

Effect of Endodontic Irrigation on Mineral Content of Root Canal Dentine: A Systematic Review and Meta-Analysis

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ABSTRACT

A systematic review and meta-analysis were conducted to evaluate the effect of endodontic irrigation on the mineral content of root canal dentine. A systematic search was performed in the following databases: PubMed, Web of Science, Scopus, Cochrane, ProQuest, and Wiley. The quality assessment of the articles was performed. The meta-analysis was carried out using the random effects model in the Stata 16 software ($p < 0.05$). The results showed that Er:YAG Laser had a significant effect on the removal of the phosphorus content of dentine (Hedges' $g = -0.49$; 95% CI: $-0.85, -0.13$; $I^2 = 0.0\%$). In addition, the EDTA 5Min had a lower removal effect compared to the control group on the magnesium content of dentine (Hedges' $g = 0.58$; 95% CI: $0.00, 1.16$; $I^2 = 0.0\%$). Other irrigations had no significant effect on other on the mineral content of root canal dentine. Evidence was found to support that most root canal irrigation protocols did not have a significantly affected in terms of the mineral content of root dentine.

Keywords: Dentine, root canal irrigants, therapeutic irrigation

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HIGHLIGHTS

- The Er:YAG Laser affected the removal of the phosphorus content of dentine.
- The EDTA 5Minute had a lower removal effect than the control group on the magnesium content of dentine.
- The effect of other irrigation on the removal of the mineral content of dentine needs additional supportive evidence.

INTRODUCTION

Root canal preparation is one of the most critical parts of successful endodontic treatment, and this step is essential in two aspects, including cleaning and shaping the root canal and cleaning tissue debris and root canal irrigation to remove and debride the root canal and disinfect the root canal system (1,2). Various chemical solutions are being introduced and widely used (3,4). On the other hand, we are confronted with forming a smear layer during instrument use, canal preparation in endodontic treatment, and plug

smears inside the dentinal tubules' openings (5,6). Therefore, treatment of the inner surface of the root canal and removal of the smear layer by chemical means, such as chelating solutions (7,8), physical means, such as the action of ultrasonic waves (9), cavitation by laser waves (10,11), or mechanical means, such as micro-brushes (12) and negative pressure tools, is facilitated (13).

Generally, it has been shown that because of morphological limitations, a significant percentage of the root canal wall areas (35%-53%)

might be untouched during root canal instrumentation (2). To compensate for this shortcoming, root canal irrigation methods have been introduced to clean, disinfect or remove the smear layer based on the following strategies: irrigation and disinfection of the canal system with a conventional syringe and activating the irrigating solution during the irrigation process (2). The activation of the irrigants can increase the chemical and physical effects of the solution in the irrigation process due to the greater twitching and dispersion of the solution in the root canal system (2,14). The irrigation solution can act by direct mechanical action, creating agitation with files such as F-file or XP-endo Finisher, tools to create subsonic movements such as Endo Activator, or ultrasonic system as a Passive Ultrasonic Irrigation (PUI) method (2,15,16). In the last two decades, the activation of the irrigants by applying pulses of a laser beam and creating cavitation in the flow of the irrigating solution has led to acceptable results in debridement and cleaning of the root surface. Photon-induced Photoacoustic Streaming (PIPS) and Shock Wave Enhanced Emission Photoacoustic Streaming (SWEEPS) methods are used with the help of this technology to do the root canal irrigation process (17,18).

On the other hand, one of the most common cases of using a laser for cleaning and removing the smear layer is under the term Laser Activation Irrigation (LAI). In this method, the laser fiber tip enters the canal up to the working length after shaping and enlarging the canal. It is applied with the radiation protocol and outward movement of the tip at a suitable time. At the same time, the required irrigating solution (distilled water) is supplied by the laser device. While in PIPS and SWEEPS systems, the laser tip does not enter the root canal and only requires to be placed into the coronal reservoir of the pulp chamber. The serial emission of consecutive laser pulses produces bubbles in the solution. The subsequent collapse of these bubbles and the continuation of this process leads to the creation of cavitations and shock waves streaming into the root canal. In this way, the cleaning and treatment of the root surface of the canal are carried out (19).

There are studies on the level of cleaning or the penetration and diffusion of the solutions. Still, there is no document in the literature about the effects of these methods on the biochemical content or mineral compounds of the dentine of the root canal wall. Numerous studies have shown that these agents impact the elemental composition and the ratio of these elements on the dentine surface (20-22). Therefore, special attention has been paid to mineral elements such as calcium, phosphorus, magnesium, and potassium and the ratio of calcium to phosphorus. Of course, other components, such as oxygen and carbon (23-25), and the organic content of dentine were also examined separately (26,27). Human dentine contains 70% minerals, 20% organic matter, and 10% water by weight (28). Determining the exact proportions of elemental content in normal or carious dentine varies depending on the elements examined; therefore, these values are obtained relatively (29). Calcium ions in hydroxyapatite crystals are one of the most essential mineral elements of dentine. It has been reported that some of the chemicals used to irrigate the root canals can change the chemical composition of dentine by re-

moving calcium and phosphorus from hydroxyapatite crystals (22). These changes in the dentine-containing elements cause changes in the biomechanical properties of dentine and, in turn, can cause a change in hardness or surface roughness and affect the formation and initiation of microcracks in dentine and their occurrence during root canal treatment (30-32). These changes in root surface element content may also be effective in some desirable functions, such as permeability to irrigation solutions and sealants (33). Finally, it can affect the bonding rate of the materials and sealers used and, ultimately, the root canal treatment (34,35). Studies in the literature have only examined and reported quantitative changes in elemental content in the dentin surface of the root canal.

