	Lateral condensation technique	Human	7 days at 37°C with 100% humidity.
Shokouhinejad, N., et al. (2013).	Mtwo rotary instruments	Cold lateral compaction technique	Human	37°C and incubated for 7 days.
Souza, M. A., et al. (2019).	ProTaper rotary system	Lateral condensation technique	Human	37°C and 95% humidity for 21 days.
Stelzer, R., et al. (2014).	ProFile Nickel Titanium Rotary System	Cold lateral compaction technique	Human	1 week
Trindade, T. F., et al. (2018).	ProTaper rotary system	Cold lateral compaction technique	Animal	Water for 24 h or 6 months
Uzunoglu, E., et al. (2015).	ProTaper rotary system	Single-cone technique	Human	37°C in 100% humidity for 2 weeks
Yavari, H., et al. (2017).	RaCe rotary system	Lateral condesantion technique	Human	95% humidity and 37°C for a week

Table 3 – Effects of irrigant solutions on POBS of sealers.

Table 3. Effects of irrigant solutions on POBS of sealers.						
	Irrigant solutions					
Author	**During endodontic treatment**	**Final endodontic treatment**	**Final rinse**	**Surfactants**	**Sealer**	**Main findings**
Albino Souza, M., et al. (2017).	2.5% NaOCl (after each change of instrument, 5x) + 3 mL of 17% EDTA (Final	DW (control); 2% CHX; Qmix; 6.5% GSE.	All roots were irrigated with 5 mL of DW	NU	AH Plus	The final decontamination protocols showed similar bond strength values and did not interfere with the bond

	rinse) for 1 min + followed by irrigation with 5 mL of DW (all groups).					strength of filling material to root canal dentin.
Antunes, P.V.S., et al (2020)	2 mL of a 1% NaOCl (all groups)	5mL of 15% EDTA; 5 mL of 0.2% chitosan solution	NP	NU	AH Plus	The final irrigation with 15% EDTA or 0.2% chitosan achieved comparable effects in terms of reducing bond strength.
Aranda-Garcia, A. J., et al. (2013).	2.5% NaOCl (all groups)	DW (control); QMiX; SmearClear; 17% EDTA	2.5% NaOCl (all groups)	NU	AH Plus	The POBS values of irrigants testing were superior to the control group. The final rinse with these solutions promoted similar POBS values.
Cecchin, D., et al. (2017).	5mL of 5% NaOCl before the use of the instrument and 5mL of NaOCl after the intrumenation; 3mL of 2% CHX gel before insertion of the instrument into the root canal and after 5 mL of DW	control group (without a naturally derived reducing agent); 5mL of 10% GSE; 5mL of 10% Green Tea (GT)	3 mL of 17% EDTA for 1 min + 5 mL of DW (all groups)	NU	AH Plus	The irrigation protocols and naturally derived reducing agents had no effect on the POBS of the resin-based sealer to root dentin.
Dalbem, F., et al. (2015).	NaCl (auxiliary chemical substance and irrigating solution)(control group); 2% CHX gel (auxiliary chemical substance) + NaCL (irrigating solution); 5.25% NaOCl (auxiliary chemical substance and irrigating solution)	NU	17%EDTA (all groups)	NU	AH Plus; MTA Fillpaex	The irrigating protocols did not influence the POBS of either sealer.

Dinesh, K., et al. (2014).	5 mL of 3% NaOCl between each instrument (all groups)	5 mL of 17% EDTA; 5 mL 17% EDTA + 5 mL of 2% CHX	NU	NU	AH Plus	The use of 2% CHX as a final rinse following 17% EDTA significantly improved the bond strength of GP/AH Plus.
Donnermeyer, D., et al. (2019).	2.5 mL of 3% NaOCl	5 mL of 3% NaOCl 3% + 5 mL of 17% EDTA 17% (contact time 5 min)	5mL of 3% NaOCl; 5 mL of 2% CHX; 5 mL of 17% EDTA; 5 mL of 20% citric acid (CA) or 5 mL of 0.9% NaCl (each solution for 5 min)	NU	AH Plus; BioRoot RCS; GuttaFlow2	The POBS of AH Plus was positively influenced by EDTA and NaOCl. EDTA had a negative effect on the POBS of BioRoot RCS. The POBS of GuttaFlow2 was not influenced by the irrigation solutions.
El-Ma'aita, A. M., et al. (2013).	1% NaOCl	17% EDTA for 1 min; control group without EDTA	NU	NU	AH Plus	Whether smear layer removal improved the bond strength between the sealer and the radicular dentin could not be detected by this test.
Ertas, H. and B. Sagsen (2015).	1mL of SS; 1% NaOCl; 17% EDTA; 17% EDTA+1%NaOCl; 2% CHX solution; 1.3%NaOCl (MTAD final rinse)	NU	5mL of the same solutions. Only in MTAD group the final flush was perfomed with 5mL of MTAD (during instrumentation 1.3% NaOCl).	NU	AH Plus	The root fillings of the groups irrigated with MTAD showed significantly lower push-out bond strength values than the groups irrigated with 1% NaOCl, 17% EDTA and 1% NaOCl, 2% CHX, and SS. MTAD reduces the bond strength of root canal sealer to root canal dentin when compared with other irrigating solutions.
Fahmy, S. H., et al. (2015).	3mL of 2.5% NaOCl at each file change	17%EDTA + 2.5% NaOCl; 17% EDTA with 0.9% T80 + 2.5% NaOCl; 17% EDTA + 2.5% NaOCl solution with	5mL of decalcifying agent + 5mL of 2.5% NaOCl for 1min + 5mL	T80	AH Plus	Tween 80 addition to the demineralizing irrigants improved the bond strength value of gutta percha/ AH Plus to radicular dentin whereas its addition to NaOCl gave lower results.

