Postoperative pain after root canal filling with different endodontic sealers: a randomized clinical trial

Abstract: The aim of this randomized clinical trial was to compare the occurrence and intensity of postoperative pain and analgesic intake after root canal treatment, using different root canal sealers. Sixty single-rooted teeth diagnosed with asymptomatic necrosis and apical periodontitis were randomly assigned to 3 experimental groups (n=20), according to the root canal sealer: AH Plus, Endofill or MTA Fillapex. Endodontic treatment was performed in two sessions, and calcium hydroxide was used as the intracanal dressing. Patients were instructed to record pain intensity as none, slight, moderate and severe. Scores from 1 to 4 were attributed to each level of pain after 24 h, 48 h and 7 days. The need for analgesic intake was also recorded. Differences in the incidence of postoperative pain and the need for an analgesic were analyzed using the chi-square test. Differences in pain intensity after treatment were analyzed using the ordinal (linear) chi-square test. 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 timepoint (p>0.05). No pain was reported after 7 days. AH Plus, Endofill and MTA Fillapex used for filling root canals resulted in the same rate of postoperative pain and need for analgesic medication.

Keywords: Pain, Postoperative; Root Canal Obturation; Clinical Study.

Introduction

Endodontic postoperative pain has been defined as an unpleasant sensation of any degree of pain that occurs after initiating root canal treatment. Postoperative pain after endodontic procedures occurs in 3 to 58% of the cases, depending on the individual and variables evaluated. Postoperative pain is commonly related to mechanical, chemical or microbiological injury to periradicular tissues. Knowing the variables related to postoperative pain allows the professional to choose the techniques and materials that will lower this pain incidence.

Root canal systems requiring treatment are traditionally filled with gutta-percha associated to an endodontic sealer. These sealers are designed to be used inside the root canal during endodontic treatment, but may come in close contact with the periapical tissues through lateral...
canals, apical foramina or leaching.\textsuperscript{8,9} Therefore, it can be expected that root canal sealers may stimulate an inflammatory response and activate sensory neurons.\textsuperscript{10,11,12} Consequently, root canal sealers may be related to postoperative pain after root canal treatment. Ruparel et al.\textsuperscript{10} suggested that root canal sealers might activate trigeminal nociceptors \textit{in vitro}, and that this activation, along with the immunologic response, may trigger pain symptoms and cause flare-ups.

Previous studies have evaluated postoperative pain after application of different root canal sealers, and have found contrasting results. A study by Ates et al.\textsuperscript{13} found no differences when a resin-based (AH Plus; Dentsply-Sirona, Ballaigues, Switzerland) and a calcium silicate-based (iRoot SP; Innovative BioCeramix Inc., Vancouver, Canada) root canal sealer were compared regarding postoperative pain. Similar results were observed by Graunaite et al.\textsuperscript{14} when comparing AH Plus and Total Fill BC Sealer (FKG Dentaire SA, La Chaux-de-Fonds, Switzerland). In contrast, Shashirekha et al.\textsuperscript{15} found a statistically significant difference when two resin-based root canal sealers: AH Plus (Dentsply, DeTrey, Konstanz, Germany) and ResinoSeal (Amrit Chemicals and Mineral Agency, India) were compared to two calcium-hydroxide root canal sealers: Sealapex (SybronEndo, Orange, USA) and Apexit Plus (Ivoclar Vivadent, Liechtenstein). Thus, the contrasting results found in endodontic literature on this topic, and the limited evidence, prompted us to further explore the relationship between postoperative pain and different endodontic sealers used for filling root canals.

The aim of this randomized, controlled and prospective clinical trial was to compare the occurrence and intensity of postoperative pain and analgesic intake after root canal treatment, using different root canal sealers: AH Plus (Dentsply, DeTrey, Konstanz, Germany), EndoFill (Dentsply, Petrópolis Ind. e Com., Rio de Janeiro, Brazil) and MTA Fillapex (Angelus, Londrina, Brazil). The null hypothesis tested was that there are no differences in the occurrence and intensity of postoperative pain and the analgesic intake using different root canal sealers for the same root canal filling protocol.