Meanwhile, the failure to use a fixed standard when reporting small values has resulted in some studies reporting these values as percentages by weight, volume, or as ppm (22, 36-38). Furthermore, these studies have used different measurement tools such as the X-Ray Fluorescence (XRF) (39), micro-energy-dispersive X-ray fluorescence spectrometry (μ EDXRF) (40), Laser-induced breakdown spectroscopy (LIBS) (20), Inductively coupled plasma atomic emission spectroscopy (ICP-AES) (41), and Energy-dispersive X-ray spectroscopy (EDS). This, in turn, has led to more confusion and difficulties in interpreting the results in the systematic review and meta-analysis studies. Therefore, due to the development of evidence-based dentistry in recent years (42,43) and the need to synthesize various studies to obtain reliable evidence in clinical decision-making, the purpose of this systematic review and meta-analysis was to investigate the effect of endodontic irrigation on the mineral content of root canal dentine.

METHODS

This systematic review was prepared following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement (<http://www.prisma-statement.org>).

Search Strategy

On 22 June 2022, we searched PubMed, Web of Science, Scopus, Embase, Cochrane, ProQuest, and Wiley databases. A three-step process was performed to determine the search keywords and design the syntax. In the first stage, after PICO analysis, the concepts needed for the search were extracted according to the research topic. Also, synonyms, abbreviations, related terms, UK/US spellings, singular/plural forms of words, and thesaurus terms (where available) were extracted and embedded in the search syntax to achieve comprehensiveness in retrieving concepts. The thesaurus MeSH and Emtree were used to complete keywords and perform thematic searches on databases that had these tools. In the last stage, the vocabulary was completed and enriched by conducting a preliminary search and analyzing the keywords of related and leading articles in this field. Therefore, the baseline syntax was (Endodont* OR Root Canal) AND (Mineral* OR Calcif*) AND (Deminerliz* OR Irrig* OR solution). Complete search strategies are presented for each database in Appendix 1. Third, the manual search of reference lists of all included studies and relevant systematic reviews was screened for any potentially eligible studies. Citation tracking was performed for all the included articles.

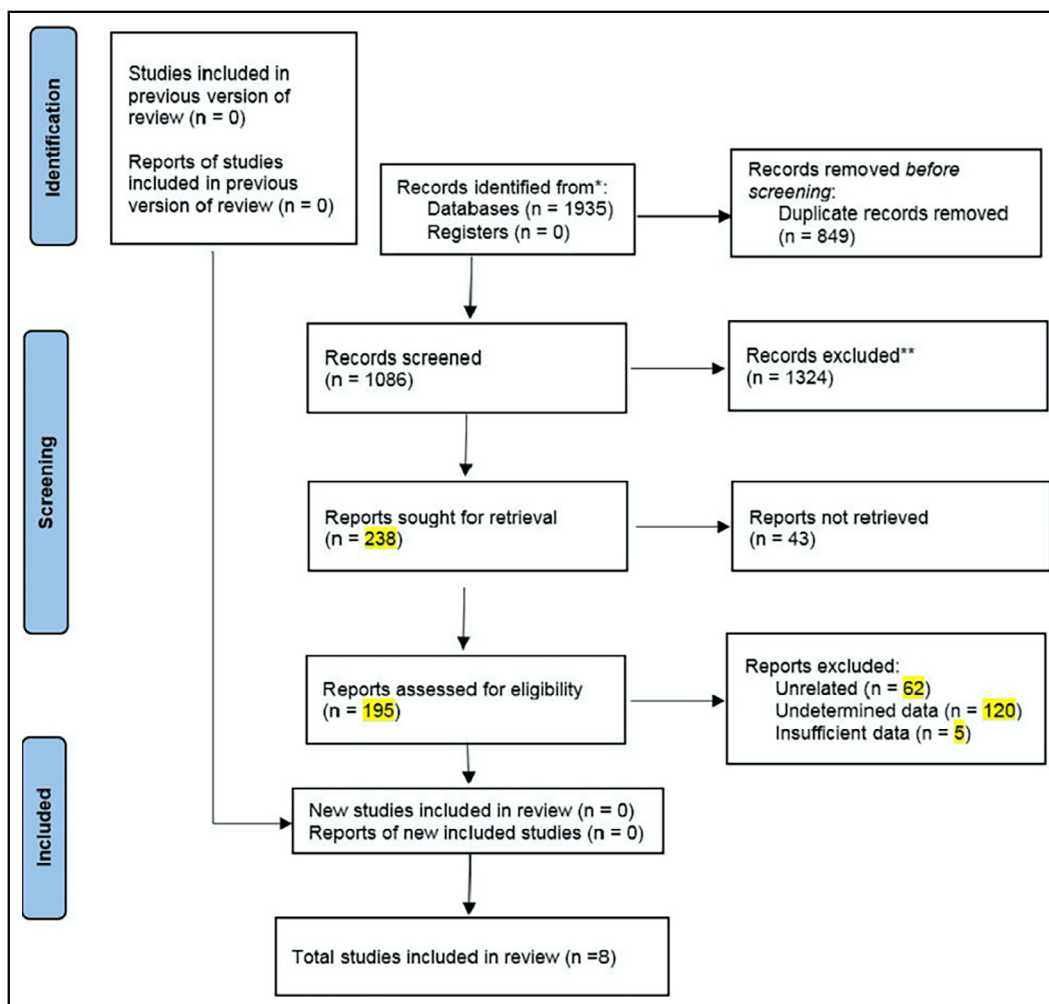


Figure 1. Flowchart of study selection procedure and exclusion criteria

PICOS Question

The population, intervention, comparison, and outcome (PICO) strategy used for the structured review question were based on the PICO strategy (PRISMA-P 2016) as follows:

- Population (P): Candidate patients for endodontics;
- Intervention (I): Endodontic irrigation using different techniques;
- Comparison (C): Removal of mineral contents of dentine with normal saline;
- Outcome (O): Removal of the mineral content.