		0.6% T80; 7% EDTA with 0.9% T80 + 2.5%NaOCl with 0.6% T80; 7% MA + 2.5% NaOCl; 7% MA with 1% T80 + 2.5% NaOCl; 7% MA + 2.5% NaOCl with 0.6% T80; 7% MA with 1% T80 + 2.5% NaOCl with 0.6% T80.	of DW for 1min.			
Forough Reyhani, M., et al. (2014).	2.5% NaOCl; SS	NU	for 2.5%NaOCl group - SS + 17% EDTA for 5 min	NU	Dorifill; MTA Fillapex	Irrespective of the sealer type, the mean bond strength to dentin after irrigation with 2.5% NaOCl+17% EDTA was higher than irrigation with normal SS solution. Removal of the smear layer increased the resistance to displacement of root filling materials.
Franceschini, K. A., et al. (2016).	2mL of distilled and deionized water (DDW) at each change of file	DDW; 1% NaOCl; 17% EDTA + Cetavlon (EDTAC), all for 10 min.	10 mL of DDW	NU	AH Plus	Final irrigation with 17%EDTAC provided higher bond strength compared with DW.
Gaddala, N., et al. (2015).	5mL of 5.25% NaOCl between each file	5mL of peracetic acid (PAA); 5mL of smear clear	DW for 1 min	NU	Kerr; Apexit plus; AH Plus	Peracetic acid when employed as final irrigant improved the bond strength of root canal sealers compared to control group but not statistically significant than smear clear.
Gandhi, B., et al. (2016).	Normal SS	10 mL of 17% EDTA + 10 mL of 5.25% of NaOCl for 5 min; 10 mL of 17% EDTA for 5 min + 10 mL of 5.25% NaOCl for 5 min + 10 mL of Casein Phosphopeptide–	NU	NU	Real Seal SE	CPP-ACP did not affect the bond strength. There was no statistically significant difference detected among the push-out bond strength of CPP-ACP and EDTA + NaOCl groups

		Amorphous Calcium Phosphate (CPP-ACP) for 10 min				
Graziele Magro, M., et al. (2014).	5 mL of 2.5% NaOCl for 1 min between each instrument	17% EDTA for 3 min + 5 mL of 2.5% NaOCl	2%CHX solution; 2% chlorhexidine digluconate gel (CHX gel); 2% CHX modified solution; 2% chlorhexidine digluconate with a surfactant (CHX Plus). The CHX formulations were kept intracanal for 3 min.	Used on CHX Plus (2% CHX with a nonionic surfactant (Triton-X)	AH Plus	CHX groups provided similar bond strength values of the root canal filling when AH Plus sealer was used, when compared with control group
Gundogar, M., et al. (2018).	2 mL 2.5% NaOCl	NP	5 mL of 17% EDTA for 1min; 5 mL of 2% CHX for 1min + DW; 5mL QMix 2in1 for 1min	NU	Endosequence BC sealer	There was a significant difference between the push out bond strengths of Endosequence BC sealer with respect to type the irrigation solution. Endosequence BC sealer showed the highest bond strength values when QMix 2in1 was used as the final irrigant. On the other hand, Endosequence BC sealer showed the lowest bond strength values when NaOCl was used as the final irrigation solution.
Guneser, M. B., et al. (2017).	3 mL 1 % NaOCl + 5 mL 17 % EDTA for 1 min	5 % NaOCl + 0.1% Benzalkonium chloride (BAK); 5 % NaOCl +	5 mL NaOCl for 1 min	0.1% BAK; 0.1% T80; 0.1% TRX	AH Plus	The bond strength in the NaOCl+TRX group was higher than that in the control, NaOCl-BAK, and

		0.1% T80; 5 % NaOCl+ 0.1% Triton X-100 (TRX)				NaOCl + T80 groups. The bond strength of both the NaOCl + BAK and NaOCl + T80 groups was similar to that of the control group.
Gupta, H., et al. (2013).	5.25% NaOCl + 5 mL of 17% EDTA for 1min	NP	5mL 2%CHX solution for 10 min	NU	AH Plus	The precipitate formed by a combination of sodium hypochlorite and chlorhexidine tends to affect the bond strength of the sealers used for obturation. The highest bond strength is noted in the AH Plus group without precipitate
Güzel, C., et al. (2018).	3 mL 2.5% NaOCl between each file.	3 mL EDTA; REDTA (17% EDTA + 0.84 g cetyltrimethylammonium bromide); EDTA-T (17% EDTA + 1.25% sodium lauryl ether sulfate.	3 mL SS (NaOCl groups); 3 mL SS (control group)	NU	AH Plus	EDTA-T, REDTA, and EDTA significantly increased the bond strength values of gutta-percha/AH Plus sealer to the root canal dentin compared with SS. Moreover, EDTA-T provided significantly higher bond strength values compared with the EDTA group. (type of EDTA compounds).
Hashem, A. A., et al. (2009).	3 mL of 2.6% NaOCl between each file size.	5 mL 17% EDTA; 5 mL 17% EDTA + 5 mL 2% CHX; 5 mL MTAD; 5 mL MTAD + 5 mL 2% CHX	NP	NU	AH Plus	The bond strength of gutta-percha/AH plus was adversely affected by MTAD and MTAD/CHX.
Kamalasa nan, R. R., et al. (2017).	3% NaOCl + 17% EDTA (final rinse) for 1 min; 5% Chlorine dioxide (ClO2) + 17% EDTA (final rinse) for 1 min; 5% ClO2 (during and final rinse); SS (during and final rinse)	NU	5 mL of deionized water	NU	AH Plus	The bond strength values of ClO2 were comparable with conventional NaOCl and EDTA combination. The bond strength of epoxy sealers to root dentin after using various irrigants and irrigation protocol used in this study is not significantly different from one another (except SS group).
Keine, K. C., et al. (2019).	1% peracetic acid (PAA); 2.5% NaOCl + 17% EDTA; 2.5%	NU	For NaOCl-EDTA-NaOCl group: 3 mL of	NU	AH Plus	There was no difference between the PAA and NaOCl-EDTA-NaOCl groups and in both these groups, the

