

Effectiveness in the removal of bioceramic sealers versus conventional sealers: systematic review and meta-analysis

Análise da eficácia de remoção de cimentos obturadores biocerâmicos versus cimentos convencionais: revisão sistemática e metanálise de estudos *in vitro*

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Izabela Volpato Marques Tookuni

Master in Integrated Dentistry

Institution: Centro Universitário Ingá (UNINGÁ)
Address: Avenida Mandacarú, 1550, Maringá - PR
E-mail: izabelavmarques@gmail.com

Marcelo Capitânio

PhD in Integrated Dentistry

Institution: Universidade Estadual de Maringá (UEM)
Address: Avenida Mandacarú, 1550, Maringá - PR
E-mail: immarceloc@gmail.com

Breno Gabriel da Silva

PhD Student in Agronomic Statistics and Experimentation

Institution: Escola Superior de Agricultura Luiz de Queiroz
Address: Av. Pádua Dias, 235, Agronomia, Piracicaba - SP, CEP: 13418-900
E-mail: brenosilva@usp.br

Isabela Inoue Kussaba

Specialist in Endodontics

Institution: Universidade Estadual de Maringá (UEM)
Address: Avenida Mandacarú, 1550, Maringá - PR
E-mail: isabelaikussaba@gmail.com

Nair Narumi Orita Pavan

PhD in Pharmaceutical Sciences

Institution: Universidade Estadual de Maringá (UEM)
Address: Avenida Mandacarú, 1550, Maringá - PR
E-mail: narumiopavan@gmail.com

Marcos Sergio Endo

PhD in Clinical Dentistry

Institution: Centro Universitário Ingá (UNINGÁ)
Address: Avenida Mandacarú, 1550, Maringá - PR
E-mail: marcossendo@gmail.com

ABSTRACT

This study aimed to carry out a systematic review to evaluate the effectiveness in removing bioceramic sealers compared to conventional sealers commonly used, evaluated through the percentage of remaining material. The electronic search was carried out in the following databases: MEDLINE (PubMed), Embase, Web of Science, Scopus, Cochrane Library, and in gray literature, at the Brazilian Digital Library of Theses and Dissertations (BDTD). Two independent researchers conducted the survey to identify the studies, without restrictions on year and language of publication, using the PICO strategy until the month of August 2020. A total of 80 titles were retrieved in the initial search, however, only 9 studies were included for the qualitative synthesis and 5 studies were included in the quantitative synthesis. The descriptive results indicated that the average time taken to remove the filling material was longer for bioceramics by approximately 67% of the studies that evaluated this condition, and with regard to the establishment of patency, no difference was detected between the sealers. It could be observed that bioceramic sealers presented a lower amount of remaining material than conventional sealers ($p = 0.01$) both in the overall analysis and in the analysis of subgroups. The removal of conventional sealer proved to be inferior to bioceramic sealers, with greater amounts of material remaining in the root canals after endodontic retreatment. The use of bioceramic sealers has gained space in the endodontic practice. However, it is not yet known whether these sealers affect the removal of root canal fillings during retreatments.

Keywords: systematic review, bioceramic sealer, endodontic sealer, meta-analysis.

RESUMO

O objetivo deste estudo foi realizar uma revisão sistemática para avaliar a eficácia na remoção de cimentos biocerâmicos em comparação com os cimentos convencionais comumente utilizados, avaliada por meio da porcentagem de material remanescente. A busca eletrônica foi realizada nos seguintes bancos de dados: MEDLINE (PubMed), Embase, Web of Science, Scopus, Cochrane Library, e na literatura cinzenta, na Biblioteca Digital Brasileira de Teses e Dissertações (BDTD). Dois pesquisadores independentes realizaram a pesquisa para identificar os estudos, sem restrições de ano e idioma de publicação, usando a estratégia PICO até o mês de agosto de 2020. Um total de 80 títulos foi recuperado na pesquisa inicial, porém, apenas 9 estudos foram incluídos na síntese qualitativa e 5 estudos foram incluídos na síntese quantitativa. Os resultados descritivos indicaram que o tempo médio de remoção do material de obturação foi maior para a biocerâmica em aproximadamente 67% dos estudos que avaliaram essa condição e, com relação ao estabelecimento da patência, não foi detectada diferença entre os cimentos. Foi possível observar que os cimentos biocerâmicos apresentaram uma quantidade menor de material remanescente do que os cimentos convencionais ($p = 0,01$), tanto na análise geral quanto na análise de subgrupos. A remoção do cimento convencional mostrou-se inferior à do cimento biocerâmico, com maior quantidade de material remanescente nos canais radiculares após o retratamento endodôntico. O uso de cimentos biocerâmicos tem ganhado espaço na prática endodôntica. Entretanto, ainda não se sabe se esses cimentos afetam a remoção das obturações dos canais radiculares durante os retratamentos.