Data Extraction and Quality Assessment

Two investigators (A. R. and M. M.) independently extracted the original data. Any disagreement was resolved by discussion. If a consensus was not reached, the results were reviewed by a third investigator (E.K). The extracted data consisted of the article title, first author name, year of publication, sample size, type of study, method of irrigation, type of mineral, mean and standard error, or confidence intervals of minerals.

Two authors independently assessed the studies for potential eligibility. Eligible studies were screened at a full-text level, and we resolved any disagreement through discus-

sion and with the help of a third investigator. Joanna Briggs Institute's (JBI) appraisal instrument was used to assess the quality of studies. JBI data extraction tool for quantitative studies was also utilized. The study selection procedure is summarized in Figure 1.

Meta-analysis

The results of the eligible studies were analyzed using a software program for meta-analysis (Stata 16). The change in the mineral contents of dentine was selected as the outcome. The sample size of each group and the mean and standard deviation of mineral contents of dentine in groups were extracted from the studies. Standardized mean difference (SMD, Hedges' g) was calculated for each included study in a random-effects model. Results were presented in forest plots. Statistical heterogeneity between studies was evaluated by the I^2 value (44). We performed the analysis based on the subgroups, i.e., the method of measuring minerals of the dentine, including EDS and Inductively coupled plasma (ICP) methods.

RESULTS

Study Selection

A total of 1,935 publications were initially found. Duplicates were removed, and 849 records were screened by title and abstract (Fig. 1). Records were excluded if they were irrele-

TABLE 1. Characteristics of included studies

First author, citation year	Year of implementations	Country	Type of study	Measurement tool
Erdemir A et al., 2005 (22)	2005	Türkiye	<i>in vitro</i>	ICP-AES
Guler C et al., 2014 (36)	2014	Türkiye	<i>in vitro</i>	ICP-AES
Cobankara FK et al., 2011 (38)	2011	Türkiye	<i>in vitro</i>	ICP-AES
Topçuoğlu HS et al., 2013 (24)	2013	Türkiye	<i>in vitro</i>	ICP-AES
Nogueira BML et al., 2018 (43)	2017	Brazil	<i>in vitro</i>	EDS
Nogo-Živanovic D et al., 2019 (52)	2019	Serbia	<i>in vitro</i>	EDS
Eren SK et al., 2018 (20)	2017	Türkiye	<i>in vitro</i>	EDS
Kazeminejad et al.*	2021	Iran	<i>in vitro</i>	EDS

*: Unpublished data. ICP-AES: Inductively coupled plasma atomic emission spectroscopy; EDS: Energy-dispersive X-ray spectroscopy

vant to the topic. Common reasons for exclusion were papers studying automatic materials or studies that did not provide numerical data. After the initial review, some arti-

cles were excluded due to study type (i.e., case reports and review papers). Eight studies met the criteria outlined in the objectives (Fig. 1).