	NaOCl (NaOCl-EDTA-NaOCl); 2.5% NaOCl; SS solution (SS).		17% EDTA for 3 minutes + 2 mL of 2.5% NaOCl for 1 minute; Other groups: 5 mL of DW for 4 minutes			root canal sealer showed higher values for bond strength to root dentin than those of the NaOCl and SS groups.
Kumar, P., et al. (2019).	5.25% NaOCl between instruments	5 mL of 17% EDTA+ 5 mL of 5.25% NaOCl	5 mL and 5 min (all groups): SS; 6.5% PA+ 5 mL DW; 25% (bambo salt) BS + 5 mL DW	NU	AH Plus	5.25% NaOCl significantly decreased the bond strength of AH Plus to dentin. Both 6.5% PA and 25% BS were capable of reversing the compromised POBS of AH Plus to NaOCl-treated dentin. Final irrigation with antioxidants such as PA and BS eliminates the risk of reduced bond strength of AH Plus to root canal walls, which ensues following the use of NaOCl as an irrigant.
Leal, F., et al. (2015).	1mL of 5.25% NaOCl; 1mL of 2% CHX gel	17% EDTA; QMix 2 in 1 for 3 min (renewed every 1 min - 1mL/min)	1 mL of NaOCl; CHX solution; DW	NU	AH Plus	The group NaOCl/EDTA/NaOCl showed significantly higher bond strength values than other groups. The final irrigation protocols affect the push-out bond strength of AH Plus to dentin.
Magro, M. G., et al. (2015).	5 mL of 2.5% NaOCl between each instrument change	17% EDTA for 3 min + 5 mL of 2.5% NaOCl	2.5% NaOCl + the root canal was aspirated and dried with paper points + 5mL of 2% CHX; 2.5% NaOCl + 5 mL of isopropyl alcohol + 5mL of 2% CHX;	NU	AH Plus	Independent of the root third evaluated, there were no differences between the control and experimental groups. The various irrigation protocols did not interfere with the bond strength values of on epoxy-based sealer.

			2.5% NaOCl + SS + 5mL of 2% CHX; 2.5% NaOCl + DW + 5mL of 2% CHX			
Mozayeni, M. A., et al. (2013).	5 mL NaOCl between each file	5 mL of 1.3% NaOCl between each instrument + MTAD protocol (4 mL rinse + 1 mL remaining in root canal for 5 min); 5 mL of 5.25% NaOCl + 5 mL of 17% EDTA for 1 min	NP	NU	AH 26	The mean bond strength of AH26 sealer to dentin walls was significantly greater using MTAD compared with combination of EDTA and NaOCl or SS.
Ok, E., et al. (2013).	2mL SS after each instrumentation	3 mL of 17% EDTA for 1 minute + 3 mL of 5.25% NaOCl for 1 minute + 5 mL of DW for 1 min	3 mL of 2% CHX solution; NaOCl + EDTA (control group)	NU	AH Plus	There was no significant difference among the bond strength of the CHX and NaOCl groups
Pheenithic haroenkul, S. and A. Panichuttr a (2016).	1 mL of 2.5% NaOCl between files	5 mL of 17% EDTA 5 min; 5 mL of 17% EDTA 5 min + 5 mL of 2.5% NaOCl 1 min; 5 mL of 17% EDTA 5 min + 5 mL of 1mg/mL EGCG 5 min; 5 mL of 1 mg/mL epigallocatechin-3-gallate (EGCG) from green tea extract 10 min	NU	NU	AH Plus	EDTA+EGCG group significantly showed the highest push out bond strength. EGCG group showed higher bond strength than EDTA group with statistical significance. There was no significant difference in the mean bond strength value between EDTA and EDTA+NaOCl group. Final irrigation with NaOCl (control group) resulted in the lowest bond strength.
Prado, M., et al. (2013).	6 mL DW; 1 mL 5.25% NaOCl + 5mL DW; 1 mL 2% CHX gel + 5 mL DW	10mL DW (all groups): 3 mL DW; 3 mL 17% EDTA; 3 mL 37% PhA	10 mL DW; 5 mL DW + 5 mL 2% CHX solution	NU	AH Plus	When NaOCl was used as the irrigant during chemomechanical preparation, significantly higher POBS values were obtained when PhA was used for smear layer removal. When CHX was used