Palavras-chave: revisão sistemática, cimento biocerâmico, cimento endodôntico, meta-análise.

1 INTRODUCTION

Endodontic treatment consists of eliminating as many microorganisms as possible from the root canal, and hermetically sealing it to prevent the proliferation of surviving bacteria or recontamination of the root canal, as one of the most common causes of endodontic failure is when root canal root was not sufficiently clean or shaped, retaining microbial remnants and necrotic tissues that persist in the apical third, which may serve as a substrate for new bacterial growth [1, 2]. A systematic review reported primary endodontic treatment failure rates from 15 to 32% [3]. Therefore, sometimes, endodontic retreatment is necessary, which, although with slightly higher failure rates [4], still remains as the first option in most cases. Furthermore, the choice of dental material [5] or post fiber type and cementation technique used for the restoration are important factors that also need to be considered [6], providing desired properties for postendodontic reconstruction, such as bioactivity [5] and better distribution of stress during mastication on the dental residue structures [6]. Procedures in retreatment include the removal of the filling material throughout the pulp cavity, followed by mechanical preparation, chemical-mechanical disinfection and subsequent root canal sealing [7]. However, filling material, especially endodontic sealers, can become adhered to the dentin because they stick adhesively, penetrating the dentinal tubules, providing them with a mechanical imbrication [8]. Furthermore, they are classified according to their main constituents: zinc oxide and eugenol, calcium hydroxide, glass ionomer, epoxy resin and the most current bioceramic sealers, also known as calcium silicate-based sealers. Bioceramic filling sealers have recently attracted attention in Endodontics due to their excellent biocompatibility and bioactivity [9]. These are bioactive and were developed to increase the quality of root canal sealing [10], mainly composed of di- and tricalcium silicate, calcium phosphate, calcium hydroxide and zirconium oxide as a radiopacifier [11]. They have properties such as alkaline pH, biocompatibility, bioactivity, non-toxicity, dimensional stability, sealing capacity and potential to increase root strength after filling [12, 13]. In addition, many of these materials have pre-mixed preparations, thus ensuring a much simpler and faster insertion. Due to their properties of adhesion to dentin, bioceramics have the reported disadvantage of being difficult to remove from the root canal walls [14], despite this, little is known about the retreatment potential of these materials. Therefore, knowing about the effectiveness in removing these new filling sealers is of paramount importance, as their use in endodontic routine has become increasingly common. The aim of this study was to systematically review the literature on the removal resistance of bioceramic filling sealers in endodontic retreatment compared to conventional sealers used in root canal filling; it was evaluated through the amounts of residual filling. The secondary

objectives were to evaluate the time taken to remove the filling material and also to establish foramen patency between these two sealers.

2 METHODS

2.1 FOCUSED QUESTION

The key question of this research was based on the PICO strategy consisting of: In extracted teeth (P), does the filling with bioceramic sealers (I) make the root canal removal (O) less effective compared to other sealers used (C)?

This systematic review was conducted according to the PRISMA protocol [15] and was also registered in the International Prospective Register of Systematic Reviews (PROSPERO) ID: CRD42020196154.

2.2 INCLUSION AND EXCLUSION CRITERIA

Inclusion criteria: *in vitro* studies; Extraction of teeth with complete rhizogenesis; Use of bioceramic sealer for root canal filling.

Exclusion criteria: lack of a group for comparison with conventional cements used for filling; Comparison group is composed of another type of bioceramic sealer or calcium silicate hybrid bioceramic sealer.

2.3 SEARCH STRATEGY

To identify potentially relevant studies, a complete electronic search was carried out in the following databases: MEDLINE (PubMed), Embase, Web of Science, Scopus, Cochrane Library, and in gray literature, at the BDTD (Brazilian Digital Library of Theses and Dissertations). The search was carried out in June, July and August 2020, with no restriction on language or year of publication. The primary selection of studies was performed independently by 2 examiners (IVMT and MC), through the Rayyan software (rayyan.qcri.org) and when there was divergence between the evaluators, a 3rd evaluator (MSE) was requested. The Kappa test for agreement of the 2 raters was 0.86, indicating a high level of agreement. Data extraction took place in the same way as mentioned above.

2.4 TERMS USED IN THE SEARCH

The search strategy included 6 Mesh (Medical Subject Heading) terms and 48 uncontrolled descriptors listed in Table 2. The searches in the other platforms were carried out

according to the guideline of each database, with the respective Mesh terms, Entree terms and Descriptors in Health Sciences suited to each database.

Table 1. Mesh terms and uncontrolled terms used to assemble the search strategy followed by String to search at Pubmed platform.

