Histopathological evaluation of the influence of root canal obturation in the repair of apical periodontitis in animals: a systematic review

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ABSTRACT

Introduction: Root canal fillings are a decisive factor in the success of endodontic treatment. This systematic review evaluated animal studies using histopathological parameters to determine the effect of root canal filling on the healing of apical periodontitis. **Methods:** A search was conducted in PubMed, Lilacs, Scielo, Science Direct and BBO using indexed and non-indexed keywords. Studies published from 2003 to 2019 were selected according to inclusion and exclusion criteria. **Results:** Five animal studies met eligibility criteria and were included in the systematic review for a qualitative analysis. **Conclusion:** The extension of the root canal filling may affect the healing of apical periodontitis when bacteria remain in the canal. Root canal sealers with antimicrobial properties were not effective in eliminating bacteria remaining in the root canal, nor in promoting the complete healing of apical periodontitis.

Keywords: Obturação do canal radicular. Periodontite periapical. Cicatrização.

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Introduction

Root canal filling is a decisive factor in the success of an endodontic treatment. Several epidemiological studies found a high prevalence of apical periodontitis in teeth with an inadequate canal filling.[1-3]

Filling extension, filling homogeneity and the characteristics of filling materials, such as biocompatibility and antimicrobial potential, may affect the health of periradicular tissues after an endodontic treatment. According to some authors, taper is the most important characteristics in the evaluation of endodontic treatment quality.[4]

The highest success rates are achieved when the filling extension is 0 mm to 2 mm short of the radiographic root apex and radiographs do not show any empty spaces in the canal, which confirms that the condensation of the filling material was adequate.[5]

Most studies that evaluated the effect of root canal filling on the healing of apical periodontitis were cross-sectional and analyzed dental radiographs. Although the samples in these studies included a large number of people, which is a great advantage, they had some limitations. As disease history is not fully understood, it is not possible to determine whether lesions are being cured or expanding. Radiographs, which provide two-dimensional views, may not show lesions in the medullary bone spaces that have not ruptured the cortical bone, nor those that grow buccolingually.[6]

The analysis of cone beam CT scans may reveal lesions not detected on conventional radiographs,[6] but the high cost of evaluating a significantly large sample makes it difficult to conduct this type of study. Moreover, few studies in the literature conducted histopathological analyses of healing after a nonsurgical endodontic treatment, mostly because of the ethical implications of this type of analysis in human beings.

This systematic review evaluated studies using histopathological parameters to determine the effect of root canal filling on the healing of apical periodontitis in animals with pulpal necrosis and periapical lesions in permanent teeth.

Material and methods

The initial clinical question for this systematic review was: Do the characteristics of root canal filling affect periapical healing in animals that undergo nonsurgical endodontic treatment of permanent teeth with pulpal necrosis and periapical lesions?

The question was formulated following the PICO framework, that is: (P) animals that underwent nonsurgical endodontic treatment of permanent teeth; (I) root canal filling; (C) filing characteristics; (O) periapical healing.

The search terms, selected from lists of indexed (MeSH) and nonindexed terms were “root canal obturation” (MeSH), “root canal filling”, “periapical repair”, “periapical healing”, “periapical lesion”, “endodontic outcome” and “apical periodontitis” (MeSH).

Studies that answered the clinical question were selected according to the following inclusion and exclusion criteria (Table 1):

Only studies published from 2003 to 2019 were included. The search was conducted in September 2019 in PubMed, Lilacs, Scielo, Science Direct and BBO using specific filters for each database because of the search characteristics of each platform. Table 2 shows the details of the search strategy for each database.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria:	Exclusion criteria:
1. Animal studies.	1. Studies with humans.
2. Endodontic treatment of permanent teeth with pulpal necrosis and periapical lesion.	2. In vitro studies.
3. Nonsurgical endodontic treatment.	3. Teeth with incomplete root formation.
4. Histopathological evaluation.	4. Teeth with anomalies, periodontal disease, perforation or resorption.
5. Evaluation of association between root canal filling characteristics – extension, homogeneity; taper; lateral sealing, sealer biocompatibility - and presence or absence of periapical healing - periapical health.	5. Reimplanted teeth.
	6. Regenerative endodontic treatment.
	7. Endodontic treatment of teeth with a vital pulp.
	8. Endodontic treatment associated with surgical treatment.
	9. Teeth without coronal restoration.
	10. Teeth with partially filled canals – prepared for post placement.
	11. Case reports; case series; literature reviews, book chapters, Master's or Doctorate dissertations, observational studies.
	12. Studies that did not evaluate association between filling characteristics and periapical healing.
	13. Endodontic treatment associated with specific systemic disease or use of systemic drugs.