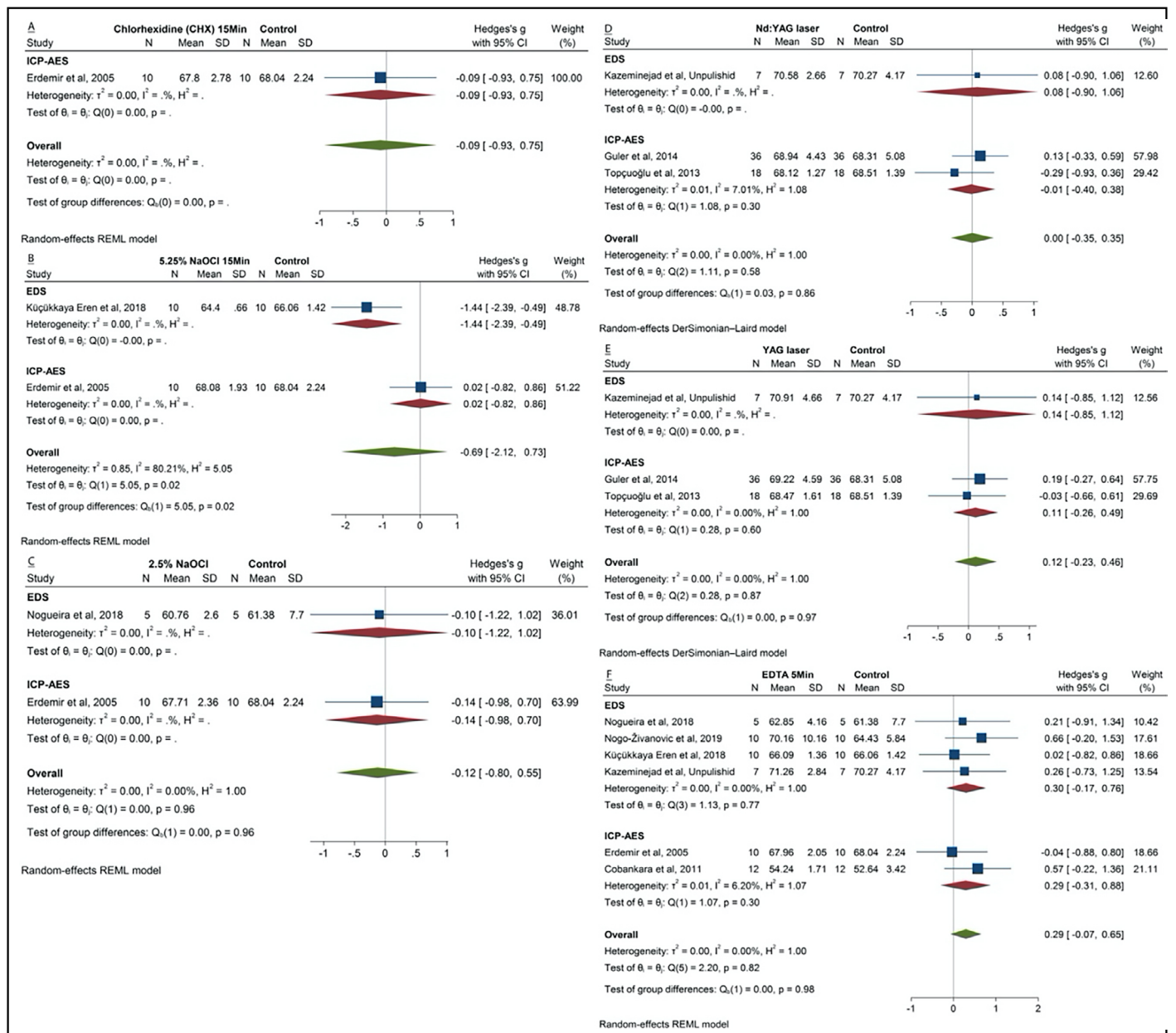


Figure 2. Forest plot of effect of endodontic irrigation on the calcium content of root canal dentine. (a) For Chlorhexidine (CHX), (b) For 5.25% NaOCl, (c) For 2.5% NaOCl, (d) For Nd:YAG laser, (e) For Er:YAG laser, (f) For Ethylenediaminetetraacetic acid (EDTA)

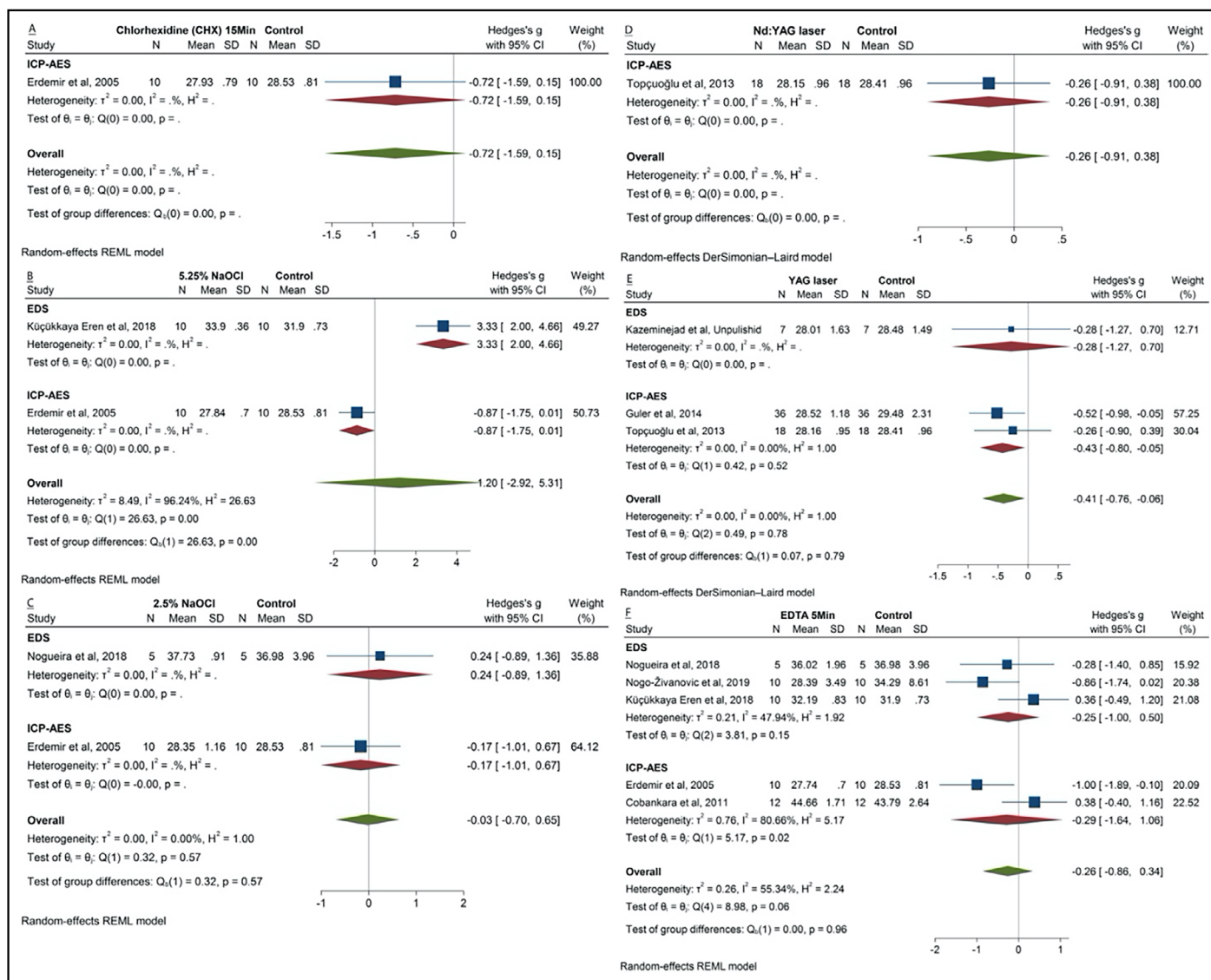


Figure 3. Forest plot of effect of endodontic irrigation on the phosphorus content of root canal dentine. (a) For Chlorhexidine (CHX), (b) For 5.25% NaOCl, (c) For 2.5% NaOCl, (d) For Nd:YAG laser, (e) For Er:YAG laser, (f) For Ethylenediaminetetraacetic acid (EDTA)