PUBMED	MESH TERMS	OTHERS
P – Extracted tooth	tooth OR "tooth extraction"	"extracted tooth" OR teeth OR "teeth extraction" OR "extracted teeth" OR "permanent tooth" OR "adult tooth"
AND	AND	AND
I – Bioceramic cement	-	bioceramic* OR "bioceramic root canal sealer" OR "bioceramic root canal sealers" OR "bioceramic sealer" OR "bioceramic endodontic sealer" OR "bioceramic endodontic sealers" OR "bioceramic-based root canal sealers" OR "bioceramic-based root canal sealer" OR "bioceramic endodontic material" OR "Root SP" OR "BC Sealer" OR "BioRoot™ RCS" OR "Endosequence BC sealer" OR "calcium silicate-based sealer" OR "calcium silicate-based endodontic sealers" OR "calcium silicate-based root canal sealer" OR "bioceramic-based sealer" OR "bio-c sealer" OR "IRoot SP" OR "bioceramic root sealer" OR bioaggregate OR "TotalFill BC Sealer" OR "EndoSeal MTA"
AND	AND	AND
C – Conventional sealers	"root canal sealants" OR "root canal filling materials" OR "canal sealants"	"root canal filling" OR "endodontic sealer" OR "endodontic filling" OR "root canal sealer" OR "root filling material" OR "root canal dressing" OR "dental root filling material"
AND	AND	AND
O - Removal of filling material	Retreatment	retreatability OR "endodontic retreatment" OR "endodontics retreatment" OR "gutta-percha removal" OR "removal of gutta-percha" OR "removing obturation material" OR "remaining filling material" OR disobturation OR desobturation OR "root canal retreatment" OR "removing root canal filling material"
STRING adopted in PUBMED	(((tooth OR "tooth extraction" OR "extracted tooth" OR teeth OR "teeth extraction" OR "extracted teeth" OR "permanent tooth" OR "adult tooth") AND (bioceramic* OR "bioceramic root canal sealer" OR "bioceramic root canal sealers" OR "bioceramic sealer" OR "bioceramic endodontic sealer" OR "bioceramic endodontic sealers" OR "bioceramic-based root canal sealers" OR	

"bioceramic-based root canal sealer" OR "bioceramic endodontic material" OR "Root SP" OR "BC Sealer" OR "BioRoot™ RCS" OR "Endosequence BC sealer" OR "calcium silicate-based sealer" OR "calcium silicate-based endodontic sealers" OR "calcium silicate-based root canal sealer" OR "bioceramic-based sealer" OR "bio-c sealer" OR "IRoot SP" OR "bioceramic root sealer" OR bioaggregate OR "TotalFill BC Sealer" OR "EndoSeal MTA")) AND ("root canal sealants" OR "root canal filling materials" OR "canal sealants" OR "root canal filling" OR "endodontic sealer" OR "endodontic filling" OR "root canal sealer" OR "root filling material" OR "root canal dressing" OR "dental root filling material")) AND (retreatment* OR retreatability OR "endodontic retreatment" OR "endodontics retreatment" OR "gutta-percha removal" OR "removal of gutta-percha" OR "removing obturation material" OR "remaining filling material" OR "disobturation" OR "desobturation" OR "root canal retreatment" OR "removing root canal filling material")

Source: Authors

2.5 LITERATURE SCREENING AND DATA EXTRACTION

Articles identified using the search terms were exported to the Rayyan software (rayyan.qcri.org) for duplicate checking. Once the duplicates were eliminated, a first screening of titles and abstracts of the articles was made according to the inclusion and exclusion criteria. After the initial selection, articles were read in full, evaluated for eligibility and qualitative synthesis through a complete screening of the text.

For analysis of each article, the following data were extracted: journal, title, authors, year, dental group, sample number, and whether there was sample calculation, groups, type of instrumentation, conventional sealer used, bioceramic sealer used, use of solvent or not, operator skill and calibration, filling material removal technique and whether there was complementation, removal of filling material time, percentage of patency, number of evaluators, evaluation method, removal results in percentage, conclusion, blinding, randomization, funding sources, conflict of interest and observations. Regarding missing data, we decided not to contact the authors of the selected studies.

