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The effectiveness of the supplementary use of the XP-endo Finisher on bacteria content reduction: a systematic review and meta-analysis

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ABSTRACT

Objectives: This systematic review evaluated the efficacy of the supplementary use of the XPendo Finisher on bacteria content reduction in the root canal system.

Materials and Methods: *In-vitro* studies evaluating the use of the XP-endo Finisher on bacteria content were searched in four databases in July 2020. Two authors independently screened the studies for eligibility. Data were extracted, and risk of bias was assessed. Data were meta-analyzed by using random-effects model to compare the effect of the supplementary use (experimental) or not (control) of the XP-endo Finisher on bacteria counting reduction, and results from different endodontic protocols were combined. Four studies met the inclusion criteria while 1 study was excluded from the meta-analysis due to its high risk of bias and outlier data. The 3 studies that made it to the meta-analysis had an unclear risk of bias for at least one criterion.

Results: No heterogeneity was observed among the results of the studies included in the metaanalysis. The study excluded from the meta-analysis assessing the bacteria counting deep in the dentin demonstrated further bacteria reduction upon the use of the XP-endo Finisher. **Conclusions:** This systematic review found no evidence supporting the supplementary use of the XP-endo Finisher on further bacteria counting the reduction in the root canal.

Keywords: Biofilms; Dental pulp cavity; Enterococcus faecalis; Review

INTRODUCTION

The main goal of endodontic treatment is to maintain teeth affected by some pulp infection, but it is necessary to eliminate or significantly reduce the microbiota in the root canal system [1-4]. Pulp infection is treated through mechanical and physical-chemical debridement of the infected tissue by associating the use of endodontic instruments with irrigating solutions [5]. However, the anatomy of the root canal system and physiological features (*i.e.*, vascularization loss after necrosis) can jeopardize the success of root canal treatment [6]. The antibacterial efficacy of the chemical-mechanical preparation depends on several factors, including a close contact of the endodontic instrument with the root canal walls. However,

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Conceptualization: Oliveira LSJ, Bragança RMF, Faria-e-Silva AL. Data curation: Oliveira LSJ, Bragança RMF, Sarkis-Onofre R, Faria-e-Silva AL Formal analysis: Oliveira LSJ, Bragança

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RMF, Sarkis-Onofre R, Faria-e-Silva AL. Investigation: Oliveira LSJ,Bragança RMF. Methodology: Faria-e-Silva AL name. Project administration: Faria-e-Silva AL. Supervision: Faria-e-Silva AL. Writing - original draft: Oliveira LSJ, Bragança RMF, Sarkis-Onofre R, Faria-e-Silva AL. Writing - review & editing: Oliveira LSJ, Bragança RMF, Sarkis-Onofre R, Faria-e-Silva AL

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Ludmila Smith de Jesus Oliveira D https://orcid.org/0000-0002-6124-6229 Rafaella Mariana Fontes de Bragança D https://orcid.org/0000-0003-4738-3005 Rafael Sarkis-Onofre D https://orcid.org/0000-0002-1514-7879 André Luis Faria-e-Silva D https://orcid.org/0000-0003-3846-4786 it has been suggested that approximately 35% of the surface of the root canal walls remain unprepared after chemical-mechanical preparation [7]. Therefore, latent bacteria can survive in these areas and prevent the remission of infection in the root canal system, resulting in failure of the root canal treatment [8].

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Recently, several supplementary techniques and instruments with different characteristics have been developed to overcome limitations on the cleaning effectiveness associated with the instrumentation step, including the XP-endo Finisher [9,10]. This complementary universal instrument is recommended for use after the root canal preparation for cleaning overly complex morphologies and areas of difficult access, such as oval-shaped root canals [11,12]. The XP-endo Finisher is compatible with files with a diameter equal to or larger than 25, and it can expand up to 6 mm of diameter when rotating. Besides, minimal damage has been observed on the root canal walls by using the XP-endo Finisher [11,12]. Changes to this instrument (*i.e.*, cross-section features) have been proposed to increase its effectiveness in touching larger areas of the root walls and removing the remaining microbiota after biomechanical preparation [4].