						during chemomechanical preparation, the use of EDTA allowed better POBS values. The use of CHX as the final irrigant did not affect the bond strength
Ravikumar, J., et al. (2014).	3 mL of 2.6% NaOCl between each file size.	2, 5 mL of 7% MA; 5 mL of 10 % CA; 5 mL of MTAD	NP	NU	AH Plus	NaOCl/MA/AH Plus yielded significantly the highest mean POBS. The significantly lowest mean POBS was recorded for group NaOCl/MTAD/AH Plus. A final rinse with MTAD might have a negative effect on the bonding ability of AH Plus sealer.
Razmi, H., et al. (2016).	SS during treatment + 10 mL of 17% EDTA for 1 min + 10 mL of 5.25% NaOCl + 20 mL of SS	2% CHX; 5.25% NaOCl	NP	NU	Adseal; AH Plus; BC sealer	The bond strength of Adseal was not affected with either NaOCl or CHX. The POBS of AH Plus was not affected by the any irrigant type. For Endosequence BC sealer, the CHX reduced the POBS.
Rocha, A. W., et al. (2012).	SS; 2.5% NaOCl; 2% CHX gel (1mL between each file)	17% EDTA for 3min + removed using the same irrigant used in the irrigation.	NP	NU	AH Plus	NaOCl adversely affected POBS of AH Plus, whereas CHX did not influence the POBS.
Shokouhinejad, N., et al. (2010).	3 mL of 5.25% NaOCl + 5 mL of 17% EDTA for 1 min; 3 mL of 1.3% NaOCl + 1 mL of BioPure MTAD for 5 min;	NP	MTAD protocol with 4 mL (only MTAD group)	NU	AH 26	The group with 5.25% NaOCl+EDTA had a significantly higher POBS than all of the other groups.
Shokouhinejad, N., et al. (2013).	3 mL of 5.25% NaOCl between each file	5 mL of 5.25% NaOCl; 5 mL of 17% EDTA for 1 min + 5 mL of 5.25% NaOCl	NP	NU	EndoSequence BC Sealer, AH Plus	The POBS of GP/AH Plus and GP/EndoSequence BC Sealer was not significantly different. The POBS of the new bioceramic sealer was equal to that of AH Plus with or without the smear layer.

Souza, M. A., et al. (2019).	2.5% NaOCl between each change of instrument + 5 mL of DW	DW; 17% EDTA; Qmix	5 mL of DW	NU	AH Plus	EDTA and Qmix groups provided the higher POBS.
Stelzer, R., et al. (2014).	0.9% SS during instrumentation	3% NaOCl; 17% EDTA; 2% CHX (5mL for 4 min)	5 mL 0.9% SS for 1 min	NU	AH Plus	Within the AH Plus groups, no significant differences existed between the irrigants and SS alone
Trindade, T. F., et al. (2018).	2 mL 2.5% NaOCl at each file change + 5 mL 17% EDTA for 3 min + 5 mL of DW	1 mL of 2% CHX for 1 min; 15% proanthocyanidin (from GSE capsules)	NP	NU	AH Plus; EndoREZ	POBS decreased with time and AH Plus had higher POBS than EndoREZ in untreated dentin; however, CHX or proanthocyanidin enhanced long-term POBS of EndoREZ.
Uzunoglu, E., et al. (2015).	2mL 3% NaOCl between each instrument + 5 mL 3% NaOCl for 1 min	5mL 17% EDTA (22°C); 5mL 17% EDTA (37°C); 5mL QMix (22°C); 5mL QMix (37°C)	5mL DW	NU	AH Plus	The samples irrigated with QMix had higher POBS values than the samples that had been irrigated with 17% EDTA regardless of temperature. Using QMix as a final irrigant can improve POBS of epoxy-resin based sealer.
Yavari, H., et al. (2017).	SS during instrumentation + 5.25% NaOCl for 3 min + 17% EDTA for 3 min	Solution containing nano particles Ag/ZnO; No final flush	NPs group: 2 mL of polymer containing Ag / ZnO for 5 min	NU	AH Plus; MTA Fillapex	The lowest mean POBS values was obtained in MTA fillapex-Ag/ZnO. AH Plus sealer had higher POBS than MTA Fillapex in all groups. Nano disinfection had significantly negative effect on the POBS of AH Plus sealer, but for MTA Fillapex sealer the difference between the NPs and the control group was not significant.
Legend: Not used (NU); Not performed (NP); Not reported (NR); Distilled water (DW); Distilled and deionized water (DDW); Chlorhexidine (CHX); Sodium hypochlorite (NaOCl); Grape seed extract (GSE); Green tea (GT); Citric acid (CA); Push-out bond strength (POBS); Maleic acid (MA); Bamboo salt (BS); Peracetic acid (PAA); Phosphoric Acid (PhA); Saline solution (SS); Chlorine dioxide (ClO2); Gutta-percha (GP); Tween80 (T80).						

Figure 1 – Flow diagram of study selection.