Study Characteristics

All of the studies included were *in vitro*. Studies were published between 2005 and 2019. Six studies were conducted in Türkiye, one in Brazil, one in Serbia, and one in Iran. Of the total studies included, four used the EDS method, and five used the ICP method to measure the remaining minerals in the dentinal surface of the tooth (Table 1).

Meta-analysis

Only one study had sufficient data to assess the effect of Chlorhexidine (CHX) on the calcium content of dentine by the ICP method. The results showed that CHX had no impact on the calcium content of dentine (Hedges' g=-0.09; 95% CI: -0.93, 0.75; I2=0.0%) (Fig. 2a). In addition, the results showed that 5.25% sodium hypochlorite (NaOCl) had a large and significant effect on the calcium content of dentine (Hedges' g=-1.44; 95% CI: -2.39, -0.49; I2=0.0%) (Fig. 2b).

Three studies provided enough data to calculate the effect of the Neodymium-doped Yttrium Aluminum Garnet (Nd: YAG) laser on the calcium content of dentine in the ICP method. The

results showed no significant effect of Nd: YAG laser and Erbium-doped Yttrium Aluminum Garnet (Er: YAG) laser on the calcium content of dentine (Hedges' g=0.54; 95% CI: -0.81, 1.89; I2=90.01%) (Fig. 2d), (Hedges' g = 0.09; 95% CI: -0.26, 0.44; I2 = 0.00%) (Fig. 2e). In addition, the results showed that the EDTA irrigant did not affect the calcium content of dentine in the EDS method (Hedges' g=0.30; 95% CI: -0.17, 0.76; I2=0.00%) and ICP method (Hedges' g=0.29; 95% CI: -0.31, 0.88; I2=6.20%) (Fig. 2f). The effect of other irrigants on the calcium content of dentine is shown in Figure 2.

Regarding the phosphorus content in the dentine after using different irrigants, the results showed that the removal of phosphorus content after irrigation with 5.25% NaOCl was significantly lower compared to the control group, and 5.25% NaOCl had a protective effect (Hedges' g=3.33; 95% CI: 2.00,4.66; I2=0.00%) in the EDS method. However, the measurement of phosphorus content in the ICP method after irrigation with 5.25% NaOCl showed no significant effect (Hedges' g=-0.87; 95% CI: -1.75, 0.01; I2=0.00%) (Fig. 3b).