The antimicrobial efficacy of the XP-endo Finisher has been evaluated in several studies using different methodologies [13-15]. However, to the best of our knowledge, the available evidence has not yet been synthesized and the role of the XP-endo Finisher in the microbiota reduction is not clear. Therefore, the aim of this study was to assess the effectiveness of the XP-endo Finisher in reducing the microbiota in the root canals system through a systematic review. The research question developed on the following PICO strategy was: "Does the supplementary use of the XP-endo Finisher (I) affect the reduction of bacteria counting (O) in infected root canals (P) when compared to not using it (C)?" The hypothesis of the study was that the additional use of the XP-endo Finisher file results in further microbiota reduction.

MATERIALS AND METHODS

This systematic review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [16]. The review protocol was not registered because the prospective international registry of systematic reviews (PROSPERO) does not allow registering systematic reviews of *in-vitro* studies. However, the systematic review protocol was developed a priori and was not modified, and it is available upon request to the authors. The PICOT strategy was: Population (P) – infected extracted teeth; Intervention (I): experimental intervention – root canal instrumentation associated with the use of the XP-endo Finisher; Control (C): control intervention – root canal instrumentation without the further use of the XP-endo Finisher; Outcome (O) – reduction on bacteria counting (without restrictions regarding the method) in the root canal system; Type of study (T) – *in vitro* studies.

Eligibility criteria

The following inclusion criteria were defined: *in vitro* studies comparing the reduction of bacteria counting after root canal instrumentation whether or not associated with the supplementary use of the XP-endo Finisher. Root canal instrumentation before the contamination of canals or the use of the XP-endo Finisher without prior instrumentation were defined as exclusion criteria. There were no restrictions regarding language or date of publication.

Table 1. Search strategy according to database

Database	Search strategy						
PubMed/MEDLINE	("Root Canal Preparation" [Mesh] OR "Root Canal Therapy" [Mesh] OR "Canal Preparation, Root" [Title/Abstract] OR "Canal Preparations Root" [Title/Abstract] OR "Preparation, Root Canal" [Title/Abstract] OR "Root Canal Preparations" [Title/Abstract] OR "Canal Therapy, Root" [Title/Abstract] OR "Root Canal Therapies" [Title/Abstract] OR "Therapy, Root Canal" [Title/Abstract]) AND ("XP endo" [Title/ Abstract] OR "XP-endo" [Title/Abstract])						
Scopus	(TITLE-ABS-KEY ("Endodontic treatment" OR "Root Canal Preparation" OR "Canal Preparation, Root" OR "Canal Preparations, Root" OR "Preparation, Root Canal" OR "Preparations, Root Canal" OR "Root Canal Preparations")) AND (TITLE-ABS-KEY ("XP endo finisher" OR "XP-endo"))						
Web of Science	(TS = (Root Canal Preparation OR Root Canal Preparations)) AND (TS = (XP endo OR XP-endo))						
Embase	('endodontic treatment':ti,ab,kw OR 'root canal preparation':ti,ab,kw OR 'canal preparation, root':ti,ab,kw OR 'canal preparations, root':ti,ab,kw OR 'preparation, root canal':ti,ab,kw OR 'preparations, root canal':ti,ab,kw OR 'root canal preparations':ti,ab,kw) AND ('xp endo':ti,ab,kw OR 'XP-endo':ti,ab,kw)						

Information sources and search

The bibliographic search aimed to identify all the studies that evaluated the effect of the XP-endo Finisher on the reduction of bacteria counting in root canal systems. The search was carried out in the following databases: PubMed/MEDLINE, Scopus, Web of Science, and Embase. The search strategy used is described in **Table 1**. The latest search was conducted in July 2020.

Study selection

The searched articles were managed by using Microsoft Excel software. After duplicates removal, 2 reviewers screened the identified articles by reading the titles and abstracts. The articles only were included after the full-text reading. Two independent reviewers (L.S.J.O. and R.M.F.B.) assessed whether the articles fulfilled the inclusion criteria. Disagreements between the reviewers were discussed until reaching a consensus. A third reviewer (A.L.F.S.) solved the remaining disagreements. The reviewers also manually searched the reference lists of the included articles for additional relevant studies.

Data extraction

The following data from the included articles were recorded: teeth used, contamination protocol, bacteria counting method, and the system used for root canal instrumentation. The protocol of data extraction was previously discussed. Data extraction was carried out by 2 independent reviewers (L.S.J.O. and R.M.F.B.) and verified by a third reviewer (A.L.F.S.) independently. Means and standard deviations of bacteria counting for the different treatments and assessment times were recorded from the included studies. Standard deviations were obtained from authors when such information was not available in the article. Data from different endodontic protocols (*e.g.*, different systems of root canal instrumentation) were combined following section 6.5.2.10 (Combining groups) of the Cochrane handbook [17].