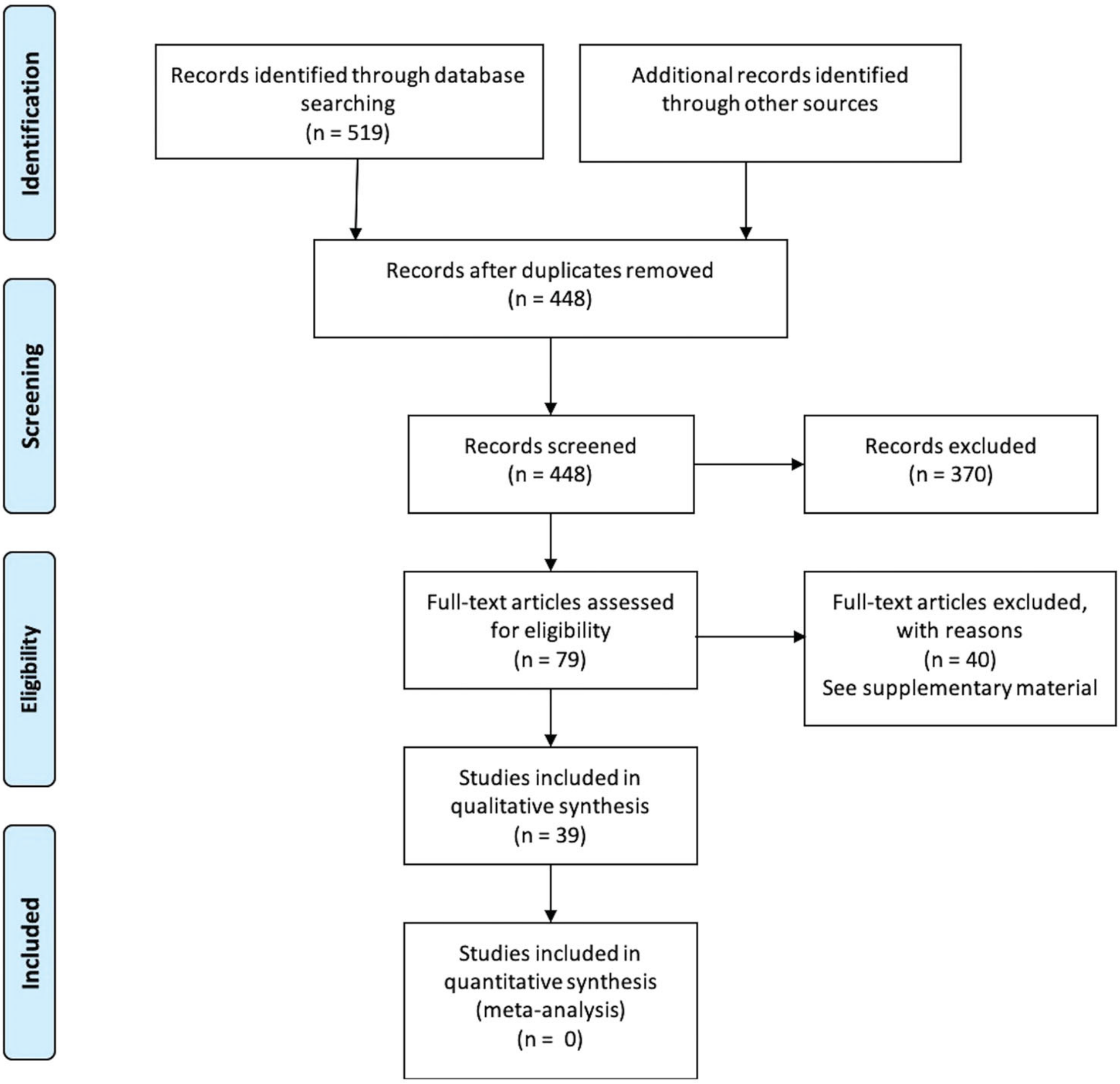
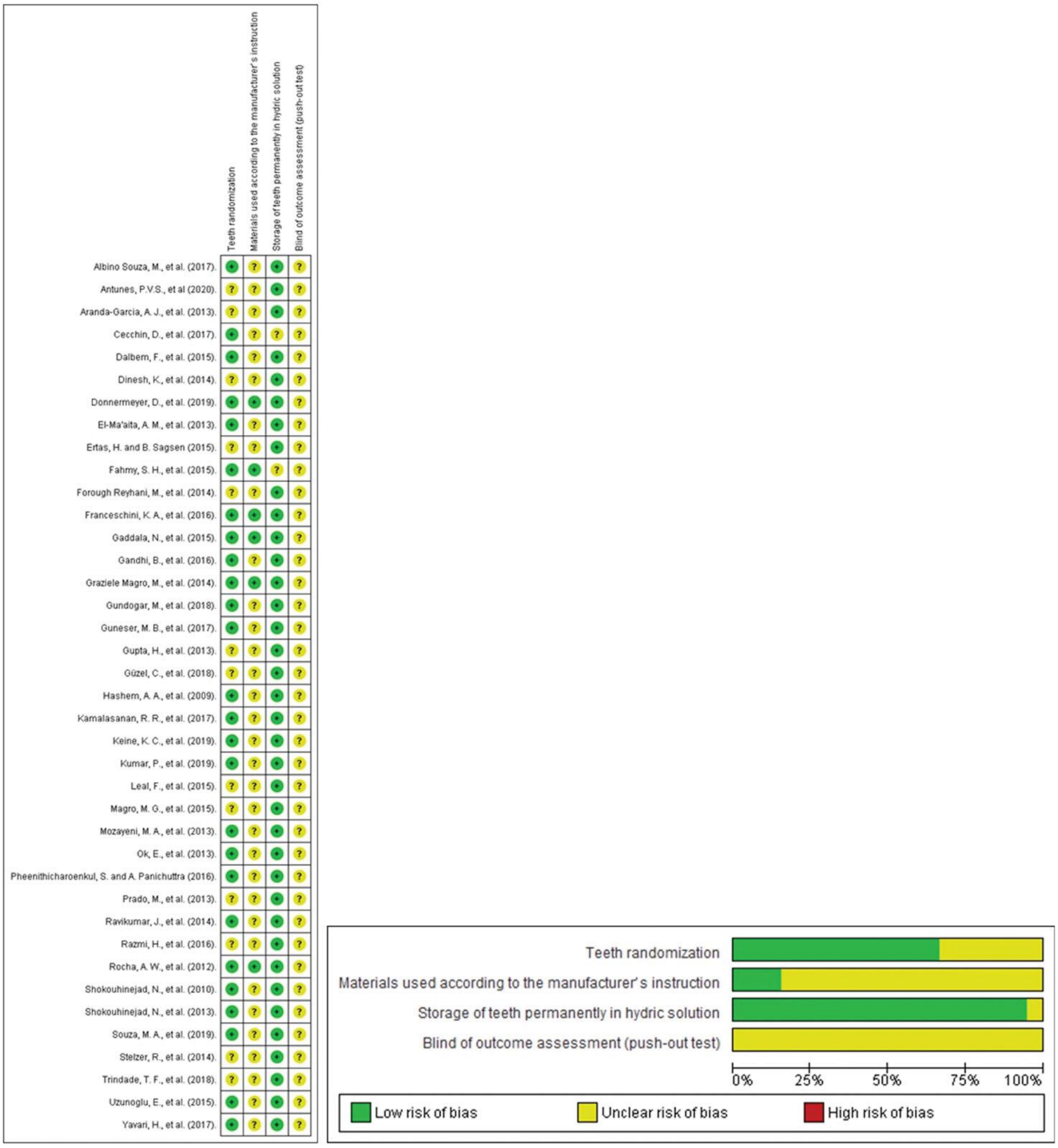