Table 2. Filters and search strategy

	PubMed	Lilacs	Scielo	Science Direct	BBO
Filters	Studies with animals;- date 2003-2019	date: 2003-2019	date: 2003-2019	date: 2003-2019	date: 2003-2019
Search strategies	((((((“root canal obturation”[Title/Abstract]) OR “root canal filling”[Title/Abstract]) OR “periapical repair”[Title/Abstract]) OR “periapical healing”[Title/Abstract]) OR “periapical lesion”[Title/Abstract]) OR “endodontic outcome”[Title/Abstract]) OR “apical periodontitis”[Title/Abstract]	root canal obturation OR root canal filling OR periapical repair OR periapical healing OR periapical lesion OR apical periodontitis OR endodontic outcome [Words] and animals [Limits] and “2003” or “2004” or “2005” or “2006” or “2007” or “2008” or “2009” or “2010” or “2011” or “2012” or “2013” or “2014” or “2015” or “2016” or “2017” or “2018” or “2019” [Country, year publication	(ab:(“root canal obturation”)) OR (ab:(“root canal filling”)) OR (ab:(“periapical repair”)) OR (ab:(“periapical healing”)) OR (ab:(“periapical lesion”)) OR (ab:(“endodontic outcome”)) OR (ab:(“apical periodontitis”)) AND year_cluster:(“2014” OR “2016” OR “2017” OR “2009” OR “2012” OR “2015” OR “2013” OR “2011” OR “2007” OR “2008” OR “2010” OR “2004” OR “2019” OR “2005” OR “2006” OR “2003”) AND type:(“research--article”)	(root canal obturation OR root canal filling OR periapical repair OR periapical healing OR periapical lesion OR endodontic outcome OR apical periodontitis) AND (dogs OR dog OR rats OR rat OR primate OR primates OR mice OR mices OR animal OR animals)	root canal obturation OR root canal filling OR periapical repair OR periapical healing OR periapical lesion OR apical periodontitis OR endodontic outcome [Words] and animals [Limits] and “2003” or “2004” or “2005” or “2006” or “2007” or “2008” or “2009” or “2010” or “2011” or “2012” or “2013” or “2014” or “2015” or “2016” or “2017” or “2018” or “2019” [Country, year publication)

Results

The search in these five databases retrieved 710 studies: PubMed – 324; Scielo – 239; Science Direct – 62; Lilacs – 49; and BBO – 36. After 100 repeated studies were excluded, the titles of 610 publications were analyzed, and the 519 that did not meet inclusion criteria were excluded. The abstracts of the remaining 91, whose titles did not contain enough information to determine whether they should be excluded, were selected for reading. Again, the 66 studies that did not meet inclusion criteria were excluded. After that, the full text of the remaining 25 studies was read. A search in the references of these studies found seven other titles that might meet inclusion criteria, which totaled 32 studies to be read fully. Eligibility criteria were again applied and, at the end of the selection, five studies were included in the qualitative analysis of this systematic review. Figure 1 shows the study selection flowchart, and Table 3 summarizes the characteristics and results of the studies included in the systematic review.

