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ORIGINAL ARTICLE

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Influence of root canal sealer composition on postoperative pain after endodontic treatment of permanent teeth: a systematic review and meta-analyses

Influência da composição do cimento endodôntico na dor pós-operatória de dentes permanentes tratados endodonticamente: uma revisão sistemática e meta-análise

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ABSTRACT

Postoperative pain is a frequent complication after root canal treatment. Its management is an important aspect of endodontic practice. Some treatment-related parameters were associated with the development of postoperative pain, including the sealer composition and extrusion. **Objective:** This systematic review aimed to answer the clinical question: Do root canal sealers composition influence postoperative pain after endodontic treatment of permanent teeth? **Material and Methods:** Electronic searches were conducted in PubMed, Scopus, Web of Science, Cochrane, LILACS, and grey literature databases until September 2021. The studies were qualitatively assessed using the RoB2 tool (Cochrane) and the certainty of evidence (GRADE). Sensitivity and pooled estimates were calculated using a random-effects model. Twelve articles were included. **Results:** The risk of bias was high in one study, low in nine, and two had some concerns. Qualitative analyses showed no influence of sealer extrusion on postoperative pain. Meta-analyses showed no significant difference in postoperative pain with moderate to very low levels of certainty between AH Plus and calcium silicate-based sealers, in a 95% confidence interval. Analysis between AH Plus, Zinc Oxide and Eugenol (ZOE), and calcium hydroxide ($Ca(OH)_2$)-based sealers were not performed due to heterogeneity and lack of data. **Conclusion:** Literature showed contrasting results in postoperative pain between AH Plus and ZOE-based sealers, with low to moderate certainty of evidence. Regarding Ca(OH)2-based sealers, a single study with a low level of certainty concluded that AH Plus presented less postoperative pain than Apexit Plus. Therefore, further studies are needed to assess the influence of these sealers on postoperative pain. Evidence showed no difference in postoperative pain between AH Plus and calcium silicate-based sealers. Sealer extrusion is a variable that requires further studies.

KEYWORDS

Postoperative pain; Root canal treatment; Sealer composition; Sealer extrusion; Systematic review.

RESUMO

A dor pós-operatória é uma complicação frequente após o tratamento endodôntico. O seu manejo é um importante aspecto na prática endodôntica. Algumas variáveis relacionados ao tratamento foram associados com o desenvolvimento da dor pós-operatória, incluindo a composição e extrusão dos cimentos endodônticos. **Objetivo:** Esta revisão sistemática objetivou responder a seguinte pergunta clínica: A composição dos cimentos endodônticos podem influenciar a dor pós-operatória de dentes permanentes tratados endodonticamente?

Material e Métodos: Buscas eletrônicas foram realizadas nas bases de dados no PubMed, Scopus, Web of Science, Cochrane, LILACS, e literatura cinzenta até setembro de 2021. Os estudos foram avaliados qualitativamente usando a ferramenta RoB2 (Cochrane) e a certeza de evidência (GRADE). A sensibilidade e as estimativas agrupadas foram calculadas usando um modelo de efeitos aleatórios. Doze artigos foram incluídos. **Resultados:** O risco de viés foi alto em um estudo, baixo em nove e dois tiveram algumas preocupações. A análise qualitativa mostrou que não há influência da extrusão do cimento na dor pós-operatória. A meta-análise mostrou que não houve diferença estatisticamente significante na dor pós-operatória entre o AH Plus e os cimentos a base de silicato de cálcio com moderada a muito baixa certeza de evdência. Análises entre os cimentos AH Plus, óxido de zinco e eugenol (OZE) e hidróxido de cálcio não foram realizados devido a heterogeneidade e falta de dados. **Conclusão:** A literatura sugere resultados contrastantes com relação a dor pós-operatória e entre os cimentos AH Plus e OZE, com baixa a moderada certeza de evidência. Já os cimentos a base de hidróxido de cálcio, um único estudo com baixa certeza de evidência concluiu que o AH Plus apresentou menos dor pós tratamento endodôntico do que o Apexit Plus. Portanto,mais estudos são necessários para avaliar a influência desses tipos de cimentos na dor pós-operatória. Com relação ao cimento AH Plus e os cimentos a base de silicato de cálcio não houve diferença estatística entre eles e a dor. A extrusão dos cimentos é uma variável que requer mais estudos.

PALAVRAS-CHAVE

Dor pós-operatória; Tratamento endodôntico; Composição dos cimentos; Extrusão dos cimentos; Revisão sistemática.

INTRODUCTION

Postoperative pain is a frequent complication after root canal treatment and such condition may have an impact on patients quality of life [1]. Generally, it ranges from mild to moderate and occurs even after optimal procedures are performed [2]. However, pain control remains a key issue in endodontic treatment [3].

Pain is multifactorial in nature [4] and can be induced by mechanical, chemical, or microbiological injuries to the periodontal tissues [5]. Endodontic sealers may affect the periradicular tissues either by direct contact or by percolating components that are released through the root canal systems [6] which may trigger an inflammatory response increasing the risk of postoperative pain [7]. Such sealers are developed to be inside the root canal system. However, unintentional extrusion may occur [8] thus causing symptoms such as pain, hyperesthesia, and paresthesia [9]. These symptoms may vary in intensity depending on the amount of extruded sealer [10].

A wide variety of root canal sealers are currently available in the market. Of these, Zinc Oxide and Eugenol (ZOE)-based, calcium hydroxide (Ca(OH)2)-based, glass ionomer, mineral trioxide aggregate, and resin-based sealers are commonly used. Additionally, bioceramic sealers have recently been launched [6,11]. Histological findings indicate that components percolated from the root canal sealers may induce local inflammatory effects [12] and its intensity is related to the sealer composition [6]. Dysregulated cytokine production during inflammatory processes is a potential contributor to the development of inflammatory diseases [13]. Interleukin-6 (IL-6) and (IL-8) release have been reported to play an important role in root canal sealer-induced periapical inflammation [13,14].

Two systematic reviews [15,16] evaluated the risk and intensity of postoperative pain with calcium silicate and epoxy resin-based sealers, but not with other types of sealers. Additionally, both studies presented contrasting results. Sponchiado et al. [15] showed no statistical difference between the composition and pain between these two sealers. Mekhdieva et al. [16] concluded that calcium silicate-based sealers were associated with significantly lower pain than epoxy resin-based sealers.

Therefore, this systematic review aimed to investigate current evidence regarding the influence of other types of sealers composition on postoperative pain after endodontic treatment. The clinical question was designed according to the Population, Intervention, Comparator, Outcome, and Study (PICOS) and should answer the following clinical question: Do root canal sealer composition influence postoperative pain after endodontic treatment of permanent teeth?

MATERIAL AND METHODS

This systematic review and meta-analysis was conducted according to the Preferred Reporting

Items for Systematic Reviews and Meta-analysis (PRISMA) statement [17] and was registered in the PROSPERO database (CRD42020211297).

Eligibility criteria

The inclusion criteria was outlined according to the Population, Interventions, Comparisons, Outcomes, and Studies. The articles should answer the following PICOS, as follow:

(P) Population included patients undergoing nonsurgical root canal treatment in permanent teeth;

(I) Intervention included root canal filling with AH Plus sealer with or without extrusion;

(C) Comparison included root canal filling with other types of sealer with or without extrusion;

(O) Outcome included postoperative pain after root canal treatment;

(S) Study design included randomized controlled trials (RCTs).

Exclusion criteria

Duplicated articles, pilot studies, literature reviews, editorial letters, book chapters, theses and guidelines were excluded.

Search strategy and study selection

An electronic search was conducted to identify relevant articles. No restrictions were imposed on the dates. Studies published in English, Portuguese and Spanish were included. The following databases were searched until September 29, 2021: PubMed, Scopus, Web of Science, Cochrane, LILACS, and OpenGrey. In addition, MeSH terms, synonyms, and free terms were used and combined to refine the search results, as presented in Table I. Experts were contacted to identify related unpublished and ongoing studies. The records were exported to Mendeley (Mendeley Ltd., UK, England); duplicates were considered only once.

Before analyzing the selected abstracts, a Kappa test was conducted to evaluate agreement among evaluators (10% of the publications were randomly selected). Subsequently, their classifications were compared, resulting in a kappa statistic of 0.90. All potentially relevant publications were selected by reading the titles and abstracts by two independent reviewers (VM and SM). Any differences between them were resolved by consensus with the third author (LSA). Studies without abstracts were also assessed for inclusion. Subsequently, the full texts of all potentially eligible studies were accessed; inclusion and exclusion criteria were then applied. Any other disagreements were resolved by consensus with the senior reviewer (LSA). Additionally, the reference lists of the included studies were manually searched to retrieve all eligible articles.

Data extraction

Data were extracted by two independent authors (VM and SM) and organized as follows:

1. First author, year of publication;
2. Sample (sample size, gender, tooth type, tooth diagnosis);
3. Endodontic treatment (irrigation, instrumentation, number of sessions, obturation technique, type of sealer);
4. Preoperative symptoms;
5. Pain assessment (pain scale, period in hours, and analgesic intake);
6. Postoperative symptoms;
7. Results.