Figure 2 – Review authors’ judgements about each risk of bias item presented as percentages across all included studies and about each risk of bias item for each included study



SUPPLEMENTARY MATERIAL.

List of included studies

1.Albino Souza M, Dalla Lana D, Gabrielli E, et al. Effectiveness of final decontamination protocols against Enterococcus faecalis and its influence on bond strength of filling material to root canal dentin. Photodiagnosis Photodyn Ther. 2017;17:92-7.

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6. CONSIDERAÇÕES FINAIS

Baseado nos principais achados dos estudos incluídos nesse trabalho, foi possível concluir que:

(I) Em relação à influência dos irrigantes nas propriedades mecânicas dos DTE, independentemente da solução de irrigação considerada, a maioria dos estudos corrobora a ocorrência de algum dano às propriedades mecânicas dos dentes tratados endodonticamente. Assim, a literatura disponível parece determinar que fatores como concentração e tempo de exposição devem ser considerados para amenizar os efeitos deletérios, sem que isso venha a interferir nas propriedades antibacterianas. Além disso, é necessário que o profissional conheça as características de cada solução para decidir qual é a mais adequada, garantindo o sucesso do tratamento endodôntico e causando danos mecânicos mínimos ao tratamento em questão;

(II) Quanto ao uso de solventes para a remoção da guta-percha durante o retratamento endodôntico, não existe solvente unânime para a remoção eficaz do material obturador. De fato, a maioria dos estudos sugere que os solventes podem inclusive prejudicar a limpeza do canal radicular e facilitar a presença de restos de GP na superfície radicular. Assim, o uso de solventes deve ser evitado, sendo seu uso considerado se o comprimento de trabalho anterior não for possível de acessar sem essa substância;

(III) Na avaliação do efeito das soluções irrigadoras na resistência de união entre os cimentos endodônticos e a dentina do canal radicular, a utilização de substâncias irrigantes capazes de desmineralizar a superfície da dentina do canal radicular e/ou remover a camada de lama dentinária remanescente pareceu aumentar ou pelo menos não reduz a força de união por *push-out*, independentemente do tipo de cimento endodôntico utilizado.

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8. APÊNDICE

Protocolo Artigo 1 - Effects of root canal irrigants on mechanical properties of endodontically treated teeth: a scoping review.

Version 1

Study protocol

06/21/2019

Study protocol

Effects of root canal irrigants on mechanical properties of endodontically treated teeth: a scoping review protocol

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REGISTRATION

This study will not be registered in a registry database (e.g., PROSPERO) due to the nature of the inclusion criteria (in vitro studies) and nature of study design (Scoping review).

OBJECTIVE

To identify if root canal irrigants influence the mechanical properties of endodontically treated teeth and which properties could be affected through a scoping review.

METHODS

The protocol of this study is based on the framework proposed by Peters et al., 2015, according to The Joana Briggs Institute (Peters et al., 2015).

Inclusion criteria

We will select studies in dentistry that considered the effect of irrigant solutions at the mechanical properties of endodontically treated teeth. It will be included studies that evaluated the effect of at least one irrigant solution on dentin, regardless of the teeth type (human, bovine and other animals) and study design. Study groups testing associated techniques such as the use of laser therapy or agitation protocols will not be considered.

Search

The search will be performed in two databases: MEDLINE (PubMed) and Scopus. We will be limited to articles written in English language. The search strategy will be based on Mesh terms of PubMed and specific terms of Scopus using the following keywords (table 1).

Table 1 – Search strategy

PUBMED
"Tooth, Nonvital"[Mesh] OR "Tooth, Nonvital" OR "Nonvital Tooth" OR "Tooth, Devitalized" OR "Devitalized Tooth" OR "Tooth, Pulpless" OR "Pulpless Tooth" OR "Teeth, Pulpless" OR "Pulpless Teeth" OR "Teeth, Devitalized" OR "Devitalized Teeth" OR "Teeth, Nonvital" OR "Nonvital Teeth" OR "Teeth, Endodontically-Treated" OR "Endodontically-Treated Teeth" OR "Teeth, Endodontically Treated" OR "Tooth, Endodontically-Treated" OR "Endodontically-Treated Tooth" OR "Tooth, Endodontically Treated" OR "dentin" AND "Root Canal Irrigants"[Mesh] OR "Root Canal Irrigants" OR "Canal Irrigants, Root" OR "Irrigants, Root Canal" OR "Root Canal Medicaments" OR "Canal Medicaments, Root" OR "Medicaments, Root Canal" OR "Chlorhexidine" OR "EDTA" OR "Sodium hypochlorite" OR "chemical irrigant" OR "NaOCl" OR "CHX" OR "ethylenediamine tetraacetic acid" AND "fracture" OR "strength" OR "resistance" OR "fatigue" OR "mechanical properties" OR "flexural strength" OR "microhardness" OR "modulus of elasticity" NOT "bond"*
SCOPUS
"Tooth, Nonvital" OR "Nonvital Tooth" OR "Tooth, Devitalized" OR "Devitalized Tooth" OR "Tooth, Pulpless" OR "Pulpless Tooth" OR "Teeth, Pulpless" OR "Pulpless Teeth" OR "Teeth, Devitalized" OR "Devitalized Teeth" OR "Teeth, Nonvital" OR "Nonvital Teeth" OR "Teeth, Endodontically-Treated" OR "Endodontically-Treated Teeth" OR "Teeth, Endodontically Treated" OR "Tooth, Endodontically-Treated" OR "Endodontically-Treated Tooth" OR "Tooth, Endodontically Treated" AND "Root Canal Irrigants" OR "Canal Irrigants, Root" OR "Irrigants, Root Canal" OR "Root Canal Medicaments" OR "Canal Medicaments, Root" OR "Medicaments, Root Canal" OR "Chlorhexidine" OR "EDTA" OR "Sodium hypochlorite" AND "fracture" OR "strength" OR "resistance" OR "fatigue" OR "mechanical properties" OR "flexural strength" OR "microhardness" OR "modulus of elasticity" AND NOT bond AND (LIMIT-TO (DOCTYPE , "ar")) AND (LIMIT-TO (SUBJAREA , "DENT"))