2.6 METHODOLOGICAL QUALITY AND RISK OF BIAS ANALYSIS

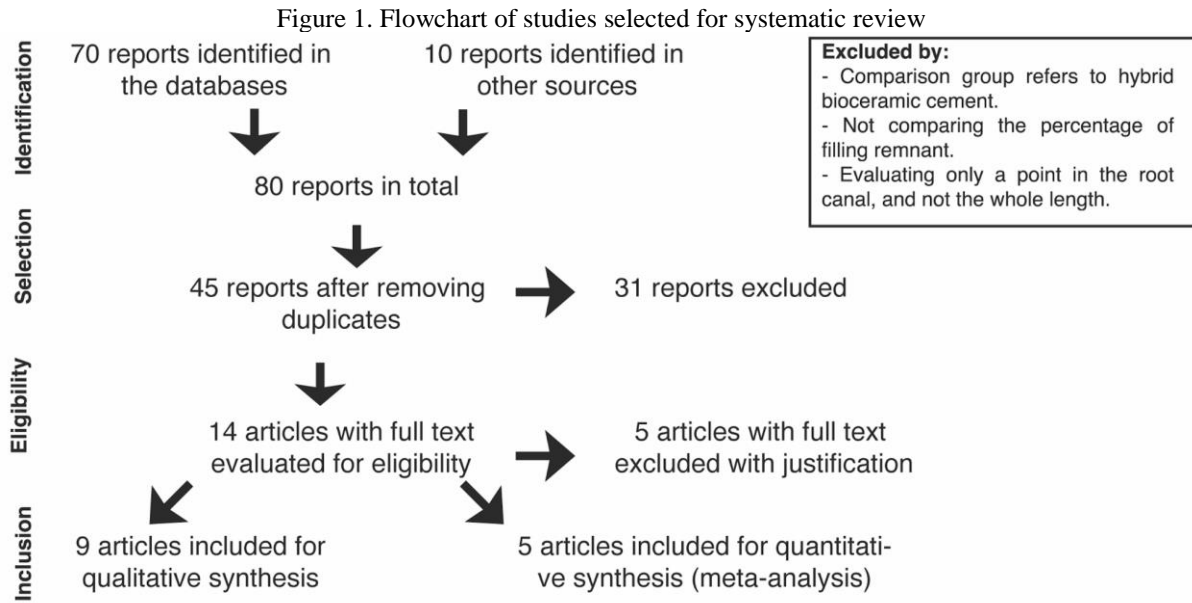
Study quality was assessed for each article through an internal 30-question data abstraction form by examining information such as the number and type of teeth, endodontic treatment and retreatment procedures, experience of the operators, evaluation method and statistical analysis. The form was also used to collect information about randomization and blinding. Thus, the risk of bias of the studies could be assessed using the Rob - Cochrane tool, following the guideline Revised Cochrane risk-of-bias tool for randomized trials (RoB 2).

2.7 DATA ANALYSIS

Initially, a descriptive analysis was performed based on data from all included studies, which were tabulated in Excel software, version 2013. Statistical analyses were run using the R 4.0.2 software (R., Auckland, New Zealand). For statistical analysis, the Shapiro-Wilk test was applied to analyze the hypothesis of normality of the mean proportions in each study group. The Student's t-test was used to compare means to check for possible differences between the groups (bioceramic and conventional). Regarding the meta-analysis, in order to express the effect size and respective 95% confidence interval, the standardized mean difference (SMD) was used, as the observations have different units of magnitude (area and volume). In order to assess heterogeneity between studies, the Cochran Q test and I² statistics were used. To graphically represent the results of the meta-analysis, the forest plot was used. The fixed effects model was considered due to the number of existing works and because they contain different elements in the samples. As there are less than 10 studies, the funnel plot and the Begg test were not used to assess possible publication bias. The adopted level of significance in all tests was 5% (p-value <0.05).

3 RESULTS

The search resulted in 80 preliminary articles, of which 27 articles were in Medline (Pubmed), 18 in Embase, 9 in Scopus, 12 in Web of Science, 4 at the Cochrane Library and 10 articles from other sources, gray literature and active search in description of references. Moreover, 1 additional article was identified through other resources. After removing duplicates, 45 articles remained, which were evaluated for title and abstract, and of these, 31 were excluded according to the inclusion and exclusion criteria. In total, 14 articles were selected for full reading and 9 were selected because they met the eligibility criteria (Figure 1).



Source: Authors

3.1 CHARACTERISTICS OF THE INCLUDED STUDIES

The detailed characteristics of the included studies are listed in Table 3.

Regarding bioceramic sealers, Endosequence BC Sealer was the sealer used in seven (77.7%) (Ersev et al. 2012); [17, 18, 19, 20, 21, 22] out of the nine studies surveyed. Among the conventional sealers, those based on epoxy resin, zinc oxide and glass ionomer were observed. The most used in the studies was the AH Plus (66.6%) [16, 23, 18, 19, 20, 21].

Table 2. Studies included after meeting the eligibility criteria. Legend: *Studies not included in the meta-analysis.