Risk of bias

The RoB2 tool was used for assessing the risk of bias (RoB) of the selected RCTs [18]. Two authors (LSG and SM) independently assessed the RoB of the included studies in a duplicate manner. Disagreements were resolved by consensus with the senior reviewer (LSA). If relevant data were missing, the authors were contacted. The sources of bias assessed were the randomization process, deviations from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain was classified as having low (+), high (x), or some concerns (-) RoB. A study was considered to have an overall high RoB if judged to be at high RoB in at least one domain or judged to have "some concerns" for multiple domains in a way that substantially lowers confidence in the result. A study was considered to have an overall some concerns RoB if judged to be at "some concerns" in at least one domain. Finally, a study was considered to have

Table I - Electronic Databases and Search Strategy

Pub Med n=463	((((((((((((root canal therapy[MeSH Terms]) OR (root canal therapy[Title/Abstract])) OR (teeth, endodontically treated[MeSH Terms])) OR (teeth, endodontically treated[Title/Abstract])) OR (endodontically-treated tooth[MeSH Terms])) OR (endodontically-treated tooth[Title/Abstract])) OR (root canal preparation[MeSH Terms])) OR (root canal preparation[Title/Abstract])) OR (tooth root therapy[Title/Abstract])) OR (endodontic therapy[Title/Abstract])) OR (endodontic treatment[Title/Abstract])) OR (root canal treatment[Title/Abstract])) AND ((((((((((((((((((((root canal filling materials[MeSH Terms]) OR (root canal filling materials[Title/Abstract])) OR (endodontic obturation[MeSH Terms])) OR (endodontic obturation[Title/Abstract])) OR (root canal obturation[MeSH Terms])) OR (root canal obturation[Title/Abstract])) OR (root canal obturations[MeSH Terms])) OR (root canal obturations[Title/Abstract])) OR (Root Canal Sealants[MeSH Terms])) OR (Root Canal Sealants[Title/Abstract])) OR (root canal cement[Title/Abstract])) OR (root canal filling[Title/Abstract])) OR (endodontic cement[Title/Abstract])) OR (endodontic sealer[Title/Abstract])) OR (root canal sealer[Title/Abstract])) OR (root canal cement extrusion[Title/Abstract])) OR (root canal filling extrusion[Title/Abstract])) OR (root canal sealer extrusion[Title/Abstract])) OR (endodontic cement extrusion[Title/Abstract])) OR (endodontic sealer extrusion[Title/Abstract]))) AND ((((((((((((((((pain[MeSH Terms]) OR (pain[Title/Abstract])) OR (pain, postoperative[MeSH Terms])) OR (pain, postoperative[Title/Abstract])) OR (postoperative pain[MeSH Terms])) OR (postoperative pain[Title/Abstract])) OR (hyperemia[MeSH Terms])) OR (hyperemia[Title/Abstract])) OR (toothache[MeSH Terms])) OR (toothache[Title/Abstract])) OR (odontalgia[MeSH Terms])) OR (odontalgia[Title/Abstract])) OR (edema[Title/Abstract])) OR (hyperesthesia[Title/Abstract])) OR (heat[Title/Abstract])) OR (swelling[Title/Abstract])) OR (touch pain[Title/Abstract]))
Scopus n=981	(TITLE-ABS-KEY (root AND canal AND therapy) OR TITLE-ABS-KEY (teeth, AND endodontically AND treated) OR TITLE-ABS-KEY (endodontically-treated AND tooth) OR TITLE-ABS-KEY (root AND canal AND preparation) OR TITLE-ABS-KEY (tooth AND root AND therapy) OR TITLE-ABS-KEY (endodontic AND therapy) OR TITLE-ABS-KEY (endodontic AND treatment) OR TITLE-ABS-KEY (root AND canal AND treatment) AND (TITLE-ABS-KEY (root AND canal AND filling AND materials) OR TITLE-ABS-KEY (endodontic AND obturation) OR TITLE-ABS-KEY (root AND canal AND obturation) OR TITLE-ABS-KEY (root AND canal AND obturations) OR TITLE-ABS-KEY (root AND canal AND sealants) OR TITLE-ABS-KEY (root AND canal AND cement) OR TITLE-ABS-KEY (root AND canal AND filling) OR TITLE-ABS-KEY (endodontic AND cement) OR TITLE-ABS-KEY (endodontic AND sealer) OR TITLE-ABS-KEY (root AND canal AND sealer) OR TITLE-ABS-KEY (root AND canal AND cement AND extrusion) OR TITLE-ABS-KEY (root AND canal AND filling AND extrusion) OR TITLE-ABS-KEY (root AND canal AND sealer AND extrusion) OR TITLE-ABS-KEY (endodontic AND cement AND extrusion) OR TITLE-ABS-KEY (endodontic AND sealer AND extrusion) AND (TITLE-ABS-KEY (pain) OR TITLE-ABS-KEY (pain, AND postoperative) OR TITLE-ABS-KEY (postoperative AND pain) OR TITLE-ABS-KEY (hyperemia) OR TITLE-ABS-KEY (toothache) OR TITLE-ABS-KEY (odontalgia) OR TITLE-ABS-KEY (edema) OR TITLE-ABS-KEY (hyperesthesia) OR TITLE-ABS-KEY (heat) OR TITLE-ABS-KEY (swelling) OR TITLE-ABS-KEY (touch AND pain)
WoS n=454	pain OR pain, postoperative OR postoperative pain OR hyperemia OR toothache OR odontalgia OR edema OR hyperesthesia OR heat OR swelling OR touch pain
Cochrane Reviews n=304	root canal therapy OR teeth, endodontically treated OR endodontically-treated tooth OR root canal preparation OR tooth root therapy OR endodontic therapy OR endodontic treatment OR root canal treatment in Title Abstract Keyword AND root canal filling materials OR endodontic obturation OR root canal obturation OR root canal obturations OR Root Canal Sealants OR root canal cement OR root canal filling OR endodontic cement OR endodontic sealer OR root canal sealer OR root canal cement extrusion OR root canal filling extrusion OR root canal sealer extrusion OR endodontic cement extrusion OR endodontic sealer extrusion in Title Abstract Keyword AND pain OR pain, postoperative OR postoperative pain OR hyperemia OR toothache OR odontalgia OR edema OR hyperesthesia OR heat OR swelling OR touch pain in Title Abstract Keyword - (Word variations have been searched)
Lilacs/BVS n=4	tw:((tw:(root canal therapy OR tooth, nonvital)) AND (tw:(root canal filling materials OR root canal obturation)) AND (tw:(acute pain OR pain, postoperative OR toothache))) AND (db:("LILACS"))

an overall low RoB if judged to be at low RoB for all domains [18].

Meta-analysis

A meta-analysis was performed to combine comparable results using subgroup analysis. Extraction data of the mean and the standard deviation with 95% confidence interval (CI) related to the post-operative pain between the types of sealer groups in the time intervals of 6, 12, 24, 48, and 72 hours were performed. A random effects model was used in the meta-analysis. The mean differences between the sealer groups were determined using inverse variance meta-analysis. I^2 was used to assess the statistical heterogeneity between studies, where values of 25%, 50%, and 75% indicated low, medium, and high heterogeneity, respectively [19]. Meta-analysis and forest plots were performed using the RevMan 5.4. Sensitivity analyses using different methods of data imputation and subgroup analyses were also planned.

Evidence synthesis (GRADE)

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system for classifying the certainty of the evidence was used to ensure the accuracy of data analysis. GRADE Pro GDT software (http://gdt.guidelinedevelopment.org) was used to summarize the results. Certainty is downgraded owing to RoB, inconsistency,

indirectness, imprecision, and publication bias [20,21]. The level of certainty among the identified evidence can be characterized from very low to high [21].

RESULTS

Search and Study selection

An electronic search identified 2,363 studies by searching the databases: 463 from MEDLINE (PubMed), 454 from Web of Science, 981 from Scopus, 304 from Cochrane Reviews, 4 from Lilacs (Virtual Health Library) and 157 registers in Clinical Trials. Of these, 288 were duplicated and removed using an automated tool. After screening titles and abstracts, 1,931 articles were excluded since they did not meet the inclusion criteria. Thirty-two articles were potentially eligible; their texts were then read in full. Three studies were included from citation search. Twelve studies were included in the systematic review (Figure 1). Appendix 1 shows the studies excluded from the full-text analysis.

Risk of bias

Nine studies had low RoB [22-30], one was considered to have a high RoB due to bias in the randomization process and deviations from the intended interventions [31], while two [32,33] were judged to be at some concerns due to bias arising from the randomization process. Details regarding downgrading are provided in Figure 2. The most frequent domain causing downgrading was bias due to the randomization process and deviations from the intended intervention. No study had attrition bias due to missing outcome data or selection of reported results.

Qualitative analysis

Tables II and III present the data extractions of the selected studies.

Of the 12 studies, two evaluated sealer extrusion and postoperative pain [27,30], nine sealer composition and pain [22-26], and one evaluated both, sealer composition and extrusion on postoperative pain [28].