For the articles reporting only baseline and final data, the outcome "reduction of bacteria counting" was calculated by the difference between the data collected from both assessments. Therefore, the means and standard deviations of differences were determined according to section 6.5.2.1 (Extracting post-intervention versus change from baseline data) of the Cochrane handbook [17]. Correlation coefficients were calculated from one of the included studies reporting the difference between baseline and final assessment, as determined by section 6.5.2.8 (Imputing standard deviations for changes from baseline) of the Cochrane handbook [17,18]. The details of data extraction are described in the **Supplementary Material**.



Assessment of the risk of bias

The risk of bias of the included studies was assessed by using adapted criteria for systematic reviews of *in vitro* studies [19-21]. Therefore, the following criteria were analyzed: similarity of specimens, specimen randomization, accordance with manufacturers' directions, standardization of inoculum, and blinding of outcome assessment. Each criterion was scored as having high, low, or unclear risk of bias by 2 reviewers (L.S.J.O. and R.M.F.B.). A third reviewer (A.L.F.S.) was used in case of some discordance.

Data analysis

Estimates of reduction of bacteria counting were obtained by comparing the standardized mean difference (SMD) between root canal instrumentation protocols whether using (experimental) or not using (control) the supplementary instrumentation with XP-endo, with an estimated 95% confidence interval. The SMD was used to allow summarizing the same outcome measured through different methods. The analyses were performed by adopting a random-effects model using Review Manager version 5.4 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The statistical heterogeneity of the treatment effect across studies was assessed by using the Cochrane Q test.

RESULTS

Study selection

A flowchart illustrating this review's search and selection is presented in **Figure 1**. The search resulted in the retrieval of 165 articles, which was reduced to 74 after removing duplicates.

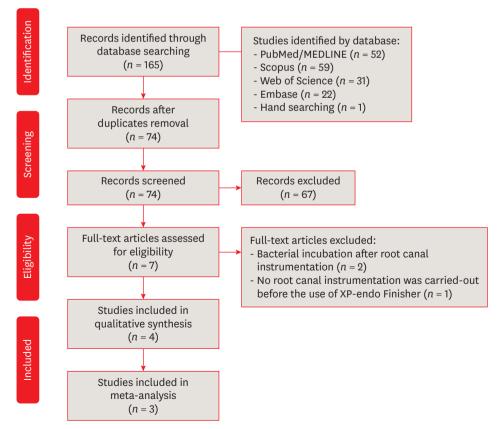


Figure 1. Flow diagram of the systematic review.



After screening titles and abstracts, only seven articles were assessed in full. Four articles met all the predefined criteria, and three made it to the meta-analysis.

Study characteristics

The characteristics of the included studies are described in **Table 2**. All included studies [18,22-24] enlarged the root canals and sterilized the specimens before the contamination procedures. Specimens were contaminated with *Enterococcus faecalis* ATCC 29212 in all studies, and the incubation times were 10 days [24], 21 days [23], 30 days [22], and 4 weeks [18], respectively. The counting of bacteria on Agar-sheep blood plates was performed in 2 studies [18,24], while the other 2 studies quantified the bacteria content using a 16S rRNA gene-targeted quantitative polymerase chain reaction (qPCR) assay [22] or Confocal laser scanning microscopy (CLSM) [23]. The root canals were instrumented with BT RaCe system (FKG Dentaire, La Chaux-de-Fonds, Switzerland) [22], XP-endo Shaper (FKG Dentaire) [23,24], iRaCe1 (FKG Dentaire) [23], Reciproc Blue (VDW, Munich, Germany) [24], Reciproc (VDW) [18], or ProTaper Next (Dentsply Maillefer, Ballaigues, Switzerland) [18].