Study	Sample size	Conventional cement	Bioceramic cement	Remnant percentage	Time (s)	Clinical patency (%)	Evaluation method	Results
Cornelissen et al., 2020	n=60	TopSeal	Endosequence BC Sealer	Conventional: 2.06 Bioceramic: 1.69	Conventional: 229.7 Bioceramic: 326.4	Conventional: 96.7% Bioceramic: 100%	Periapical radiography (AREA)	There was no significant difference in the percentage of remaining material between the cements. The time for total retreatment was significantly longer in the bioceramic groups.
Dornneyer et al., 2017	n=192	AH Plus	BioRoot RCS Endo CPM Sealer	Conventional: 13.5 Bioceramic: 3.86	Conventional: 240.6 Bioceramic: 190.0	Conventional: 100% Bioceramic: 100%	Photo 8x Operative microscope (AREA)	OH Plus showed significantly higher percentage of remaining material and longer retreatment time (<0.001).
Ersev et al., 2012	n=120	AH Plus Hybrid Root SEAL Activ GP	Endosequence BC Sealer	Conventional: 13.96 Bioceramic: 13.75			Periapical radiography (AREA)	When comparing cements, the only significant difference was detected between AH Plus/manual and Activ GP/manual with respect to the percentage of remnant material in the total area of the root canal (P < 0.05).
Zuolo et al., 2016	n=64	Pulp Canal Sealer	Endosequence BC Sealer	Conventional: 2.59 Bioceramic: 6.83	Conventional: 166.3 Bioceramic: 216.6	Conventional: 100% Bioceramic: 84.38%	Micro CT (VOLUME)	Groups with teeth filled with Pulp Canal Sealer (PCS) had less filler remaining than groups with teeth filled with Endosequence (BCS). Roots filled with BCS also required longer time for retreatment than those filled with PCS.

Crozeta et al., 2021	n= 28	AH Plus	Endosequenc e BC Sealer	Conventional: 28.30 Bioceramic: 16.06		Micro CT (VOLUME)	There was a significant difference between the type of cement used; the filling with BC Sealer cement showed lower amounts of remaining material when compared to AH Plus.
Kakoura & Pantelidu, 2018*	n=68	AH 26	BioRoot RCS TotalFill BC Sealer	Conventional: 84.4 Bioceramic: 93.3	Conventional:95% Bioceramic: 100%	MEV 100x and 1000x	There was no significant difference between the percentage of filling remnant between the groups.
Kim et al., 2019*	n= 57	AH Plus	Endosequenc e BC Sealer EndoSeal MTA			Micro CT (AREA)	There was no statistically significant difference between retreatment between all cements and one- and two-root canals. However, in C-molars, EndoSeal showed the highest values of remaining material, followed by AH Plus and BC Sealer. The percentage of remaining material was significantly higher in the C-shaped canals when compared to the one- and two-root canals (p<0.05).

Oltra et al., 2017*	n=56	AH Plus	Endosequenc e BC Sealer	Conventional with solvent: 100% Conventional without solvent: 100% Bioceramic with solvent: 93% Bioceramic without solvent: 14%	Micro CT (VOLUME)	The AH Plus + chloroform group showed a significant reduction when compared to the AH Plus group without chloroform, BC Sealer + chloroform and BC Sealer without chloroform when the entire length was analyzed. The AH Plus group without chloroform showed less remaining material when compared to the BC sealer without chloroform, however, with no significant difference.
Suk et al., 2017*	n= 36	AH Plus	Endosequenc e BC Sealer		Micro CT (VOLUME)	There was no statistical difference between the AH Plus and Endosequence BC groups after retreatment with PTU.

Source: Authors

3.2 QUALITATIVE DESCRIPTIVE ANALYSIS

As a secondary objective, the mean time taken to remove the filling material of conventional and bioceramic sealers was evaluated. Among the studies included, only three performed this assessment of the mean time to remove the filling. Two studies (66.6%) indicated a longer retreatment time with bioceramic sealer [17, 22] versus one study (33.3%) that obtained a longer time with conventional sealer, in this case, based on epoxy resin [23].

Only five studies evaluated foramen patency, among them, two reported a higher occurrence of patency when using bioceramic sealers [24, 22], two observed the opposite, that is, a higher occurrence of patency when using conventional sealers [17, 18] and one study obtained patency in 100% samples, with no differences between conventional and bioceramic sealers [23].

Regarding the filling technique used, there was a higher prevalence of the use of the single cone (66.6%) [16, 23, 24, 21, 22, 20], followed by continuous wave (33.3%) [17, 18, 21], lateral condensation and vertical compaction (11.1%) [19, 22].

The method used for removal of the filling material in the studies was through the use of manual, rotary and reciprocating files, and some studies presented methods for complementing this removal through the use of ultrasound, XP Endo Finisher, YAG laser [19, 20]. 77.7% studies used a sequence of rotary files [16, 17, 23, 19, 18, 24, 21], 44.4% used reciprocating files for retreatment [17, 23, 22, 20] and only two studies used groups composed of hand files [16, 23].