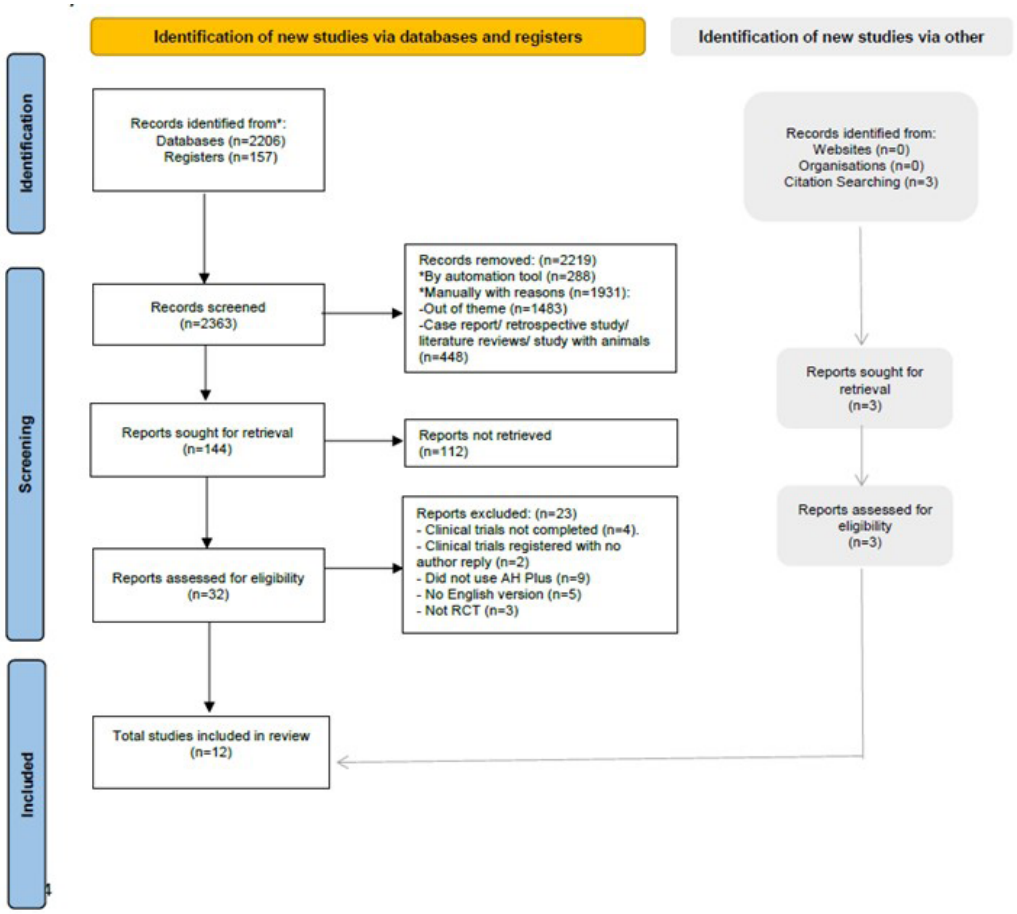

Figure 1 - PRISMA flowchart of the manuscripts screened through the review process.

Table II - Evidence table summarizing the characteristics of the included studies

Author	Sample				Endodontic treatment					
	Sam ple size	Gender	Tooth diagnosis	Tooth type	Irrigation solu- tion	Instrumentation	N° sessions	Obturation tech- nique	Sealers	Pre operative symptom
Ambika and Satish [26]	90	NI	NI	NI	NI	NI	1	NI	Endosequence BC; MTA; AH Plus	NI
Paz et al. [31]	30	NI	pulpitis, pulp necrosis, and retreatment	NI	2.5% NaOCl	ProTaper Next	1 or 2	Cold lateral condensation	BioRoot RCS; AH Plus	NI
Graunaite et al. [29]	61	25 males 36 females	Asymptomatic apical periodontitis	Single /multi- rooted	2% NaOCl	ProTaper Gold	1	Warm vertical condensation	AH Plus; Total Fill BC	No
Atav et al. [28]	160	67 males 89 females	Pulp necrosis and vital teeth	Single /multi- rooted	2.5% NaOCl	One Shape	1	Herofill™ Soft-Core obturator	iRoot SP; Innovative BioCeramix; AH Plus	Yes
Fonseca et al. [27]	64	26 males 38 females	Pulp necrosis	Single rooted	2.5% NaOCl	Reciproc VDW	1	Single cone	AH Plus; Sealer Plus BC	No
Ferreira et al. [25]	60	19 males 41 females	Pulp necrosis	Single /multi- rooted	2.5% NaOCl	Wave One Gold	2	Single cone and vertical compaction	AH Plus; EndoFill MTA Fillapex	No
Gudlavalleti et al. [33]	99	45 males 54 females	Chronic irreversible pulpitis	Multi-rooted	3% NaOCl	Protaper Universal	1	Cold lateral condensation	Tubli-Seal EWT; Apexit Plus; AH Plus	Yes
Cunha et al. [23]	69	33 males 27 females	pulpitis and pulp necrosis	Multi-rooted	2.5% NaOCl	Protaper Next	2 to 4	Single cone + accessory cones	AH Plus; Sealer 26	Yes
Tan et al. [22]	171	76 males 87 females	Pulp necrosis and vital teeth	Single /multi- rooted	1,25% NaOCl	Rotatory files	1 or more	Single cone and Warm vertical Compaction	AH Plus; TotalFill BC	Yes
Shim et al. [32]	108	36 males 31 females	NI	Single /multi- rooted	2.5% NaOCl	Protaper Next	2 to 4	Single cone and Continuous wave	AH Plus; Endoseal MTA	Yes
Drumond et al. [30]	330	36 males 31 females	Asymptomatic irreversible pulpitis	Multi-rooted	2% chlorhexidine gel	Wave One Gold	1	Single cone and Warm vertical Compaction	AH Plus; BC Sealer; Bio-C Sealer	No
Aslan et al. [24]	96	34 males 50 females	Asymptomatic irreversible pulpitis	Multi-rooted	5% NaOCl	Reciproc VDW	1	Single cone	AH Plus; Endoseal MTA; Endosequence BC	No

NI = not informed.

Table III - Summary of the parameters and results collected for each study

Author	Pain assessment				Results
	Pain scale	Period (hours)	Analgesic intake	Postoperative symptoms	
Ambika and Satish [26]	VAS	24, 72, 120, 168	NI	Pain	None of the patients reported postoperative pain after 3rd day. No patient reported severe pain at any time interval. Postoperative pain during the 1h and 1, 3 days intervals was significantly different (p <0.05) between groups.
Paz et al. [31]	Modified VAS	24, 48, 72, 96, 120, 144, 168	Ibuprofen 600 mg	Pain	Bioceramic referred postoperative pain more frequently than resin sealer. There were statistically significant differences in post-operative pain intensity only between day 1 and day 6 and between day 1 and day 7 (p = 0.002) respectively.
Graunaite et al. [29]	VAS	24, 48, 72, 168	Nonsteroid analgesics	Pain	There was no statistically significant difference between the tested root canal sealers regarding postoperative pain at any time points assessed (P > .05).
Atav et al. [28]	Huskisson VAS	6, 12, 24, 72	Ibuprofen 200 mg	Pain	There was no significant difference between groups in the incidence of postoperative pain; however, iRoot SP sealer was associated with less analgesic intake compared to AH Plus sealer. No correlation between sealer extrusion-pain intensity and analgesic intake.
Fonseca et al. [27]	VAS	24, 48, 72	Ibuprofen 600 mg	Pain	No statistically significant difference between the groups with regard to pain level and intake of analgesics (p > 0.05). Sealer Plus BC presented a statistically significant more extrusion (59.37%) than AH Plus (28.12%). Sealer extrusion was not associated with pain.
Cunha et al. [23]	NI	[a]	NI	Pain	No effect of sealer composition was observed. Apical repair incidences and asymptomatic teeth were, respectively, 90.5 and 89.3, 96.8 and 90.0% during 1 and 2 years of follow-up.
Ferreira et al. [25]	Descriptive	24, 48, 168	Ibuprofen 600 mg	Pain	No significant differences were detected among the groups in terms of either incidence or intensity of postoperative pain, or need for analgesic intake, at any time point (p>0.05).
Gudlavalleti et al. [33]	VAS	8, 24, 48	Ibuprofen 200 mg	Pain	There was statistically significant difference seen in all three groups (p=0.0001) at all the time points (8h, 24h and 48h).
Tan et al. [22]	Likert	24, 72, 168	Ibuprofen[c]	Pain	There was no significant difference in pain experience between teeth filled using AH Plus or TotalFill BC Sealer 1, 3, and 7 days after obturation.
Shim et al. [32]	VAS	24, 48, 72, 96, 120, 144, 168	NI	Pain	Endoseal MTA and AH Plus had equivalent effects on postoperative pain incidence and intensity.
Drumond et al. [30]	Modified NRS	6, 12, 24, 48, 168	Acetaminophen 500 mg	Pain	The occurrence of unintentional apical extrusion of calcium silicate–based root canal sealers present similar postoperative pain results compared with resin-based sealers with low-intensity pain.
Aslan et al. [24]	VAS	6, 12, 24, 48	Ibuprofen 400 mg	Pain	There were no significant differences among the groups in terms of postoperative pain at any time points assessed (P>0.05) nor for analgesic intake of patients among the groups (P>0.05).

NI = not informed; NRS = numeric rating scale; VAS = visual analogue scale; [a]period of 1 and 2 years; [c]milligrams not informed.