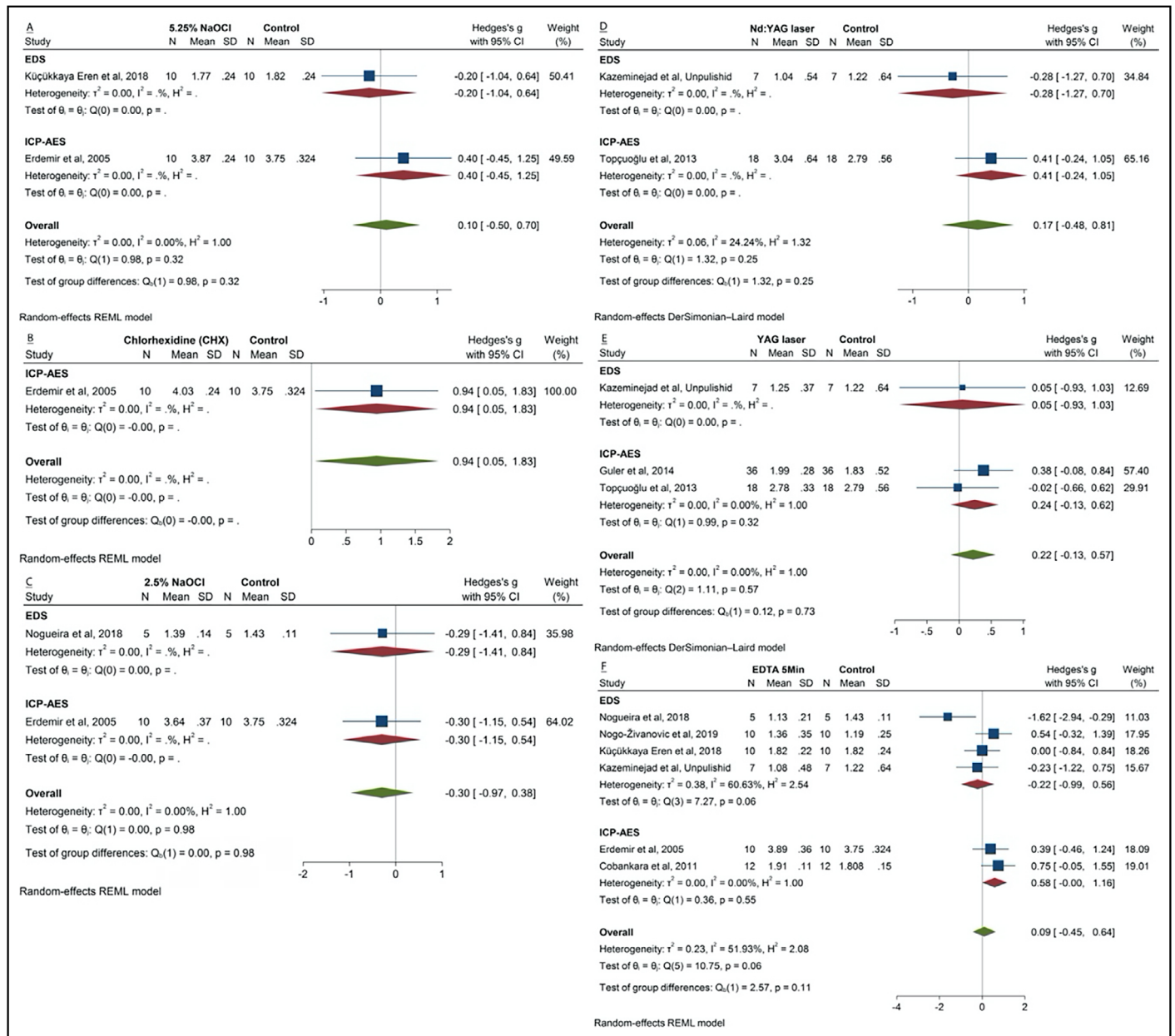


Figure 4. Forest plot of effect of endodontic irrigation on the magnesium content of root canal dentine. (a) For 5.25% NaOCl, (b) For Chlorhexidine (CHX), (c) For 2.5% NaOCl, (d) For Nd:YAG laser, (e) For Er:YAG laser, (f) For Ethylenediaminetetraacetic acid (EDTA)

Regarding the effect of Er:YAG laser on the phosphorus content of dentine by ICP method, three studies had sufficient data that showed the Er:YAG laser had a moderate and significant effect on the removal of phosphorus content in dentine (Hedges' $g = -0.49$; 95% CI: $-0.85, -0.13$; $I^2 = 0.00\%$) (Fig. 3e).

Three studies provided sufficient data about the EDTA irrigant by EDS method. The results showed that irrigation with EDTA had no significant effect on the phosphorus content of dentine (Hedges' $g = -0.25$; 95% CI: $-1.00, 0.50$; $I^2 = 47.94\%$) (Fig. 3f). The impact of other irrigants on dentine's phosphorus content is presented in detail in Figure 3.

Regarding the magnesium content after using different irrigants, three studies measured the amount of magnesium content in the ICP method. Analysis of this data showed that Er:YAG laser had no significant effect on the magne-

sium content of dentine (Hedges' $g = 0.30$; 95% CI: $-0.06, 0.66$; $I^2 = 0.00\%$) (Fig. 4e). In addition, four studies examined the magnesium content in the EDS method after irrigation with EDTA. The results showed that this irrigant had no significant effect on the magnesium content of dentine (Hedges' $g = 0.22$; 95% CI: $-0.99, 0.56$; $I^2 = 60.63\%$) (Fig. 4f). The impact of other irrigants on the magnesium content of dentine is presented in Figure 4.

The effect of Nd:YAG laser and Er:YAG laser irrigants on the calcium-to-phosphorus ratio content is presented in Figure 5. As shown, the effect of Nd:YAG laser on the calcium-to-phosphorus ratio of dentine in the ICP method was insignificant (Hedges' $g = 0.19$; 95% CI: $-0.62, 0.99$; $I^2 = 39.81\%$) (Fig. 5a). In addition, the effect of Er:YAG laser on the calcium-to-phosphorus ratio content in the ICP method was higher compared to the