Screening

Initially, the search will be undertaken using EndNote program (EndNote X9, Thomson Reuters, New York, NY). Two researches will identify articles by first analyzing titles and abstracts for relevance and the presence of the eligibility criteria. Retrieved records will be classified as include, exclude, or uncertain. The full-text articles of the included and uncertain records will be selected for further eligibility screening by the same 2 reviewers. Discrepancies in screening of titles/abstracts and full text articles will be resolved through a discussion. In case of disagreement, the opinion of a third reviewer will be garnered.

Charting the results

We will create a form using the Excel program, which will be test by three reviewers to reach a consensus of data collections. Then, one of the reviewers will extract the data and another will check. The following data will be collected: study design; irrigation solutions tested; concentration of the solution; exposure time; final rinse; teeth type (human, bovine or other animal); teeth conditions - if were split, filled, restored, using a dowel and if so the type of dowel); mechanical properties evaluated and main findings. In case of identification of reviews (systematic or not), the following data will be collected: inclusion criteria, number of included articles, number of included articles grouped by mechanical test, main findings, level of evidence generated reported by authors and conclusions.

Data analysis

A descriptive analysis will be performed considering the study design and different irrigants tested using tables, graphs and maps.

REFERENCES

Peters MDJ, Godfrey CM, McInerney, Khalil H, Parker D, and Baldini Soares C. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc. 2015. 13(3):141-146. Available: http://www.ncbi.nlm.nih.gov/pubmed/26134548

Protocolo Artigo 2 - Effectiveness of solvents for gutta-percha dissolution/removal during endodontic retreatments: a scoping review

Study protocol

Effectiveness of solvents for gutta-percha dissolution/removal during endodontic retreatments: a scoping review

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REGISTRATION

This study will not be registered in a registry database (e.g., PROSPERO) due to the nature of the inclusion criteria (in vitro studies) and nature of study design (Scoping review).

OBJECTIVE

To assess and discuss the necessity and effectiveness of using solvents for gutta-percha dissolution/removal during endodontic retreatments in comparison to the effect of mechanical instrumentation executed without solvents, through a scoping review.

METHODS

The protocol of this study is based on the framework proposed by Peters et al., 2015, according to The Joana Briggs Institute guidelines (Peters et al., 2015).

Inclusion criteria

We will select studies in dentistry that considered the effectiveness of solvents in guttapercha dissolutions in endodontic retreatments, which compared the performance of such agents to the use of instrumentation techniques without solvents. It will be included studies that evaluated the effect of at least one solvent solution on gutta-percha, regardless of the teeth type (human, bovine and other animals) and regardless of how the outcome was measured. In relation to the adopted studies design, it will be included reviews which discussed the gutta-percha removal/dissolution on endodontic retreatment. Study groups testing others root filling materials (not gutta percha) will not be considered.

Search

The search will be performed in two databases: MEDLINE (PubMed) and Scopus, limited to articles written in English language. The search strategy will be based on Mesh terms of PubMed and specific terms of Scopus using the following keywords (table 1).

Table 1 – Search strategy

PUBMED
“Solvent” OR “Solvents” OR “Gutta-percha Solvent” OR “Chloroform” OR “Eucalyptol” OR “Orange Oil” OR “Endosolv E” OR “Xylene” AND "GuttaPercha"[Mesh] OR "Gutta-Percha removal" NOT “Sealing” NOT “Bond”
SCOPUS
"Solvent" OR "Solvents" OR "Gutta-percha Solvent" OR "Chloroform" OR "Eucalyptol" OR "Orange Oil" OR "Endosolv E" OR "Xylene" AND "GuttaPercha" [mesh] OR "Gutta-Percha removal" AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re")) AND (LIMIT-TO (LANGUAGE , "English"))

Screening

Initially, the search will be undertaken using EndNote program (EndNote X9, Thomson Reuters, New York, NY). Two researches will identify articles by first analyzing titles and abstracts for relevance and the presence of the eligibility criteria. Retrieved records will be classified as include, exclude, or uncertain. The full-text articles of the included and uncertain records will be selected for further eligibility screening by the same 2 reviewers. Discrepancies in screening of titles/abstracts and full text articles will be resolved through a discussion. In case of disagreement, the opinion of a third reviewer will be garnered.