Figure 2 - Quality assessment of selected studies (the Cochrane Collaboration tool for assessing risk of bias – RoB2).

One study used single-rooted teeth [27], four multi-rooted [23,24,30,33], five multi- and single-rooted teeth [22,25,28,29,32], and two did not inform the type of teeth [26,31]. The average number of teeth per study was 115.5, with a minimum of 30 and a maximum of 330.

Concerning the number of sessions, seven studies were carried out in a single session [24,26-30,33], and five studies in multiple sessions [22,23,25,31,32].

Postoperative pain was assessed in all studies. Six studies evaluated pain using a visual analogue scale (VAS) [24,26,27,29,32,33], one using a modified VAS form [31], one using a descriptive scale [25], one using a Likert scale [22], one using a modified visual rating scale [30], one not using a binary scale (pain present or absent) [23], and one using the Huskisson VAS form [28].

Six studies did not report analgesic intake [23,26,30-33]. Only two studies [24,28] assessed NSAID intake at 6 and 12 h, showing a higher intake in the first 6 h in both studies. At both time intervals, there was no statistically significant difference in analgesic intake between the groups. Six studies [22,24,25,27-29] assessed NSAID intake at 24 h, with no statistical difference in any of the groups. At 48 h, two studies [24,25] reported that very few patients took analgesics; however, there was no difference among the groups. The same trend was observed at 72 h [22,28].

Regarding sealer composition, seven studies [22-25,28,29,32] compared pain intensity between AH Plus (Dentsply Maillefer, Konstanz, Germany) and calcium silicate-based sealers. They found no statistical difference between the groups regarding the level of pain. On the other hand, two studies found statistically significant differences in postoperative pain intensity between the groups [26,31]. Paz et al. [31] reported that the AH Plus group reported postoperative pain less frequently than the Bioroot group (Septodont, Saint Maur-des-Fosses, France). However, Ambika and Satish [26] reported that AH Plus presented with more postoperative pain than MTA Fillapex (Angelus, Londrina, Brazil) and Endo Sequence BC (Brasseler, Savannah, GA, USA) at all time intervals.

Two studies compared pain intensity between AH Plus and ZOE-based sealers [25,33] Ferreira et al. [25] found no statistical difference between AH Plus and Endofill (Dentisply, Petrópolis, Brazil). In contrast, Gudlavalleti et al. [33] concluded that AH Plus resulted in less postoperative pain than Tubliseal (SybronEndo, Glendora, CA, USA).

A single study comparing pain intensity between AH Plus and Ca $(OH)_2$-based sealers [33] concluded that AH Plus presented less postoperative pain than Apexit Plus (Ivoclar, Vivadent, De Trey, Germany).

Studies that evaluated sealer extrusion and postoperative pain [27,28,30] showed no association between extrusion and pain occurrence. Atav et al. [28] concluded that AH Plus had more extrusion than iRoot SP (Innovative BioCeramix Inc., Canada). Fonseca et al. [27] found that Sealer Plus BC (MK Life, Porto Alegre, RS, Brazil) had a significantly higher incidence of extrusion than AH Plus. Drumond et al. [30] found that unintentional apical extrusion of AH Plus presented with postoperative pain similar to those of EndoSequence BC (Brasseler, Savannah, GA, USA) and Bio-C (Angelus, Londrina, PA, Brazil).

Quantitative analysis

Homogeneous data from the included studies were compared using meta-analysis. Two eligible studies were excluded [23,24]. Data of one study [24] could not be extracted. In this case, the corresponding author was contacted by email; however, missing data were not provided. Another study [23] reported the total number of patients who developed postoperative pain as present or absent, but did not inform the sealers group.

The meta-analyses of studies with continuous data [27-30] demonstrated that the comparison between the level of pain and AH Plus vs. calcium silicate-based sealers showed no significant difference between groups at all time intervals ($p > 0.05$) (Figure 3).

Regarding the meta-analyses of studies with binary data [22,25,26], there was no statistically significant difference in pain intensity in any of the reported periods. Subgroup tests showed that the size effect between AH Plus and calcium silicate-based sealers was the same at all time intervals ($p > 0.05$) (Figure 4).

Studies that compared pain intensity between AH Plus and ZOE-based sealers [25,33],

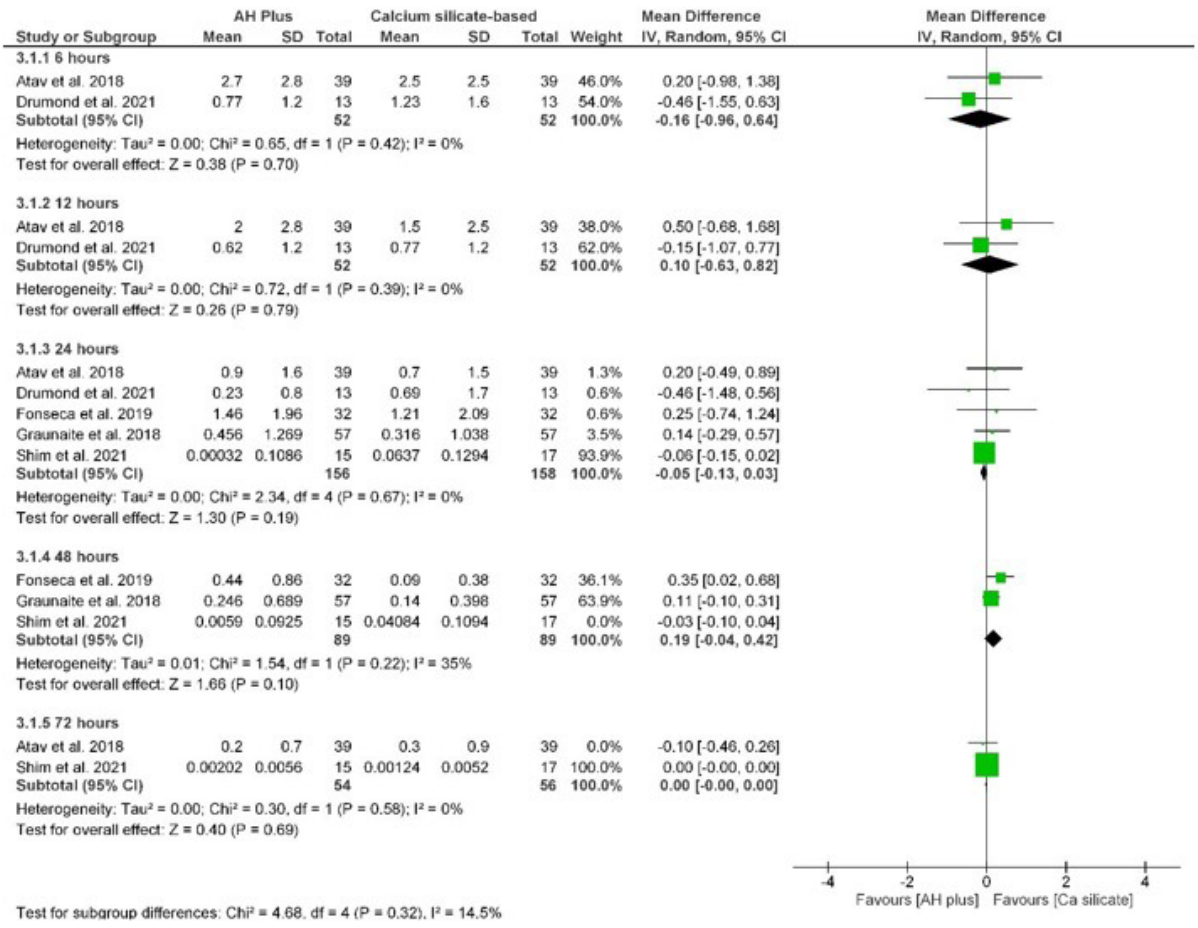

Figure 3 - Forest plots of postoperative pain between AH Plus vs Calcium silicate-based sealers groups (6, 12, 24, 48, and 72 hours).