Assessment of the risk of bias

The authors' judgments on each risk of bias item for the included studies are presented in **Figure 2**. All studies had a low risk of bias to items "similarity of specimens" and "accordance with manufacturers' directions." Only one study [24] properly reported the procedure used to randomize the specimens among the treatments. Two studies [18,22] reported that the teeth were randomly assigned to one of the experimental groups, however, with no detail as to the method used; therefore, they were scored as unclear risk of bias. Meanwhile, the other study [23] did not address the randomization of specimens and this item was scored as high risk of bias. Three studies reported [18,23,24] that the inoculum concentration was adjusted

Study	Alves et al., 2016 [11]*	Bedier et al., 2018 [23]	Carvalho <i>et al.</i> , 2019 [24]	Tüfenkçi & Yılmaz, 2020 [18]		
Teeth used	Mandibular molars	Mandibular molars	Mandibular incisors	Mandibular first molars		
Contamination protocol	1. Enlargement using BioRaCe BR2 (25/04) instrument.	1. Enlargement up to a size 25 K-file	 Enlargement up to a size 25 K-file. Smear layer removal with EDTA. 	0		
	 Smear layer removal with EDTA and 2.5% NaOCl. Specimens filled and immersed in TSB. Sterilization in an autoclave. Specimens contamination with <i>E. faecalis.</i> 	 Sterilization in an autoclave Immersion of specimens in BHI. Specimens contamination with <i>E. faecalis</i> (1 × 10⁸ CFUs/ mL). Incubation for 21 days at 37°C. 	 Immersion of specimens in BHI. Sterilization in an autoclave. Specimens contamination with <i>Exfaecalis</i> (3 × 10⁸ CFU/mL). Incubation for 10 days at 37°C. 	 NaOCI. Immersion of specimens in BHI. Sterilization in an autoclave. Specimens contamination with <i>E</i> faecalis (1 × 10⁷ CFU/mL). Incubation for 4 weeks at 37°C. 		
Bacteria counting	6. Incubation for 30 days at 37°C.1. Rinsing with a sterile saline	1. Rinsing with a sterile saline	1. Rinsing with a sterile saline	1. Rinsing with a sterile saline		
method	solution. 2. Bacteria recovered with sterile paper points.	solution. 2. A sample measuring (2 × 2 × 4 mm in thickness) was	solution. 2. Bacteria recovered with sterile stainless-steel a size 25 Hedstron	solution. 2. Bacteria recovered with sterile n paper points.		
	 Content transferred to tubes containing Tris-EDTA buffer. DNA extraction and 	removed from mild-third. 3. Staining procedure. 4. Washing with PBS.	file and paper points. 3. Content transferred to tubes containing BHI.	 Content transferred to tubes containing phosphate-buffered solution. 		
	quantification of <i>E. faecalis</i> cells by using a 16S rRNA gene- targeted qPCR assay.	5. Percentage of dead bacteria at a depth of 50 µm was assessed using a CLSM.	4. Counting the CFU/mL on Agar- sheep blood plates after 48 hour of incubation at 37°C.	4. Counting the CFU/mL on Agar- s sheep blood plates after 24 hours of incubation at 37°C.		
Systems used for root canal instrumentation	BT RaCe system (FKG Dentaire, La Chaux-de-Fonds, Switzerland)	XP-endo Shaper (FKG Dentaire) and iRaCe (FKG Dentaire)	XP-endo Shaper (FKG Dentaire) and Reciproc Blue (VDW, Munich, Germany)	ProTaper Next (Dentsply Maillefer, Ballaigues, Switzerland) and Reciproc (VDW)		

 Table 2. Characteristics of included studies

BHI, brain heart infusion; CFU/mL: colony-forming unit per milliliter; CLSM, confocal laser scanning microscopy; EDTA, ethylenediaminetetraacetic acid; NaOCl, sodium hypochlorite; PBS, phosphate buffer saline; qPCR, quantitative polymerase chain reaction; TSB, trypticase soy broth. *Only the phase 1 of the study was included.



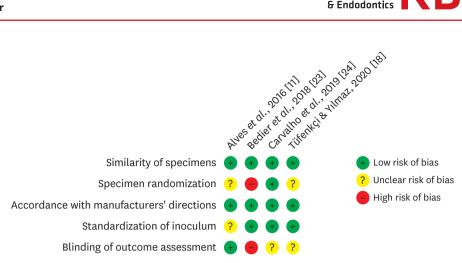


Figure 2. Authors' judgments about each risk of bias criterion for the included studies.

(low risk of bias), whereas one study [22] reported no prior standardization of inoculum (unclear risk of bias). No procedure to blind the outcome assessment was reported by any of the included studies. However, the study [22] assessing the bacteria counting through qPCR assay was scored as low risk of bias because it is unlikely that the outcome was influenced by the operator. Otherwise, in one study [23], this item was classified as a high risk of bias because the measurement area was selected by the operator using confocal laser scanning microscopy (CLSM). In the studies [18,24] assessing bacteria counting on Agar-sheep blood plates, this item was scored as having an unclear risk of bias.