Charting the results

We will create a form using the Excel program, which will be tested by three reviewers to reach a consensus of data collections. Then, one of the reviewers will extract the data and another will check it. The following data will be collected: study design; method/technique used for obturation; cement used for obturation; method/technique used for instrumentation during retreatment (manual or rotary); solvent solutions tested; exposure time; moment of use of the solvent (final rinse/ during instrumentation); control groups used, method to access the presence of gutta percha; characteristics of the teeth (human, bovine or other animal/ straight or curved roots, among others); and study main findings. In case of identification of reviews (systematic or not), the following data will be collected: inclusion criteria, number of included articles, main findings, level of evidence generated reported by authors and conclusions.

Data analysis

A descriptive analysis will be performed considering the study design and different solvents tested using tables, graphs and maps.

REFERENCES

Peters MDJ, Godfrey CM, McInerney, Khalil H, Parker D, and Baldini Soares C. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc. 2015. 13(3):141-146. Available: http://www.ncbi.nlm.nih.gov/pubmed/26134548

Protocolo Artigo 3 - Effect of root canal irrigants on push-out bond strength of endodontic sealers: a systematic review

Study protocol

Effect of root canal irrigants on push-out bond strength of endodontic sealers: a systematic review protocol

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REGISTRATION

This study will not be registered in a registry database (e.g., PROSPERO) due to the nature of the inclusion criteria (in vitro studies).

OBJECTIVE

To assess what are the effects of root canal irrigants on push-out bond strength of endodontic sealers in endodontic treated teeth, through a systematic review.

METHODS

The reporting of protocol of this study is based on the PRISMA for systematic review protocols (Moher et al., 2015).

Inclusion criteria

We will select studies in dentistry, written in English language, that considered the effects of root canal irrigants on push-out bond strength of endodontic sealers, which compared the influence of such agents during the endodontic treatment and/or at final irrigation, regardless if chelating agents or surfactants were used, regardless of the teeth type (human or animal) and regardless of the instrumentation type or obturation method. The outcome (bond strength) should be measured by the push-out test. In relation to the adopted studies design, only in vitro studies will be included. Study groups testing others root filling materials (not gutta percha) will not be considered. We will consider groups that the use irrigants with passive and active irrigation.

Search

The search will be performed in two databases: MEDLINE (PubMed) and Scopus, limited to articles written in English language. The search strategy will be based on Mesh terms of PubMed and specific terms of Scopus using the following keywords (table 1). We will perform a manual search in the references of the included articles in order to identify additional studies.

Table 1 – Search strategy

PUBMED
("Root Canal Irrigants"[Mesh] OR "Root Canal Irrigants" OR "Canal Irrigants, Root" OR "Irrigants, Root Canal" OR "Root Canal Medicaments" OR "Canal Medicaments, Root" OR "Medicaments, Root Canal" OR "Chlorhexidine" OR "EDTA" OR "Sodium hypochlorite" OR "chemical irrigant" OR "NaOCl" OR "CHX" OR "ethylenediamine tetraacetic acid")) AND ("sealer" OR "canals sealer" OR "Root Canal Sealer")) AND push out bond strength)
SCOPUS
"Root Canal Irrigants" OR "Canal Irrigants, Root" OR "Irrigants, Root Canal" OR "Root Canal Medicaments" OR "Canal Medicaments, Root" OR "Medicaments, Root Canal" OR "Chlorhexidine" OR "EDTA" OR "Sodium hypochlorite" OR "chemical irrigant" OR "NaOCl" OR "CHX" OR "ethylenediamine tetraacetic acid" AND "sealer" OR "canals sealer" OR "Root Canal Sealer" AND push AND out AND bond AND strength AND (LIMIT-TO (SUBJAREA , "DENT")) AND (LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (DOCTYPE , "ar") OR LIMIT-TO (DOCTYPE , "re"))

Screening

Initially, the search will be undertaken using EndNote program (EndNote X9, Thomson Reuters, New York, NY). Two researches will identify articles by first analyzing titles and abstracts for relevance and the presence of the eligibility criteria. Retrieved records will be classified as include, exclude, or uncertain. The full-text articles of the included and uncertain records will be selected for further eligibility screening by the same 2 reviewers. Discrepancies in screening of titles/abstracts and full text articles will be resolved through a discussion. In case of disagreement, the opinion of a third reviewer will be garnered.

Data Extraction

We will create a form using the Excel program, which will be tested by three reviewers to reach a consensus of data collections. Then, one of the reviewers will extract the data and another will check it. The following data will be collected: author, year, irrigant solutions protocol used during and/or on final endodontic treatment (including concentration, how many times, amount used and whether surfactants were used with irrigant solutions); chelating agents used during the treatment; method/technique used for instrumentation during retreatment (manual or rotary); method/technique used for obturation;sealer used for obturation (calcium silicate-based, epoxy resin-based,siliconebased and methacrylate-based sealers); control groups used; type of the teeth (human or animal); time between obturation and push-out test; and study main findings and results of push-out test.

Risk of Bias

The risk of bias of included studies will be assessed based on previous studies (SarkisOnofre et al., 2014; Schestatsky et al., 2019). The following parameters will be considered: teeth randomization, materials used according to the manufacturer's instruction, storage of teeth permanently in hydric solution, blind of outcome assessment. The parameters used were discussed by the researchers involved and judgment will be carried out by one researcher and verified by another one. Assessment of risk of bias will be conducted using Review Manager 5.3 software.

Data analysis

Our first to plan is to perform a descriptive analysis (tables and graphs) identifying the effects of root canal irrigants on push-out bond strength of endodontic sealers considering different techniques and substances used. Our second plan is to perform a subgroup analysis considering different groups of sealer and the influence of different method/technique used for obturation.

REFERENCES

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