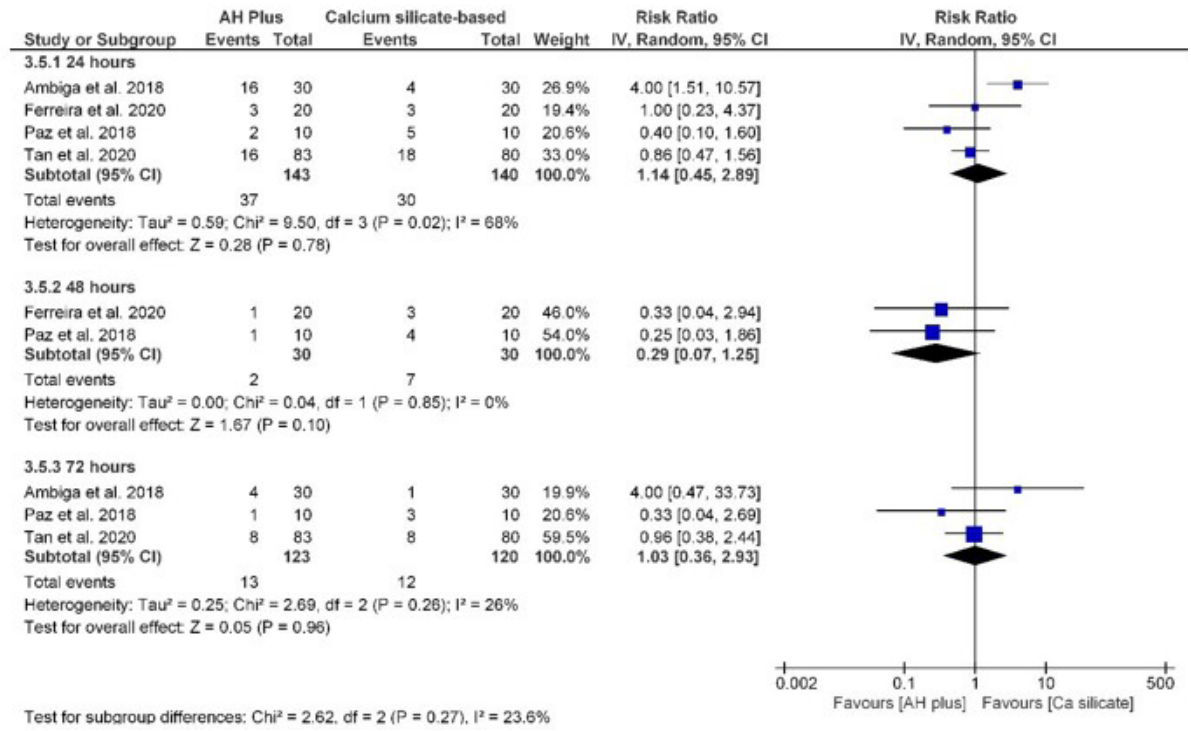

Figure 4 - Forest plots of the relative risk (RR) for postoperative pain between AH Plus vs Calcium silicate-based sealers groups (24, 48, and 72 hours).

the meta-analysis could not be performed due to outcome variability.

A meta-analysis to assess the intensity of pain between AH Plus and Ca (OH)2-based sealers could not be performed because only one study presented data [33]. Atav et al. [28] also evaluated devital teeth with AH Plus and iRoot SP; Paz et al. [31] assessed teeth with AH Plus and two different obturation techniques; and Shim et al. [32] evaluated AH Plus and Endoseal MTA in multirooted teeth. Therefore, additional meta-analyses were performed, including those data, and no statistical differences were observed (Appendices 2 and 3).

Evidence synthesis (GRADE)

The overall certainty varied from moderate to very low for all the syntheses. All analyses were downgraded due to imprecision (low number of participants) and RoB (Table IV). For each outcome, analysis of the certainty of evidence was performed based on the time intervals investigated. For imprecision (pain intensity), a threshold of 1 point on the 10-point VAS [34], as well as a minimum sample of 400 was used.

DISCUSSION

The literature suggests several etiological factors of postoperative pain, including sealer extrusion [3] and composition [6] This systematic review aimed to investigate current evidence regarding the influence of various types of sealer composition on postoperative pain after endodontic treatment. In this review AH Plus sealer (Dentsply, De Trey, Konstanz, Germany) was chosen as the control group. AH-Plus is a resin-based sealer and represents the gold standard in clinical practice and in *in vitro* studies and is the reference material for other types of sealers [24].

As root canal sealers may frequently come into contact with perirradicular tissues, biocompatibility is of paramount importance [35]. Some *in vitro* studies have reported conflicting results regarding biocompatibility [36,37]. Nonetheless, these findings should be cautiously interpreted, as the results of *in vitro* toxicity tests may not correlate with *in vivo* response [35]. The results of our meta-analyses between AH Plus and calcium silicate-based sealers confirmed the results of most of the selected studies; there was no statistical difference in pain intensity at any time interval. This can be attributed to the fact that, except for paraformaldehyde-containing materials, most contemporary root canal sealers are either biocompatible or show cytotoxicity only prior to setting [38]. This may not be sufficient to induce an intense inflammatory reaction, which may justify the non-difference between the groups in the selected studies. Another scenario, may suggest that both AH Plus and calcium silicate-based sealers were adequate.

The individual results of the eligible studies showed no association between sealer extrusion and the occurrence or intensity of postoperative pain [27,28,30]. This phenomenon might be due to the small surface of contact between the filling material and the periapical tissue. In all selected studies, the authors reported that there was no significant amount of extruded sealer. Cases of gross overfilling are generally associated with clinical symptoms and sealer composition [39]. Another issue that must be pointed out is that in the methodology of the selected articles that assessed post-operative pain and sealer extrusion, there was no control group (no sealer extrusion). Therefore, this design cannot determine whether any deviation in the results from the treatment group is a direct result of the variable. Thus, sealer extrusion is a variable that requires further clinical evaluation.

The intake of NSAID after endodontic treatment significantly reduces postoperative pain [40]. The studies included in this systematic review reported that analgesics/anti-inflammatory consumption was low, with no statistical difference between groups with regards to pain level. The lack of significant difference in analgesic intake may be indicative of the fact that despite the occurrence of postoperative pain, it may not be clinically relevant. The endodontic treatment includes a complex of procedures such as chemomechanical debridement and obturation. Pain after root canal treatment is expected and it might also be referred to sensitivity caused by pressure of the clamp, injection of local anesthetic or by instrumentation and chemical irrigation solutions [24]. Another factor to be consider is preoperative pain. Some studies demonstrated that preoperative pain is a strong predictor of postoperative pain [1,22,24]. In this systematic review only four studies included patients free of symptoms [24,25,27,29]. Therefore, future studies assessing pain should include patients

Table IV - Quality of evidence and strength of recommendations of the selected studies (GRADE)

Certainty assessment							N° of participants or Events/total		Absolute or relative effects (95% CI)	Overall certainty
N° of datasets	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consid-erations	Intervention	Comparator		
AH-Plus vs. ZOE-based (8 hours)										
1	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	33	33	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. ZOE-based (24 hours)										
2	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	53	53	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. ZOE-based (48 hours)										
2	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	53	53	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. ZOE-based (72 hours)										
1	RCT	Not serious	Not serious	Not serious	Serious[b]	None	20	20	No difference between groups	⊕⊕⊕◯ MODERATE
AH-Plus vs. Calcium silicate-based (6 hours) - Continuous data										
2	RCT	Not serious	Not serious	Not serious	Serious[b]	None	52	52	No difference between groups MD: -0.16 [-0.96, 0.64]	⊕⊕⊕◯ MODERATE
AH-Plus vs. Calcium silicate-based (8 hours) - Continuous data										
1	RCT	Not serious	Not serious	Not serious	Serious[b]	None	13	13	No difference between groups	⊕⊕⊕◯ MODERATE
AH-Plus vs. Calcium silicate-based (12 hours) - Continuous data										
2	RCT	Not serious	Not serious	Not serious	Serious[b]	None	52	52	No difference between groups MD: 0.10 [-0.63, 0.82]	⊕⊕⊕◯ MODERATE
AH-Plus vs. Calcium silicate-based (24 hours) - Continuous data										
5	RCT	Not serious†	Not serious	Not serious	Serious[b]	None	156	158	No difference between groups MD: -0.05 [-0.13, 0.03]	⊕⊕⊕◯ MODERATE
AH-Plus vs. Calcium silicate-based (48 hours) - Continuous data										
2	RCT	Not serious	Not serious¥	Not serious	Serious[b]	None	89	89	No difference between groups MD: 0.19 [-0.04, 0.42]	⊕⊕⊕◯ MODERATE
AH-Plus vs. Calcium silicate-based (72 hours) - Continuous data										
2	RCT	Not serious†	Not serious	Not serious	Serious[b]	None	54	56	No difference between groups MD: 0.00 [-0.00, 0.00]	⊕⊕⊕◯ MODERATE
AH-Plus vs. Calcium silicate-based (96 hours) - Continuous data										
1	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	15	17	No difference between groups*	⊕⊕◯◯ LOW
AH-Plus vs. Calcium silicate-based (120 hours) - Continuous data										

CI = confidence interval; MD = mean difference; RR = relative risk; [a]Datasets provide results with risk of bias for some criteria, and likely to seriously alter the results; [b]Limited amount of data included in the synthesis (number of subjects evaluated less than the threshold suggested by GRADE of 400); [c]I^2 value greater than 50% ($P<0.05$); †The subgroup test showed that the study with a high risk of bias did not affect the direction or significance of the effect; therefore, it was kept in the synthesis and it was considered that the evidence was not affected for this topic; ¥Since the imprecision item would be affected anyway, it was opted to exclude the study by Shim et al. [32] and to make the evidence more consistent. ⊕◯◯◯ = Very low; ⊕⊕◯◯ = Low; ⊕⊕⊕◯ = Moderate.

Table IV - Continued...