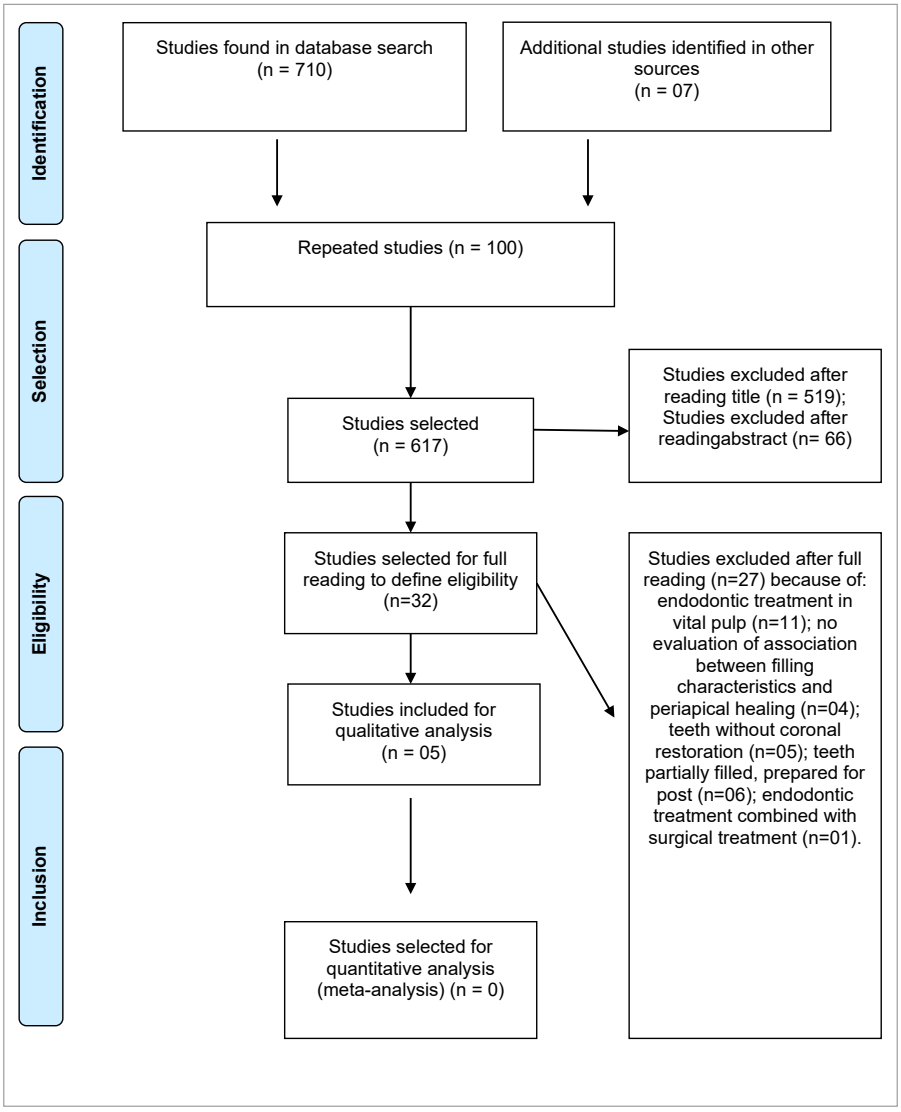

Figure 1. Flowchart of systematic search of studies.

Table 3. Summary of characteristics and results of the studies included in the systematic review.

Study	Species	No. of samples	Teeth used	Preparation technique	Canal filling extension	Irrigation
Leonardo et al.[27] (2003)	Dogs	3 dogs (44 canals)	Premolars	Crown-down Up to #70 file	2 mm short of radiographic apex	2.5% NaOCl
Fabricius et al.[18] (2006)	Monkeys	8 monkeys (175 canals)	Not described.	Not described.	Not described.	1.0% NaOCl and 10% H2O2
Sabeti et al.[38] (2006)	Dogs	7 dogs (56 canals)	Premolars	Crown-down Up to #70 file	1.5 mm to 2 mm from radiographic apex	5.25% NaOCl
Borlina et al.[26] (2010)	Dogs	2 dogs (40 canals)	Incisors and premolars	Crown-down Up to #55 file	Extension to cemento-dentinal junction (tactile method)	2.5% NaOCl
Gomes-Filho et al.[25] (2013)	Dogs	2 dogs (64 canals)	Incisors, canines and premolars	Technique not specified. Up to #40 K file	1 mm short of radiographic apex	2.5% NaOCl

Discussion

The technical characteristics of root canal fillings, such as their extension and the absence of empty spaces, are important factors in the success of endodontic treatments.[7-10] The composition and biocompatibility of sealers have also been evaluated in studies to determine the best materials for these treatments. The healing of apical periodontitis seems to be affected by sealer biocompatibility, and sealer components should induce mineralization and have antimicrobial effects.[11,12]

Different methods have been used to evaluate the healing of apical periodontitis. Periapical radiographs are the most common tests for the follow-up of endodontic treatments, but López et al (2014)[13] found that this type of radiograph provides limited information about periapical lesions and should not be used in scientific investigations.