Of the studies analyzed, five (55.5%) evaluated the amount of filling remnant through microtomography (Micro-CT) (de Siqueira Zuolo et al. 2016); [18, 19, 20, 21], followed by radiographic evaluation (22.2%) [16, 22], scanning electron microscopy (11.1%) [24] and digital photography through the operating microscope [23] (11.1%).

Therefore, regarding the question of the PICO strategy, 55.5% found no significant difference in the percentage of material remaining after removal either with conventional sealer or with bioceramic sealer [16, 19, 24, 21, 22], however, to obtain this answer, the statistical analysis and meta-analysis were applied.

3.3 QUANTITATIVE ANALYSIS (META-ANALYSIS)

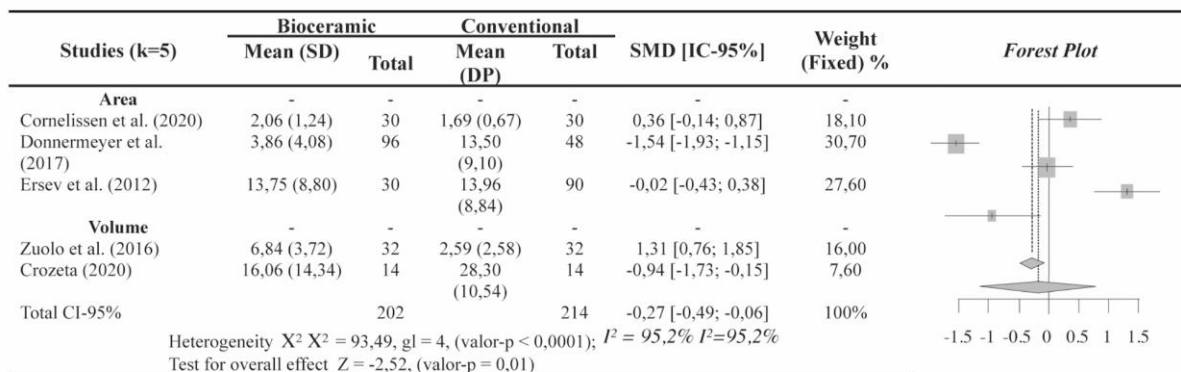
3.3.1 General meta-analysis

The meta-analysis was performed based on the main objective of evaluating the amount of material remaining between bioceramic and conventional sealers. The hypothesis of normality of the mean percentages of materials in the conventional and bioceramic groups was

accepted (p-value=0.45 and p-value=0.38, respectively). Student’s t-test evidenced no significant differences between the mean percentages of materials between the groups (p-value=0.55). Due to dissimilar characteristics in the studies, regarding the unit of magnitude used (area and volume), the standardized mean difference (SMD) was used as a metric for the effect size, which is expressed by dividing the differences in the means of the two groups by the common standard deviation between them, noting that these were significant, that is, there were differences between the two groups, in which the result indicates a superior effect in relation to the amount of bioceramic material remnant, with a mean difference of -0.27 (95% CI [-0.49; -0.06]; p-value = 0.01).

The result of the effect size for the comparative groups was superior for the studies of [23] (-1.54; 95% CI[-1.93; -1.15]) and [16] (-0.02; 95% CI[-0.43; 0.38]), corroborating the values of Weight(Fixed)% (30.70% and 27.60% respectively), in which the size of the square observed in the Forest Plot reflects their weight, and the horizontal lines represent the 95% CI, and the effect size common to the groups is graphically represented by the diamond, as seen in the Forest Plot, where its center corresponds to the effect size (-0.27) and its ends to the 95% CI [-0.49; -0.06], noting heterogeneity between studies using the Cochran’s Q test (p-value<0.0001) and $I^2= 95.2\%$, with an I^2 value of 0% indicating no heterogeneity, while the values of 25%, 50%, and 75% are considered low, moderate and high [25] (Figure 2).

Figure 2. Result of the meta-analysis of the standardized mean differences in relation to the bioceramic and conventional groups.



Source: Authors

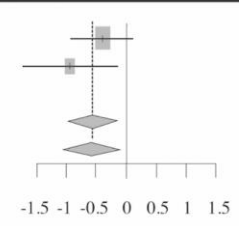
3.4 SUBGROUP META-ANALYSIS

For the meta-analysis in subgroups, given the observation of a very high heterogeneity in the overall analysis involving all types of sealers, the selected studies were separated by commercial brands in order to make a comparison between bioceramic and conventional

sealers. However, only two studies presented the same bioceramic sealer and the same conventional sealer, allowing comparisons. The standardized mean difference (SMD) was used as a metric for the effect size, as well as in the overall meta-analysis. With regard to this new analysis, in which the material used for the conventional group was AH Plus and the bioceramic was Endosequence BC Sealer, the results showed significant differences (Table 5), with a superior effect for the bioceramic material, with a mean difference of -0.55 (95% CI [-0.98; -0.12]; p-value = 0.01), (Figure 3).