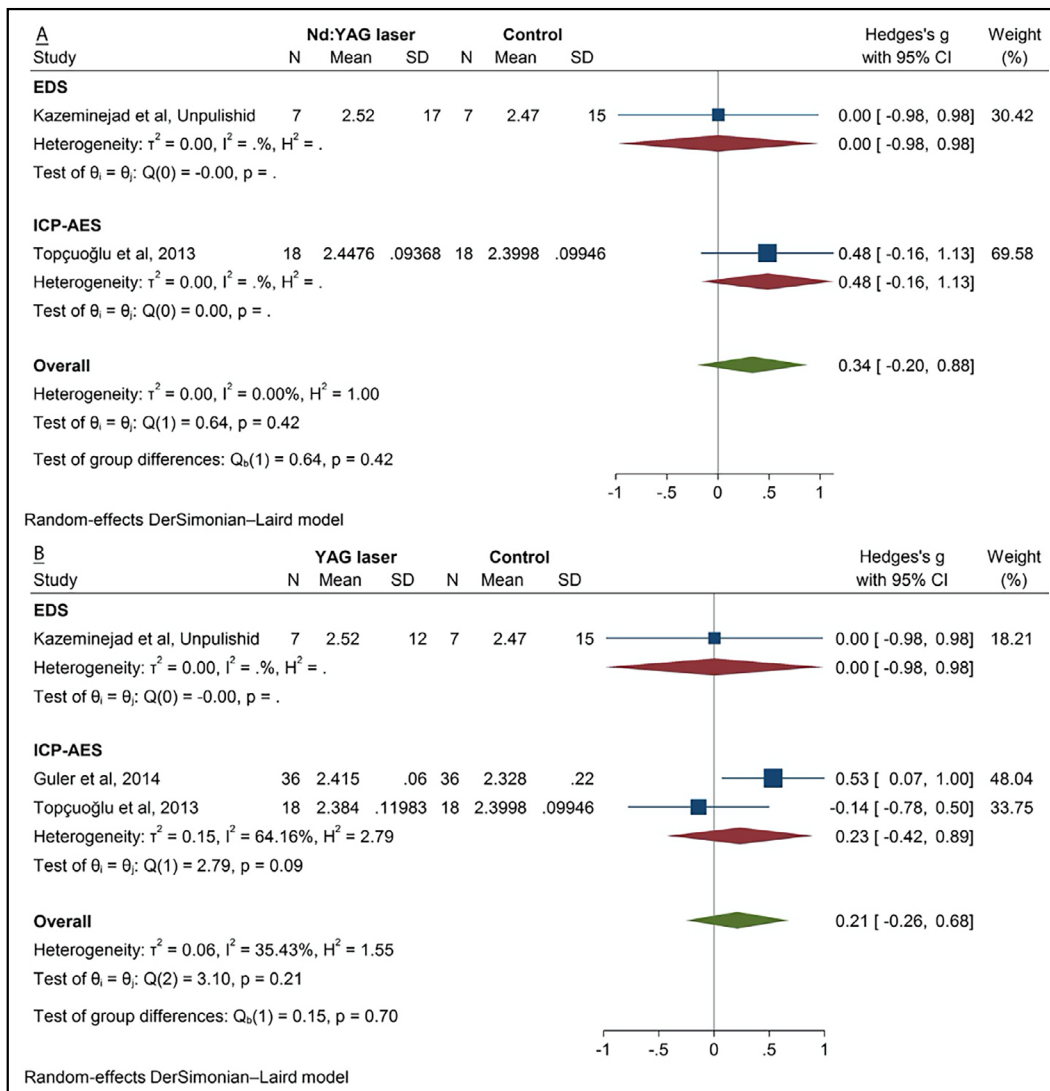


Figure 5. Forest plot of effect of endodontic irrigation on the calcium to phosphorus ratio content of root canal dentine. (a) For Nd:YAG laser, (b) For Er:YAG laser

control group. However, due to the high heterogeneity, this effect was insignificant (Hedges' $g=2.08$; 95% CI: -1.87, 6.02; $I^2=98.65\%$) (Fig. 5b).

Publication of Bias in Studies

Funnel plot and Egger's regression test were not used to assess publication bias since the number of included studies was less than 10 (45).

Risk of Bias

All studies in the meta-analysis posed an intermediate risk of bias, primarily due to blinding and adequate follow-up of reported results (Table 2).

DISCUSSION

This systematic review and meta-analysis study provides partial support for the effect of irrigation on removing mineral dentine among receiving irrigate types. This study reviewed the studies performed on dentine mineral content for calcium, phosphorus, magnesium, and potassium elements after using standard solutions and methods for root canal irrigation and treating the dentine surface in the root canal. The primary

findings of this review of the effect of 5.25% NaOCl found statistically significant effects on phosphorus content, while other root canal irrigation had a large non-significant effect on mineral dentine. However, these findings should be interpreted with caution based on the limited number of studies and small samples.

This is the first comprehensive meta-analysis on the effect of irrigation on removing mineral dentine, which clearly illustrated a significant impact. The findings seem robust, as the analysis was based on two technologies (ICP-AES and EDS). In addition, this analysis could explore the source of heterogeneity to confirm the stability of the results.

The present study showed that irrigation with 5.25% NaOCl significantly affected calcium content on the dentine surface. The residual amount of calcium was largely lower in the group irrigated with 5.25% NaOCl than in the group irrigated with distilled water; however, it was not statistically significant. In addition, irrigation with 5.25% NaOCl significantly affected residual phosphorus in the root canal dentine. This can be because calcium and phosphorus are the main components

TABLE 2. Risk of bias assessment for interventional study using JBI's critical appraisal tool

First author, citation year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total
Erdemir A et al., 2005 (22)	Y	Y	Y	Y	NA	N	NA	Y	Y	Y	Y	8
Guler et al., 2014 (36)	Y	Y	Y	Y	NA	N	NA	Y	Y	Y	Y	8
Cobankara et al., 2011 (38)	Y	Y	Y	Y	NA	N	NA	Y	Y	Y	Y	8
Topçuoğlu HS et al., 2013 (24)	Y	Y	Y	Y	NA	N	NA	Y	Y	Y	Y	8
Nogueira BML et al., 2018 (43)	Y	Y	Y	Y	Y	N	NA	Y	Y	Y	Y	9
Nogo-Živanovic D et al., 2019 (52)	Y	Y	Y	Y	Y	N	NA	Y	Y	Y	Y	9
Eren SK et al, 2018 (20)	Y	Y	NA	Y	NA	N	NA	Y	Y	Y	N	7
Kazeminejad et al.*	Y	Y	Y	Y	NA	N	NA	Y	Y	Y	Y	8

*: Unpublished data. Y: Yes; N: No; NA: Not applicable

Q1: Were the inclusion criteria in the sample clearly defined?

Q2: Is the subject of the study and the environment described in detail?

Q3: Was true randomization used for assignment of participants to treatment groups?

Q4: Were treatment groups similar at the baseline?

Q5: Was allocation to treatment groups concealed?

Q6: Were treatment groups treated identically other than the intervention of interest?

Q7: Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?

Q8: Were outcomes measured in the same way for treatment groups?

Q9: Were outcomes measured in a reliable way?

Q10: Was appropriate statistical analysis used?