Cone beam CT scans are better than periapical radiographs to detect apical lesions.[14,15] However, histopathological tests remain the gold-standard to evaluate periapical healing.[16]

The extension of root canal fillings is an important factor in the healing of apical periodontitis.[5]

Schaeffer et al (2005)[17] conducted a systematic review of the literature and meta-analysis and found that the highest success rate was achieved when the root canal filling was short of the root apex.

Most studies that evaluated the effect of filling extension on apical periodontitis healing used radiographs or CT scans of endodontically treated teeth. Therefore, they did not determine other factors that might affect healing, such as the quality of cleaning and shaping and the control of infection in the root canal system.

Only one study included in our review conducted a histopathological evaluation of the effect of filling extension on the healing of apical periodontitis. Fabrícius et al (2006)[18] found that, when bacteria remained in the canal, a filling extension > 2.5 mm was associated with no periapical healing. When no bacteria remained in the canal after cleaning and shaping, healing took place regardless of the extension of the canal filling. They also found that bac-

Foramen instrumentation	Smear layer removal/ Intracanal medication	Type of root canal filling	Variable under analysis	Results
Yes Up to #30 K file	Yes 17% EDTA for 3 min/ Yes Ca(OH)2 + PMCC for 15 days	Lateral condensation of gutta percha and sealer	Type of sealer (Sealapex; AH Plus; Sealer Plus)	Sealapex and AH Plus had satisfactory results and promoted periapical healing. Sealer Plus had unsatisfactory results and resulted in tissue irritation.
Not described.	No/No	Gutta percha and chloropercha Technique not specified	Root filling extension - < 0.5 mm from apex; 0.5 mm to 2.5 mm from apex > 2.5 mm from apex; overfilled	When no bacteria remained in root canal, periapical healing occurred regardless of filling extension. When bacteria remained in the canal, unsuccessful healing was correlated with poor-quality fillings.
Yes Up to #40 K file	Yes 17% EDTA for 3 min/ No	Lateral condensation of gutta percha and sealer	Presence or absence of root filling (sealing)	No statistically significant difference in periodontitis healing between obturated and nonobturated teeth
20 teeth with foramen widening, up to #25 K file, and 20 teeth without foramen widening	Yes 17% EDTA for 3 min/ Yes Ca(OH)2 + saline for 21 days	Lateral condensation of gutta percha and sealer	Foramen widening (with/without) and type of sealer (Sealer 26; Endomethasone)	Foramen widening and Sealer 26 were better for healing of chronic periapical lesions.
Yes Up to #20 K file	Yes 17% EDTA for 3 min/ No	Lateral condensation of gutta percha and sealer	Type of sealer (Sealapex; Endo-CPM-Sealer; MTA-Fillapex)	Sealers had similar healing patterns. Preparation of infected canals filled with these sealers did not promote complete healing of periapical lesions.

teria that remain in the root canal after filling were significantly associated with lesion persistence, a finding also reported by other authors. According to Chandra (2009),[19] several factors, such as quality of canal filling, may affect the result of an endodontic treatment, but success relies primarily on the elimination of the endodontic infection.

Nair (2004)[20] found that the main cause of endodontic treatment failure is the presence of bacteria in the root canal system. Ng et al (2008),[21] in a systematic review and meta-analysis, evaluated studies that used radiographs to investigate the effect of the filling extension on the success of endodontic treatments in human beings. The author found no statistically significant differences when filling extension was > 2 mm or 0-2 mm short of the radiographic apex and there were no periapical lesions before the treatment. However, when there were previous lesions, the rate of success of teeth with filling extensions 0-2 mm short of the radiographic apex was statistically higher than that of fillings at > 2 mm from the radiographic apex. Therefore, periapical tissue fluids may percolate into the empty space of the apical third of the canal and provide nutrients for the proliferation of residual microorganisms.

On the other hand, Souza et al (2018)[22] evaluated the effect of filling extension on the healing of periapical lesions in human beings.They found no statistically significant differences between the control group, in which canals were filled to 1 mm short of the radiographic root apex, and the experimental group, in which filling extensions ranged from 2 mm to 7 mm short of the radiographic apex. They concluded that cleaning and shaping of the root canal seemed to be the determinant factor in the promotion of periapical lesion healing.