Data analysis

The meta-analysis on values of bacteria counting reduction according to whether or not the XPendo Finisher was used is presented in **Figure 3**. The study [23] assessing bacteria counting with CLSM was excluded from the meta-analysis due to its high risk of bias. Moreover, the sensitivity analysis showed that this outlying study inflated the heterogeneity ($I^2 = 79\%$), also justifying its removal according to section 10.10.3 (Strategies for addressing heterogeneity) of the Cochrane handbook [17]. No heterogeneity ($I^2 = 0\%$) was observed in the meta-analysis among the results of the included studies, and the summarized effect demonstrated no further reduction on bacteria counting due to the supplementary use of the XP-endo Finisher (p = 0.15). Publication bias was not assessed due to the small number of studies included in the meta-analysis.

Study	Expe	Experimental		Control		Weight	Std. Mean difference						
	Mean	SD	Total	Mean	SD	Total	(%)		IV, R	andom,	95% CI		
Alves et al., 2016 [11] -298		419,000	9	-298,723	419,001	9	10.2	-0.00 [-0.92, 0.9	92]				
Carvalho et al., 2019 [24] –182		73,308	40	-205,350	95,044	40	44.8	0.27 [-0.18, 0.7	71]				
Tüfenkçi & Yılmaz, 2020 [18	8] -22,550,000	2,527,642	40	-23,025,000	1,830,441	40	45.0	0.21 [-0.23, 0.6	65]				
Total (95% CI)			89			89	100.0	0.21 [-0.08, 0.	.51]		•		
0,	$= 0.00; \chi^2 = 0.20$	6, df = 2 (p =	= 0.88);	$I^2 = 0\%$				-4		-2	0	2	4
Test for overall effect Z	= 1.43 (p = 0.15)									avours erimenta	al]	Favours [control]	

Figure 3. Forest plots showing the estimated effect of whether associating (Experimental) or not (Control) the use of XP-endo Finisher with root canal treatment on the bacteria counting reduction.

CI, confidence interval; SD, standard deviation.



DISCUSSION

This systematic review found only 4 *in vitro* studies addressing the effect of the supplementary use of the XP-endo Finisher on bacteria reduction in the root canal systems. One study [23] was excluded from the meta-analysis due to its high risk of bias, and also because including the data (outlier) of this study resulted in high heterogeneity. This data discrepancy can be possibly explained by the differences in the bacteria counting method. The use of CLSM allowed detecting the presence of bacteria up to 50 μ m deep in the dentin, while the other studies included in the review collected only the bacteria content inside the root canal using paper points [18,22,24] or a Hedstrom file [24]. It has been demonstrated that *E. faecalis* has an inherent ability to invade dentinal tubules and its removal is more difficult from inside the tubules [25]. In fact, the means of bacteria reduction observed using CLSM ranged from 11.8% to 62.9% [23], while it was as high as 99% in the other studies [18,22,24].

Regarding the supplementary use of the XP-endo Finisher, using CLSM demonstrated a further bacteria reduction irrespective of the system used in prior instrumentation (11.8 to 33.3 for the control, 45.2 to 62.9 for the experimental group). On the other hand, the meta-analysis showed no improvement due to the use of the XP-endo Finisher. Interestingly, 2 of the studies included in the meta-analysis concluded that the XP-endo Finisher as a supplementary approach was able to improve the disinfection ability of the chemicalmechanical instrumentation [22,24]. These conclusions were drawn because of the type of data analysis carried out. One study [22] compared (Wilcoxon test) the bacteria content measured before and after the supplementary use of the XP-endo Finisher, not considering the reduction due to the prior instrumentation. The supplementary use of the XP-endo Finisher reduced the bacteria content from 277 ± 694 to 86 ± 192 of *E. faecalis* counts (mean reduction of 70.5%). However, the initial *E. faecalis* counts in the root canals were $299,000 \pm$ 419,000, indicating that either using the XP-endo Finisher or not reduced more than 99.9% of the initial bacteria content. A similar reduction was observed in the other study [24], leading to the conclusion that the supplementary use of the XP-endo Finisher was effective. The authors of that one study used 2-way repeated-measures analysis of variance to analyze the data, and comparisons among the means observed after the chemical-mechanical preparation were used to draw the conclusions. An important point of that study was that initial bacteria contents were different across the evaluated interventions, and a lower mean overall reduction was observed for the protocols using the XP-endo Finisher (182,616 ± 73,290 colony-forming unit [CFU]/mL) than for the controls (205,350 ± 95,040 CFU/mL).