Q11: Was the trial design appropriate, and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

of hydroxyapatite crystals, so irrigation with NaOCl could increase their removal. However, irrigation with Nd: YAG laser had the opposite effect compared to the impact of 5.25% NaOCl. The amount of residual calcium was higher in the Nd: YAG laser group than in the control group. This can be due to the physical effect of the laser on removing the dentine of the root canal walls, while in the control group, this process was not done in the removal of minerals, leading to an overestimation of the amount of phosphorus in the control group. Also, in the dentine microstructure, collagen fibers are surrounded and protected by nanocrystalline apatite-carbonate structures. Therefore, due to the low molecular weight of NaOCl, it is distributed in the collagen matrix of dentine. The oxidative degradation of collagen in the underlayer of mineralized dentine leads to forming a brittle dentine structure on its surface, called the collagen-poor mineral ghost layer. Moreover, this layer can be easily vulnerable to chelating solutions such as EDTA, and minerals like calcium and phosphorus extraction can be done more conveniently (35).

Since we did not find any other systematic review on this topic in the literature, we could not make any comparison in this regard. In this sense, according to the studies eligible for meta-analysis in this review, those focusing on the changes in the microstructure and composition of the surface dentine of the root canal can be addressed.

In this study, different irrigation methods indicated a decrease in the amount of calcium. However, although this decrease was higher after using EDTA than laser-assisted irrigation (Nd: Yag, Er: Yag), it was not statistically significant. Chlorhexidine and sodium hypochlorite also had little effect on the remaining calcium content. Studies have shown that calcium removal could affect flexural strength, roughness, fracture toughness, and erosion of root dentine structure (30,38,46). In addition, after removing the mineral phase of dentine, the surface col-

lagens are exposed and easily dissolved by EDTA, causing a decrease in the elasticity coefficient of dentine tissue. These changes can make dental tissue susceptible to microfractures (47,48).

On the other hand, calcium and phosphorus are the main inorganic components of hydroxyapatite. It has been shown that changes in the ratio of these two elements can affect the hardness, permeability, and adhesion of dental materials and tissue dissolving ability of dentine (22,49). However, whether these changes are clinically significant requires studies on the biomechanical properties of dentine.

Magnesium is present in trace amounts in the dentine tissue. This element plays an essential role in promoting the mineralization process, and its deficiency can decrease odontoblasts and slow down the process of dentine formation. Therefore, it makes dentine stronger (32,38). The studies showed that the amount of magnesium increased in the intervention groups. However, it has been stated that this could be due to calcium replacement with magnesium (50-52).

In the case of potassium, although it is always present in the cellular structure, no specific clinical effects on the biomechanics of dentine have been reported. The results of our study also showed no significant change in the reduction rate (43,50).

Strengths and Limitations

To our knowledge, this systematic review and meta-analysis study is the first and most comprehensive to examine the effect of irrigation on removing mineral dentine. We assessed two technologies (ICP-AES and EDS) concerning mineral dentine changes and performed a subgroup analysis to determine the source of heterogeneities. However, the limitations of the present study were the lack of control for potential confounding variables in primary studies and the limited number of studies on the effect of irrigation on removing mineral dentine.

CONCLUSION

According to this study, all the root canal irrigation protocols examined in this study did not significantly differ concerning the mineral content of root dentine, and any of them does not have superiority for changing the mineral content, providing the expected efficiency and effectiveness. Considering the limitations of the present study and the small number of studies included in the meta-analysis, the results should be interpreted and used with caution.

Disclosures

Conflict of interest: The authors deny any conflict of interest.

Peer-review: Externally peer-reviewed.

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Authorship contributions: Concept – E.K., M.N.; Design – A.R.; Supervision – E.K., A.R.; Funding - E.K., E.G.; Data collection and/or processing – M.N., M.M.; Analysis and/or interpretation – E.K., A.R., M.M.; Literature search – M.N., M.M.; Writing – E.K., M.N., E.G., A.R., M.M.; Critical Review – E.K., A.R.

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APPENDIX 1. Search strategy and terms used to identify studies

Database	Search strategy	Results
WOS	TOPIC: ((Endodont* OR Root Canal) AND (Mineral* OR Calcif*) AND (Demineraliz* OR Irrig* OR solution)) Timespan: All years. Indexes: SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, ESCI, CCR-EXPANDED, IC.	425
PubMed	((Mineral*[Title/Abstract] OR Calcif*[Title/Abstract]) AND ("Root Canal Irrigants"[Mesh])) OR (((Endodont* [Title/Abstract] OR Root Canal [Title/Abstract]) AND (Mineral*[Title/Abstract] OR Calcif*[Title/Abstract])) AND (Demineraliz*[Title/Abstract] OR Irrig*[Title/Abstract] OR solution [Title/Abstract]))	369
Scopus	(TITLE-ABS-KEY (endodont* OR root AND canal)) AND (TITLE-ABS-KEY (mineral* OR calcif*)) AND (TITLE-ABS-KEY (demineraliz* OR irrig* OR solution))	561
Embase	(endodont*:ti,ab,kw OR 'root canal':ti,ab,kw) AND (mineral*:ti,ab,kw OR calcif*:ti,ab,kw) AND (demineraliz*:ti,ab,kw OR irrig*:ti,ab,kw OR solution:ti,ab,kw)	275
Cochrane	(Endodont* OR Root Canal) AND (Mineral* OR Calcif*) AND (Demineraliz* OR Irrig* OR solution) in Title Abstract Keyword - (Word variations have been searched)	53
Wiley	"Endodont* OR Root Canal" in Abstract and "Mineral* OR Calcif*" in Abstract and "Demineraliz* OR Irrig* OR solution" in Abstract	214
ProQuest	su((Endodont* OR Root Canal) AND (Mineral* OR Calcif*) AND (Demineraliz* OR Irrig* OR solution)) OR ab ((Endodont* OR Root Canal) AND (Mineral* OR Calcif*) AND (Demineraliz* OR Irrig* OR solution)) Total=1935 After deleting duplicates=1086	38