The result of the effect size for the comparative groups was superior for the study by Ersev et al. (2012) (-0.39; 95% CI[-0.90; 0.11]), corroborating the value of Weight (Fixed) (70.30%), in which the size of the square observed in the Forest Plot reflects their weight and the horizontal lines represent the 95% CI, and the effect size common to the groups is graphically represented by the diamond, as seen in the Forest Plot, where its center corresponds to the effect size (- 0.55) and its ends to the 95% CI [-0.98; -0.10=2], pointing to homogeneity between studies using the Cochran’s Q test (p-value=0.25) and $I^2=23.70\%$.

Figure 3. Result of the meta-analysis of standardized mean differences for the bioceramic and conventional groups considering the studies by [16] and [20].

Studies (k=2)	Bioceramic EndoSequence BC Sealer		Conventional AH Plus		SMD [CI-95%]	Weight (Fixed) %	Forest Plot
	Mean (SD)	Total	Mean (SD)	Total			
Area	-	-	-	-	-	-	
Ersev et al. (2012)	13,75 (8,80)	30	17,25 (8,65)	30	-0,39 [-0,90; 0,11]	70,30	
Volume	-	-	-	-	-	-	
Crozeta (2020)	16,06 (14,34)	14	28,30 (10,54)	14	-0,94 [-1,73; -0,15]	29,70	
Total IC-95%		44		44	-0,55 [-0,98; -0,12]	100,00	
Heterogeneity $\chi^2 \chi^2 = 1,31$, $gl = 1$, (valor-p = 0,25); $I^2 = 23,70\%$ $I^2 = 23,70\%$ Test for overall effect $z = -2,55$, (valor-p = 0,01)							

Source: Authors

3.5 METHODOLOGICAL QUALITY AND RISK OF BIAS

Of the 9 studies included for the qualitative analysis, 7 described that they were randomized; however, only 3 reported the method in which this was done. Of these 3 studies, only 2 were blinded. Thus, according to our assessment, most studies had a moderate risk of bias and 1 had a high risk, as there was no blinding and randomization (Figure 4).

Figure 4. Risk of bias analysis by the Rob – Cochrane tool.

Study ID	D1	D2	D3	D4	D5	Overall	
CORNELISSEN 2020	+	!	+	+	!	!	+
ZUOLO 2016	!	!	+	+	!	!	!
DONNERMEYER 2017	!	!	+	+	!	-	-
ERSEV 2012	+	!	+	+	!	!	
KAKOURA 2018	!	!	+	+	!	!	D1
OLTRA 2017	!	!	+	+	!	!	D2
KIM 2015	!	!	+	+	!	!	D3
SUK 2017	!	!	+	+	!	!	D4
CROZETA 2020	!	!	+	+	!	!	D5

Source: Authors

4 DISCUSSION

In the descriptive analysis, most studies reported no difference when comparing the amount of remaining material between bioceramic and conventional sealers. However, when the overall meta-analysis of the studies was performed, a significant difference was detected, which benefits the group of bioceramic sealer in the removal of the filling material ($p=0.01$), corroborating the analysis of subgroups where a statistically significant difference was observed favoring the retreatment of Endosequence BC Sealer sealer when compared to the conventional AH Plus ($p=0.01$). In addition, no study achieved complete removal of the filling material.

One of the explanations for the difficulty of removal observed in studies using the conventional sealer AH Plus may be because it forms a covalent bond between the epoxy rings and amino groups present in collagen fibrils of dentin [26]. An elucidation of the difficulty of using bioceramics, however, can occur through the union formed by the release of products that react on the dentin surface causing a rupture of collagen fibers and consequently porosity, forming an ion exchange layer and minerals between dentin and sealer [27, 24]. This can be seen in the study by [28], who shows that there is no difference between the bond strength between AH Plus and Endosequence BC Sealer.

Several factors should be considered when related to endodontic reintervention, including the solubility of the endodontic sealer. [29] compared the solubility of several conventional and bioceramic sealers, and observed that the sealers TotalFill BC Sealer and BioRoot RCS showed greater solubility when compared to the other conventional sealers tested,

in addition, the AH Plus sealer provided the lowest solubility among all sealers tested. Since the formulation of TotalFill BC Sealer is very similar to Endosequence BC Sealer and IRoot SP, the results found for these sealers can be similar. Therefore, a sealer with better solubility than the other, although with similar bond strength, may be easier to remove from the inside of the root canal, especially when the filling has been performed a long time ago, which may justify our results found in the overall and subgroup meta-analysis, which showed a smaller amount of remnants when using the bioceramic Endosequence BC Sealer compared to AH Plus.