Only one of the studies included in the meta-analysis concluded that the supplementary use of the XP-endo Finisher did not improve the bacteria reduction in the root canal caused by chemical-mechanical instrumentation [18]. Unlike the other studies [22,24], this conclusion was based on the difference in bacteria content observed before and after the root canal instrumentation. In addition to statistical significance, it is essential to conclude the studies based also on the clinical significance of the findings. Therefore, a clinically relevant difference across treatments should be stated when the experimental protocol yields outcome changes that may alter a clinician's decisions regarding the treatment of a patient [26]. The overall reduction of bacteria content seems to be more relevant than only comparing the ultimate counting of bacteria remaining in the root canal, thus, the former outcome was chosen in this systematic review.



Regarding the analysis of bias, there are no well-defined criteria to assess the risk of bias in in-vitro studies, and the studies included in the present systematic review were analyzed by adapting prior criteria adopted in other reviews that evaluated *in vitro* studies [19-21]. Therefore, some methodological features with the potential to introduce some bias to the results were defined a priori. Both similarity and randomization of specimens aim to assure that some morphological differences of teeth (*i.e.*, root curvature) do not affect the assessed outcome [27]. All included studies defined criteria to include the teeth in the experiment, but only one single study [24] properly reported the method of specimen randomization among the experiment's conditions. Moreover, no study included in this review described the blinding of the outcome assessment, which is important to reduce some possible influence of evaluators on the outcomes. In fact, it is necessary to improve the reporting of the methodology of *in vitro* studies, and the use of guidelines could clarify whether or not important aspects related to both quality and risk of bias in these studies were adopted [27,28]. An important report in the study that was assessed as a potential risk of bias was the standardization of the inoculum used for specimen contamination. As bacteria reduction was the analyzed outcome, a similar bacteria content among specimens at baseline is important to assure a reliable data analysis, but one study reported no procedure to standardize the inoculum [22]. Interestingly, although using the same specimens for both experimental and control protocols reduced the risk of bias, the highest variation coefficient was observed for this study [22] indicating some consequence of the absence of standardization of the inoculum.

All included studies used either a single file reciprocating or multiple files under continuous rotation before the supplementary use of the XP-endo Finisher; the manufacturers' directions were strictly followed in all protocols evaluated. No significant difference in the bacteria reduction was observed across the different chemical-mechanical instrumentations in the studies evaluating more than one system [18,23,24]. It has been demonstrated that the instrumentation systems using either reciprocating or rotatory motion yield similar bacteria reduction [29]. Regarding the irrigating solutions, 2 studies [22,23] removed the smear layer using 17% ethylenediaminetetraacetic acid (EDTA) followed by neutralization with 2.5% sodium hypochlorite; 1 study [24] used only sodium hypochlorite (0.9% or 2.5%), and the fourth study [18] neither removed the smear layer nor used an irrigating solutions can facilitate the bacteria reduction achieved with the mechanical instrumentation by dissolving the organic content [30,31]. However, similar bacteria reduction (\approx 99%) was observed for all three studies included in the meta-analysis although the irrigation protocol can affect the cleaning ability of the chemical-mechanical instrumentation.

The findings of this systematic review are limited since only four studies met the inclusion criteria, while only 3 of them presenting some items judged as unclear risk of bias were included in the meta-analysis [18,22,24]. Moreover, the single study [23] evaluating the bacteria content deep in the dentin was classified as high risk of bias considering the randomization of specimens and blinding of outcome assessment. Finally, publication bias was not assessed due to the small number of studies included in the meta-analysis. Therefore, the results of this systematic review demonstrating that the use of the XP-endo Finisher does not affect the bacteria reduction assessed into the root canal should be interpreted with caution.



CONCLUSIONS

The present systematic review found no evidence supporting the supplementary use of the XP-endo Finisher to further reduce bacteria counting of the root canal after chemical-mechanical preparation.

SUPPLEMENTARY MATERIAL

Supplementary Material

Data extraction

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