Certainty assessment							N° of participants or Events/total		Absolute or relative effects (95% CI)	Overall certainty
N° of datasets	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Comparator		
1	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	15	17	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. Calcium silicate-based (144 hours) - Continuous data										
1	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	15	17	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. Calcium silicate-based (168 hours) - Continuous data										
2	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	28	30	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. Calcium silicate-based (24 hours) - Binary data										
4	RCT	Serious[a]	Serious[c]	Not serious	Serious[b]	None	37/143	30/140	No difference between groups RR: 1.14 [0.45, 2.89]	⊕◯◯◯ VERY LOW
AH-Plus vs. Calcium silicate-based (48 hours) - Binary data										
2	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	2/30	7/30	No difference between groups RR: 0.29 [0.07, 1.25]	⊕⊕◯◯ LOW
AH-Plus vs. Calcium silicate-based (72 hours) - Binary data										
3	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	13/123	12/120	No difference between groups RR: 1.03 [0.36, 2.93]	⊕⊕◯◯ LOW
AH-Plus vs. Calcium silicate-based (168 hours) - Binary data										
2	RCT	Not serious	Not serious	Not serious	Serious[b]	None	3/103	6/100	No difference between groups	⊕⊕⊕◯ MODERATE
AH-Plus vs. $Ca(OH)_2$-based (8 hours) - Continuous data										
1	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	33	33	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. $Ca(OH)_2$-based (24 hours) - Continuous data										
1	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	33	33	No difference between groups	⊕⊕◯◯ LOW
AH-Plus vs. $Ca(OH)_2$-based (48 hours) - Continuous data										
1	RCT	Serious[a]	Not serious	Not serious	Serious[b]	None	33	33	No difference between groups	⊕⊕◯◯ LOW

CI = confidence interval; MD = mean difference; RR = relative risk; [a]Datasets provide results with risk of bias for some criteria, and likely to seriously alter the results; [b]Limited amount of data included in the synthesis (number of subjects evaluated less than the threshold suggested by GRADE of 400); [c]I^2 value greater than 50% ($P<0.05$); †The subgroup test showed that the study with a high risk of bias did not affect the direction or significance of the effect; therefore, it was kept in the synthesis and it was considered that the evidence was not affected for this topic; ¥Since the imprecision item would be affected anyway, it was opted to exclude the study by Shim et al. [32] and to make the evidence more consistent. ⊕◯◯◯ = Very low; ⊕⊕◯◯ = Low; ⊕⊕⊕◯ = Moderate.

without preoperative pain, since it may be a confounding factor in the analysis.

The authors utilized the Cochrane Collaboration tool for assessing risk of bias - RoB2. Through this tool, they evaluated the randomization process, deviations from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result. The domain with the most significant limitations was the randomization process. Randomized clinical trials are considered the gold standard among all investigation methods, as they are capable of producing direct scientific evidence with a lower probability of error for clarifying a cause-effect relationship between two events. In terms of risk of bias, nine studies had a low RoB [22-30], two were judged to be at some concerns in at least one domain [32,33], and one was considered to have a high RoB [31]. A correct randomization process ensures that no pattern exists between the assignment of subjects into groups and in any characteristics of the subjects. Every subject will be similar to those assigned to either the treatment or control group. Allocation concealment, in which the operator cannot identify which group the patient will be placed into, should also be given importance. In relation to selection bias, three studies presented an unclear randomization process; allocation concealment was not informed [31,33]. No attrition bias was observed due to missing data. Some authors acknowledged the missing data and reported the reasons; however, there was no substantial loss of study participants without an imbalanced attrition between the groups. Another relevant aspect of risk of bias is the blinding of participants, personnel, operator, and examiners in relation to assessing treatment and outcome as well as avoiding performance bias. The blinding of participants and personnel was performed in most of studies [22-30,32]. Blinding of the operator was not performed in all studies due to the color and consistency of the sealers. Thus, being aware that operator blindness is not always possible, examiner masking should be considered a minimum. Blind outcome assessment was performed in five studies [22,23,26,28,30]. Selective reporting was performed in all studies; their limitations were reported.

Although this systematic review followed a rigorous methodology and attempted to reduce all biases by following strict criteria, its findings should be viewed considering some limitations. Variations of the visual analog scale for pain assessment were used in different studies. Additionally, postoperative pain analysis was conducted at different time intervals. To address this variability, all scales were resized to a 1–10 scale, but it is unsure to precise if this could have relevance in the analysis. Regarding time, the meta-analyses were grouped according to this variable. Another limitation concerns the language in which the article was written. Articles written in English, Portuguese, and Spanish were selected. Only publications written in other languages were excluded due to the inability to access them in full and extract complete data. In future studies it is recommend using standardized scales for which there is an overall consensus.

Although efforts were made to retrieve all relevant data, publication bias could not be ruled out. Moreover, the unclear RoB for some of the included studies could not be verified because of the authors' non-response. Therefore, the findings of the present systematic review need to be confirmed by further well-designed studies.

CONCLUSIONS

The quality of evidence supporting the relationship between root canal sealer composition and postoperative pain varied from moderate to very low. There was no significant difference between AH-Plus and calcium silicate-based sealers in the occurrence of postoperative pain. Further RCTs with high methodological evidence are needed to assess postoperative pain with other sealers. Sealer extrusion is also a variable that requires further clinical evaluation. Future well-designed RCTs should be performed to evaluate the influence of sealer extrusion on postoperative pain by using a comparative group without sealer extrusion.

Author's Contributions

VGM: Conceptualization, Methodology: eletronic search, studies selection, data extraction, tables, writing of the manuscript; Validation, Formal Analysis, Investigation, Resources, Data Curation. SRSM: Conceptualization, Methodology: eletronic search, studies selection, data extraction, tables, figures; Writing – Original Draft Preparation, Writing – Review & Editing,

Software: GRADE, Risk of Bias; Validation, Formal Analysis, Investigation, Resources, Data Curation. GAMV: Software: GRADE and Risk of Bias, Validation, Formal Analysis, Data Curation. LAAA: Writing – Review & Editing, Visualization of the final Draft. LSA: Conceptualization, Writing – Review & Editing, Visualization, Supervision, Project Administration, Funding Acquisition.

Conflict of Interest

The authors deny any conflicts of interest related to this study. The manuscript is original and has not been published previously, nor is under consideration elsewhere.

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Regulatory Statement

This systematic review was conducted through a search strategy in electronic databases. The search was restricted to publications in peer-reviewed journals, dissertations or theses, in which approval for ethics committee were obtained in their original work.

REFERENCES

1. Alves ANG, Cabau L, Pavan NNO, Marques IV, Viana BAS, Stulp P, et al. Post-obturation pain and its relationship with reference time and other risk factors. Braz Dent Sci. 2022;25(3):e3519. http://doi.org/10.4322/bds.2022.e3519.
2. AlRahabi MK. Predictors, prevention, and management of postoperative pain associated with nonsurgical root canal treatment: a systematic review. J Taibah Univ Med Sci. 2017;12(5):376-84. http://doi.org/10.1016/j.jtumed.2017.03.004. PMid:31435267.
3. Seltzer S, Naidorf IJ. Flare-ups in endodontics: I. Etiological factors. J Endod. 1985;11(11):472-8. http://doi.org/10.1016/S0099-2399(85)80220-X. PMid:3868692.
4. Comparin D, Moreira EJL, Souza EM, De-Deus G, Arias A, Silva EJNL. Postoperative pain after endodontic retreatment using rotary or reciprocating instruments: a randomized clinical trial. J Endod. 2017l;43(7):1084-8. http://doi.org/10.1016/j.joen.2017.02.010. PMid:28477995.
5. Genet JM, Hart AA, Wesselink PR, Thoden Van Velzen SK. Preoperative and operative factors associated with pain after the first endodontic visit. Int Endod J. 1987;20(2):53-64. http://doi.org/10.1111/j.1365-2591.1987.tb00590.x. PMid:3471726.
6. Zhang W, Peng B. Tissue reactions after subcutaneous and intraosseous implantation of iRoot SP, MTA and AH Plus. Dent Mater J. 2015;34(6):774-80. http://doi.org/10.4012/dmj.2014-271. PMid:26632225.
7. Siqueira JF Jr. Microbial causes of endodontic flare-ups. Int Endod J. 2003;36(7):453-63. http://doi.org/10.1046/j.1365-2591.2003.00671.x. PMid:12823700.
8. Willershausen I, Callaway A, Briseño B, Willershausen B. In vitro analysis of the cytotoxicity and the antimicrobial effect of four endodontic sealers. Head Face Med. 2011;7(1):15. http://doi.org/10.1186/1746-160X-7-15. PMid:21831282.
9. Souza C Jr, Machado R, Batts RA, Garcia LFR. Inferior alveolar nerve paresthesia after overfilling into the mandibular canal, confirmed by cone-beam computed tomography: a case report. Braz Dent Sci. 2021;24(2):1-8. http://doi.org/10.14295/bds.2021.v24i2.2421.
10. Batista RFC, Hidalgo MM, Hernandes L, Consolaro A, Velloso TRG, Cuman RKN, et al. Microscopic analysis of subcutaneous reactions to endodontic sealer implants in rats. J Biomed Mater Res A. 2007;81(1):171-7. http://doi.org/10.1002/jbm.a.30918. PMid:17120202.
11. Geurtsen W. Biocompatibility of root canal filling materials. Aust Endod J. 2001;27(1):12-21. http://doi.org/10.1111/j.1747-4477.2001.tb00445.x. PMid:11481874.
12. Huang FM, Chou MY, Chang YC. Induction of cyclooxygenase-2 mRNA and protein expression by epoxy resin and zinc oxide-eugenol based root canal sealers in human osteoblastic cells. Biomaterials. 2003;24(11):1869-75. http://doi.org/10.1016/S0142-9612(02)00584-7. PMid:12615477.
13. Gabay C. Interleukin-6 and chronic inflammation. Arthritis Res Ther. 2006;8(Suppl 2):S3. http://doi.org/10.1186/ar1917. PMid:16899107.
14. Huang FM, Tsai CH, Yang SF, Chang YC. Induction of interleukin-6 and interleukin-8 gene expression by root canal sealers in human osteoblastic cells. J Endod. 2005;31(9):679-83. http://doi.org/10.1097/01.don.0000155227.86046.a2. PMid:16123706.
15. Sponchiado EC Jr, Vieira WDA, Normando AGC, Pereira JV, Ferraz CCR, Almeida JFA, et al. Calcium silicate-based sealers do not reduce the risk and intensity of postoperative pain after root canal treatment when compared with epoxy resin-based sealers: a systematic review and meta-analysis. Eur J Dent. 2021;15(2):347-59. http://doi.org/10.1055/s-0041-1724157. PMid:33759149.
16. Mekhdieva E, del Fabbro M, Alovisi M, Comba A, Scotti N, Tumedei M, et al. Postoperative pain following root canal filling with bioceramic vs. traditional filling techniques: a systematic review and meta-analysis of randomized controlled trials. J Clin Med. 2021;10(19):4509. http://doi.org/10.3390/jcm10194509. PMid:34640531.
17. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. PMid:33782057.
18. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898. http://doi.org/10.1136/bmj.l4898. PMid:31462531.
19. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev.