Other factors that should be taken into account are the type of filling used and the method of removing the filling material. Most studies included in this review used the single-cone or continuous wave techniques. The single cone technique is indicated for use with bioceramic sealers [30]. As advantages, this technique is easy to handle, has low cost, and is fast [31, 32]; [33]. However, it can increase the presence of porosities when used with large volumes of filling material [34].

On the other hand, thermoplastification techniques, such as the continuous wave technique, can affect the total volume of the filling by reducing the amount of voids in the canal [35, 36]. However, when compared to single-cone and continuous wave techniques, the study by [33] showed no difference in the presence of voids between the techniques, exhibiting a similar behavior, with a significant difference only in the cervical third, where the continuous wave technique presented superior results. This formation of voids and "gaps" between the material and the dentin wall can interfere with the removal of this material, since, if there is a greater presence of voids, the file to remove this material will probably enter these spaces more easily.

Numerous techniques are applied to remove filling material during retreatment using manual, rotary and reciprocating files [37, 38, 39] solvents, passive ultrasonic irrigation (PUI) [40], and GentleWave Procedure [41]. In studies included in this review, the majority opted for the rotary technique (77.7%), which is in agreement with several studies that demonstrated that the use of nickel-titanium (NiTi) rotary instruments during retreatment proves effective, with good cleaning and safety capacity [42, 43]. In the selected studies, only two also compared reciprocating versus rotating files during retreatment [17, 23]; in both, there was no difference in the final percentage of remnant material when the techniques were compared.

In addition, there are several studies showing that regardless of the technique used, remaining materials can still be found in the root canal system [44, 45, 46, 47], corroborating this review in which none of the studies achieved a complete removal of filling material regardless of the type of sealer or removal technique used [16, 17, 23, 18, 19, 24, 21, 22, 20].

When the foraminal patency was observed, there was no difference between the establishment of patency between the sealers in the evaluated studies. The use of solvents can influence the removal of filling material and consequently the achievement of patency, however, only one study used solvent and showed a great difference in the removal of bioceramic sealer (93%) when compared to non-use of solvent (14%) [18]. Although there is no consensus on the benefits of using solvents and these have been shown to be ineffective in increasing the removal of endodontic sealers, according to some studies [48, 49], little is known about their influence on bioceramic sealers. A study by [50] showed effectiveness in the removal of bioceramic sealer (TotalFill BC Sealer) when using a 10% formic acid-based solvent.

With regard to the time for filling removal, 66.6% studies observed a longer mean time for the bioceramic sealer group [17, 22]. Corroborating a study found in the literature, which reported a doubled mean time when removal was performed in the Endosequence BCS group compared to AH Plus [51]. On the other hand, 33.3% studies in our systematic review showed a longer time with conventional sealer [23]. This difference may be related to the type of bioceramic sealers used in the studies by [17] and [22] were the Endosequence BC Sealer, contrary to the study by [23], who used the Endo CPM Sealer and BioRoot RCS sealers.

In relation to the evaluation methods of the studies, most of the included studies used the Micro-CT (55.5%), considered as the gold standard [49], recently included for evaluation of the preparation of the canals and removal of the filling material [52, 53], since in addition to enabling a three-dimensional image, it also has the ability to preserve specimens [54]. With regard to other assessment methods, periapical radiography, although recognized in the literature, has as a limitation a two-dimensional analysis of a 3D structure [43, 55] and other methods, such as Scanning electron microscopy and operative microscopy, although also widely used, can lead to the loss of part of the sample due to sectioning for evaluation.

A possible limitation of the study was the high heterogeneity found in the overall meta-analysis (I^2 : 95.2%). For this reason, the difference in standard means was used for the statistics, which is more reasonable for heterogeneous studies [28]. Additionally, to overcome this limitation, a meta-analysis of subgroups was performed, grouping the studies by commercial brands of sealers, where it was only possible to include two trials due to similar characteristics, where a low heterogeneity I^2 was verified: 23.7%, and results that corroborate the findings of the overall meta-analysis, favoring the removal of bioceramic sealers.

Another limitation found was the analysis of methodological quality and risk of bias, as there is no specific tool for analyzing *in vitro* studies, most studies were found to have a

moderate risk of bias. The present review was based on laboratory tests only, thus, its findings should be carefully interpreted and translated into the clinical practice. More clinical studies should be conducted to substantiate the evidence. However, despite all the observed limitations, these results show important findings since bioceramic sealers are being increasingly used in clinical routine.

5 CONCLUSION

In conclusion, with moderate strength of evidence, bioceramic sealers resulted in smaller amounts of remaining fillings when compared to conventional sealers, thus providing a greater effectiveness of removal from root canals according to the techniques presented in the different studies. However, regardless of the type of sealer, removal technique or filling used, the results of the studies show that complete removal of the filling material was not achieved.

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