The presence of the filling, although not impeding, hinders the percolation of nutrients and the growth of bacteria inside the canal.[23,24] Therefore, in canals without endodontic infection, such as those with a vital pulp, or those in which cleaning and shaping substantially reduced endodontic infection, fillings with extensions longer than 2 mm short of the radiographic root apex may not compromise healing.

In cases of overfilling, with extravasation of filling material into periapical tissues, success rates are lower.[17] Nair (2004)[20] and Ricucci et al (1998)[4] found higher success rates when filling material was contained inside the root canal, which prevented foreign body reactions of the periapical tissues against the filling material. One of the studies included in this review corroborates these findings.[18]

This review included three studies that evaluated the effect of the composition of endodontic sealers on the healing of apical periodontitis in animals.[25-27]

Gomes-Filho et al (2013)[25] found that sealers with antibacterial activity, such as MTA Fillapex, Endo-CPM-Sealer and Sealapex, do not eliminate residual microorganisms from the canal or promote the complete healing of periapical lesions. The antimicrobial activity of calcium hydroxide-based and MTA-based sealers is explained by the release of hydroxyl ions into the environment, which increases tissue pH. An alkaline environment affects bacterial metabolism and compromises bacterial survival.[11,24]

However, some authors raise questions about the effective antibacterial activity of these sealers in the long term.[28-30] According to Morgental et al (2011),[31] MTA Fillapex had no antibacterial activity seven days after setting, despite its high pH. Those authors also found that Endo-CPM-Sealer did not have any antimicrobial activity before or after sealer setting. Kuga et al (2013)[12] conducted an in-vitro study and found that Sealapex provided a higher pH than MTA Fillapex, but antimicrobial activity was not different from each other.

These studies may explain the findings reported by Gomes-Filho et al (2013),[25] who reported that bacteria remained in canals filled with MTA Fillapex, Endo-CPM-Sealer and Sealapex. According to Holland et al (2017),[32] the most important factor for the healing of periapical tissues is the absence of infection and no contact of filling material with periradicular tissues.

Sealapex has antimicrobial and mineralizing activity and is biocompatible[33]. Tanomaru Filho et al (1998)[34] found good periapical healing when Sealapex was used for root filling of dog teeth. AH Plus and Sealer 26 are also classified as low cytotoxicity sealers.[35] Therefore, and according to other studies included in this review, these sealers lead to satisfactory periapical healing.[26,27] Paraformaldehyde, contained in Endomethasone, may produce tissue irritation,[36] which may explain the unsatisfactory results reported by Borlina et al (2010).[26] Perassi et al (2004)[37] found that Endomethasone is cytotoxic and, in a study with rats, this sealer induced greater TNF-α release than Sealapex.

One of the studies selected for this review evaluated the importance of the sealing provided by root canal filling in the healing of apical periodontitis. According to Sabeti et al (2006)[38] apical periodontitis may heal regardless of whether the canal is filled. Burkovski et al (2018)[39] raised questions about the importance of root canal filling, as it does not seal the root canal system in the absence of an adequate coronal restoration.

This systematic review did not find any animal studies that evaluated other factors, such as taper, homogeneity or empty spaces, and that associated fillings with healing of apical periodontitis. Therefore, our focus was on filling extension, type of sealer and sealing.

Conclusion

The analysis of the studies included in this systematic review of the literature revealed that a root canal filling may affect the healing of apical periodontitis in animals, and that it may be associated with the microbial load that remains in the canal system after cleaning and shaping. Of the parameters under analysis, filling extension affected healing when bacteria remained inside the canal after treatment. When infection was effectively controlled, filling extension and sealing provided by filling did not seem to affect healing. The analysis of sealer characteristics revealed that fillings with Sealapex (calcium hydroxide-based sealer) AH Plus and Sealer 26 (epoxy resin-based sealers) seemed to promote periapical healing. MTA Fillapex, Endo-CPM-Sealer and Sealapex did not eliminate the bacteria that remained in the root canal and did not promote the complete healing of apical periodontitis, although they all have some antimicrobial properties.

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