2019;10(10):ED000142. http://doi.org/10.1002/14651858.ED000142. PMid:31643080.

20. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ. 2004;328(7454):1490-4. http://doi.org/10.1136/bmj.328.7454.1490. PMid:15205295.

21. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. J Chronic Dis. 2011;64(4):401-6. http://doi.org/10.1016/j.jclinepi.2010.07.015. PMid:21208779.

22. Tan HSG, Lim KC, Lui JN, Lai WMC, Yu VSH. Postobturation Pain Associated with Tricalcium Silicate and Resin-based Sealer Techniques: A Randomized Clinical Trial. J Endod. 2021;47(2):169-77. http://doi.org/10.1016/j.joen.2020.10.013. PMid:33098889.

23. Cunha SA, Soares CJ, Rosatto CMP, Vieira JVSM, Pereira RAS, Soares PBF, et al. Effect of endodontic sealer in young molars treated by undergraduate students: a randomized clinical trial. Braz Dent J. 2020;31(6):589-97. http://doi.org/10.1590/0103-6440202003258. PMid:33237229.

24. Aslan T, Dönmez Özkan H. The effect of two calcium silicate-based and one epoxy resin-based root canal sealer on postoperative pain: a randomized controlled trial. Int Endod J. 2021;54(2):190-7. http://doi.org/10.1111/iej.13411. PMid:32929721.

25. Ferreira NS, Gollo EKF, Boscato N, Arias A, Silva EJNLD. Postoperative pain after root canal filling with different endodontic sealers: a randomized clinical trial. Braz Oral Res. 2020;34:e069. http://doi.org/10.1590/1807-3107bor-2020.vol34.0069. PMid:32696911.

26. Ambika S, Satish K. Evaluation of pain after endodontic obturation with three different rootcanal sealers: a randomized control trail [Internet]. Geneva: WHO; 2018 [cited 2023 Sept 22]. Available from: http://www.who.int/trialsearch/Trial2.aspx?TrialID=CTRI/2018/05/013932

27. Fonseca B, Coelho MS, Bueno CEDS, Fontana CE, Martin AS, Rocha DGP. Assessment of extrusion and postoperative pain of a bioceramic and resin-based root canal sealer. Eur J Dent. 2019;13(3):343-8. http://doi.org/10.1055/s-0039-3399457. PMid:31794999.

28. Atav Ates A, Dumani A, Yoldas O, Unal I. Post-obturation pain following the use of carrier-based system with AH Plus or iRoot SP sealers: a randomized controlled clinical trial. Clin Oral Investig. 2019;23(7):3053-61. http://doi.org/10.1007/s00784-018-2721-6. PMid:30397735.

29. Graunaite I, Skucaite N, Lodiene G, Agentiene I, Machiulskiene V. Effect of resin-based and bioceramic root canal sealers on postoperative pain: a split-mouth randomized controlled trial. J Endod. 2018;44(5):689-93. http://doi.org/10.1016/j.joen.2018.02.010. PMid:29571915.

30. Drumond JPSC, Maeda W, Nascimento WM, Campos DL, Prado MC, de-Jesus-Soares A, et al. Comparison of postobturation pain experience after apical extrusion of calcium silicate- and resin-based root canal sealers. J Endod. 2021;47(8):1278-84. http://doi.org/10.1016/j.joen.2021.05.008. PMid:34058249.

31. Paz A, Vasconcelos I, Ginjeira A. Evaluation of postoperative pain after using bioceramic materials as endodontic sealers. EC Dental Science. 2018;17(10):1739-48.

32. Shim K, Jang YE, Kim Y. Comparison of the effects of a bioceramic and conventional resin-based sealers on postoperative pain after nonsurgical root canal treatment: a randomized controlled clinical study. Materials. 2021;14(10):2661. http://doi.org/10.3390/ma14102661. PMid:34069521.

33. Gudlavalleti B, Patil AA. Comparative evaluation of postoperative pain after root canal treatment using three different sealers, Viz., Tubli-Seal EWT, Apexit Plus, AH Plus: an in-vivo study. J Clin Diagn Res. 2020;14(1):ZC04-09. http://doi.org/10.7860/JCDR/2020/42767.13417.

34. Bodian CA, Freedman G, Hossain S, Eisenkraft JB, Beilin Y. The visual analog scale for pain: clinical significance in postoperative patients. Anesthesiology. 2001;95(6):1356-61. http://doi.org/10.1097/00000542-200112000-00013. PMid:11748392.

35. Lodiene G, Morisbak E, Bruzell E, Ørstavik D. Toxicity evaluation of root canal sealers in vitro. Int Endod J. 2008;41(1):72-7. http://doi.org/10.1111/j.1365-2591.2007.01321.x. PMid:17931390.

36. Rodríguez-Lozano FJ, García-Bernal D, Oñate-Sánchez RE, Ortolani-Seltenerich PS, Forner L, Moraleda JM. Evaluation of cytocompatibility of calcium silicate-based endodontic sealers and their effects on the biological responses of mesenchymal dental stem cells. Int Endod J. 2017;50(1):67-76. http://doi.org/10.1111/iej.12596. PMid:26660310.

37. Loushine BA, Bryan TE, Looney SW, Gillen BM, Loushine RJ, Weller RN, et al. Setting properties and cytotoxicity evaluation of a premixed bioceramic root canal sealer. J Endod. 2011;37(5):673-7. http://doi.org/10.1016/j.joen.2011.01.003. PMid:21496669.

38. Siqueira JF Jr. Reaction of periradicular tissues to root canal treatment: benefits and drawbacks. Endod Topics. 2005;10(1):123-47. http://doi.org/10.1111/j.1601-1546.2005.00134.x.

39. Sari Ş, Duruturk L. Radiographic evaluation of periapical healing of permanent teeth with periapical lesions after extrusion of AH Plus sealer. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2007;104(3):e54. http://doi.org/10.1016/j.tripleo.2007.03.024. PMid:17709070.

40. Mehrvarzfar P, Abbott PV, Saghiri MA, Delvarani A, Asgar K, Lotfi M, et al. Effects of three oral analgesics on postoperative pain following root canal preparation: a controlled clinical trial. Int Endod J. 2012;45(1):76-82. http://doi.org/10.1111/j.1365-2591.2011.01950.x. PMid:21902704.

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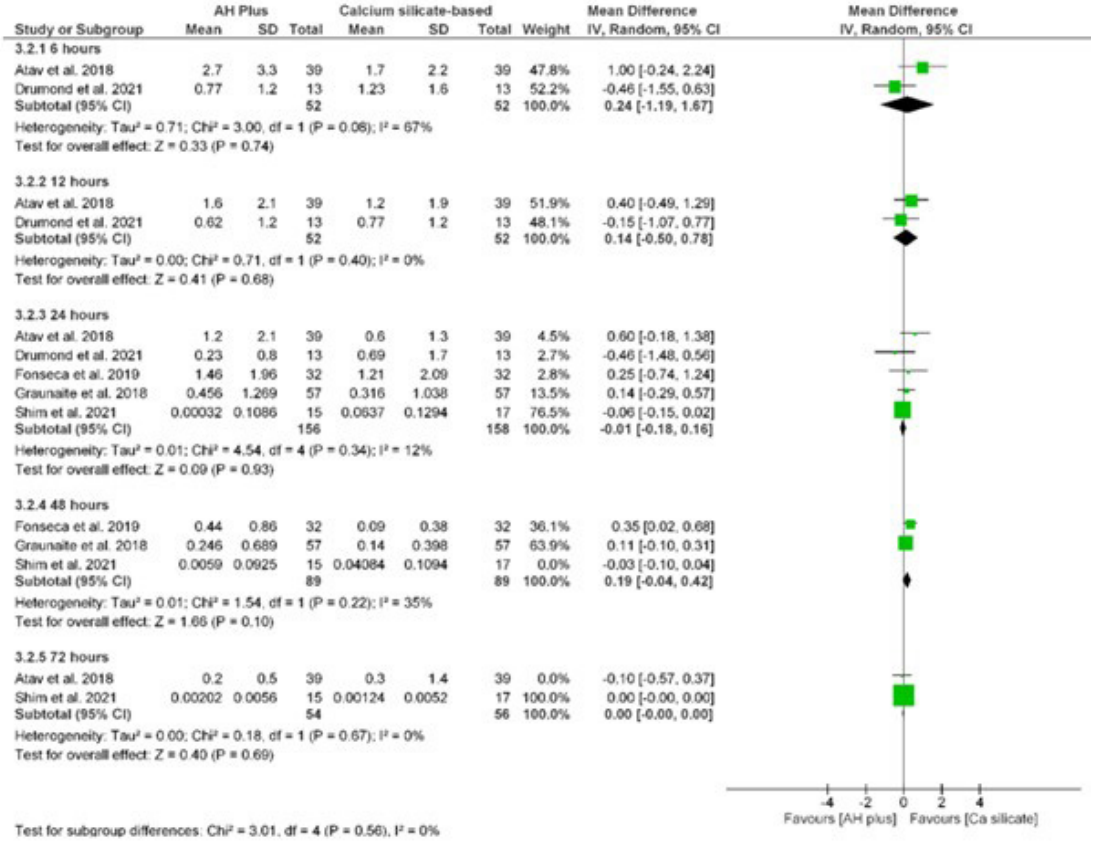
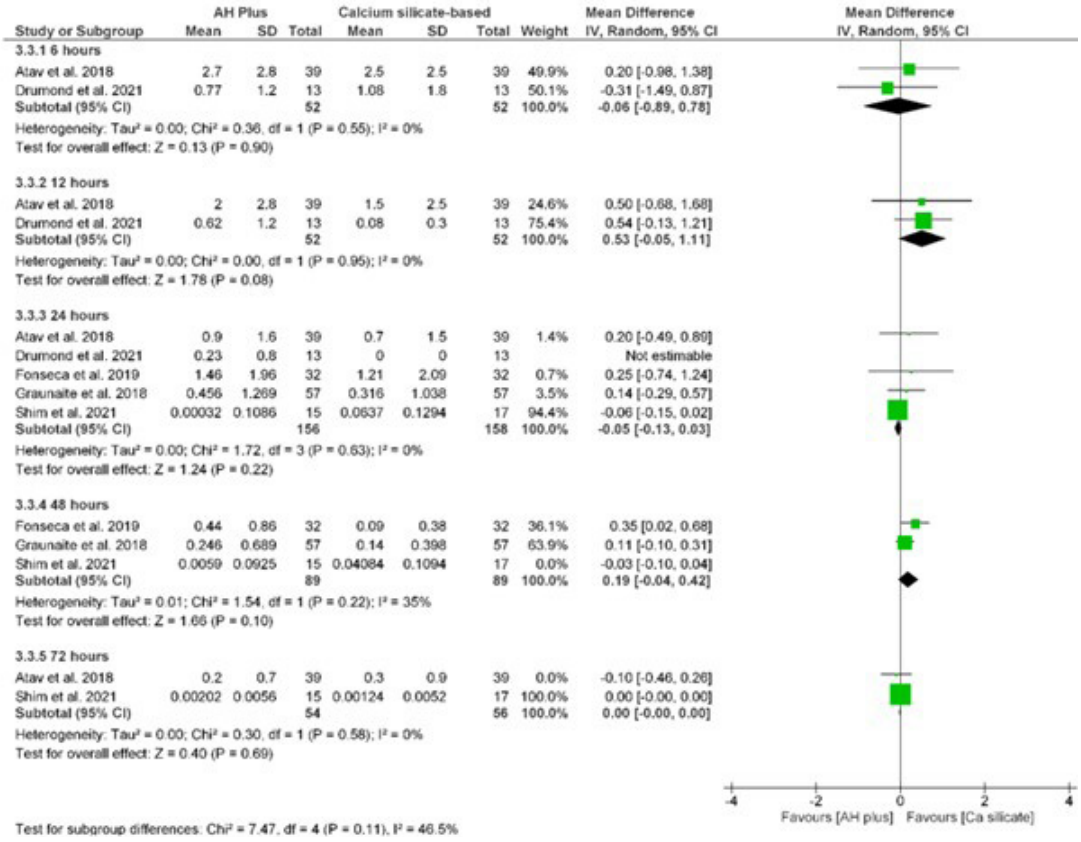
Appendix 1. Studies excluded in the full-text analyses with reasons

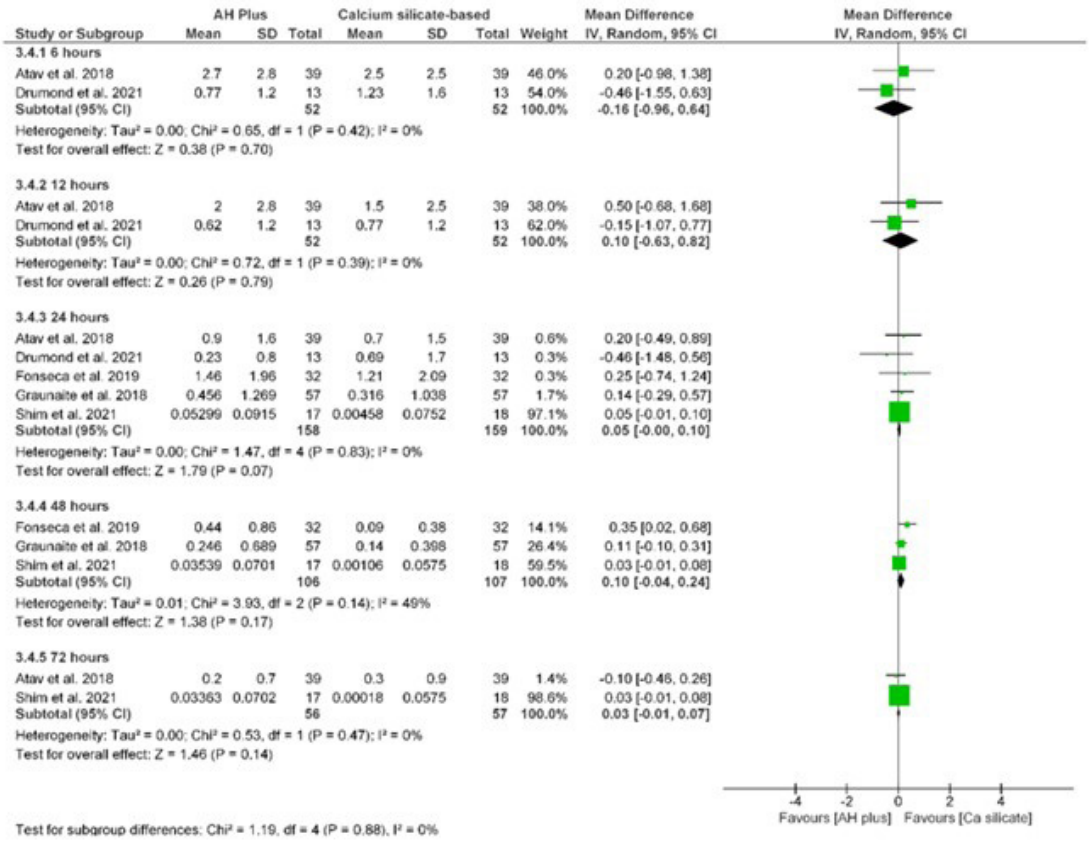
	Author, year	Reason for exclusion	Indexing in databases (DOI)/ INSS
1	Thakur, 2013	No RCTs	10.4103/0972-0707.120944
2	Shashirekha, 2018		10.4103/JCD.JCD_224_18
3	Yu, 2021		10.1007/s00784-021-03814-x
4	Alacam, 1985	AH-Plus not tested	10.1016/S0099-2399(85)80233-8
5	Goreva, 2004		15111950
6	Sadaf, 2014		25598754
7	Sharma, 2019		23952822
8	Javidi, 2020		10.30476/DENTJODS.2020.83231.1041
9	Nabi, 2020		15509702
10	Sadaf, 2021		10.9734/jpri/2021/v33i42A32418
11	NCT04935736		-
12	NCT03874949		-
13	Wang, 2003	No english, portuguese or spanish version	10067248
14	Chen, 2006		16718852
15	Tang, 2009		10.3969/j.issn.1673-8225-2009.29.040
16	Xu, 2013		10.3724/SP.J.1008.2013.01029
17	Shu, 2018		10.19439/j.sjos.2018.06.017
18	CTRI / 2021/04/032815	Not finished	-
19	NCT03732170		-
20	CTRI/2019/02/017745		-
21	CTRI/2018/10/015919	No author reply	-
22	NCT04228913		-
23	NCT02981693		-

Appendix 2. Forest plots of postoperative pain between AH Plus vs Calcium silicate-based sealers groups (6, 12, 24, 48, and 72 hours)





Appendix 2. Continued...



Appendix 3. Forest plots of the relative risk (RR) for postoperative pain between AH Plus vs Calcium silicate-based sealers groups (24, 48, and 72 hours)