### Methodology

#### Study design

This study was a randomized clinical trial comparing three endodontic sealers (AH Plus, EndoFill and MTA Fillapex), and was registered at www.clinicaltrial.gov (ClinicalTrials.gov Identifier: NCT03841877) and reported according to the guidelines of CONSORT clinical trials.\textsuperscript{16} This research project was approved by the local research ethics committee (number 2.516.565) and was performed in compliance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Sample size calculation was based on a previous study.\textsuperscript{17} It considered an error of alpha = 0.05 and a power of 0.9, and indicated a required sample size of 18 in each group. Assuming possible loss, 60 patients were included in the study.

#### Participant selection

Patients referred for endodontic treatment to the Dental School of the Federal University of Pelotas (Brazil) between September 2017 and December 2018 were invited to participate in this study. They were given complete information on the purpose and methods of the study, and those who agreed to participate signed an informed consent form.

**Inclusion criteria:** patients older than 18 years, referred to undergo endodontic treatment and diagnosed with pulp necrosis in anterior teeth and premolars. Participants who presented more than one indication for endodontic treatment were included more than once in the sample; however, the treatments were not performed at the same time, but rather, at an interval of 14 days between the end of one treatment and the beginning of another.

**Exclusion criteria:** teeth with previous endodontic treatment or positive response to pulpal sensitivity test, presence of a root fracture, teeth that could not be isolated with a rubber dam, or whose root length could not be reached, and patients who had complications during previous treatments. Patients who were younger than 18 years, or had cognitive difficulties, and who were pregnant, or had uncontrolled systemic diseases, were also excluded.
Randomization and blinding

Stratified randomization was performed according to the different dental groups (anterior or premolars), using a table of computer-generated random numbers (www.randomization.com). Allocation was concealed using opaque envelopes numbered consecutively. The envelopes were opened by an assistant not involved in the research, but only when the endodontic sealer was going to be inserted into the root canal. Patients were randomized for the endodontic sealer used (AH Plus, EndoFill and MTA Fillapex). Table 1 states the endodontic sealers used and their composition. The operator knew which sealer would be used only right before filling the root canal. The patients were blinded to the sealer.

Clinical interventions

The operators were last-year undergraduate students and a graduate student, trained for the procedures and techniques used, and always supervised by the responsible researcher. Diagnosis of pulpal necrosis was determined by negative response to the cold test, and confirmed by absence of bleeding when entering the pulp chamber. After receiving local anesthesia (2% lidocaine with epinephrine 1:100,000 – Nova DFL, Rio de Janeiro, Brazil), an access cavity was made using a spherical high-speed diamond bur. Upon reaching the pulp chamber, a rubber dam was placed, and the operating field was disinfected. Abundant initial irrigation with 5 ml 2.5% NaOCl was performed, followed by exploration of root canals with a size #10 K-file (Dentsply Maillefer, Ballaigues, Switzerland). The root canal length was determined using an apex locator (RomiApex A-15; Romidan Dental Solution, Israel), and root canals were prepared by using Wave-one Gold files (Dentsply Maillefer, Ballaigues, Switzerland), according to the manufacturer’s directions. These files were chosen based on the anatomy of the root canal, and were used with a gentle in-and-out pecking motion at 2-3 mm amplitude. The instrument was removed from the root canal after 3 in-and-out movements. These movements were repeated until the working length was reached. The root canals were irrigated with 5 mL 2.5% NaOCl, and apical patency was achieved with a size #10 K-file. After instrumentation, the root canals were flooded with 5 mL 17% EDTA for 3 minutes. Next, a final rinse was performed with 5 mL 2.5% NaOCl. An aliquot of approximately 40 ml of NaOCl was used during the treatment. Then the root canals were dried with sterile paper points, filled with a calcium hydroxide-based dressing, and sealed with composite resin.

After 7 days, infiltrative anesthesia and rubber dam isolation were performed, and the intracanal dressing was removed with manual files and irrigation with 5 mL 2.5% NaOCl. Root canals were filled using the single cone and vertical compaction technique with gutta-percha compatible with the root canal preparation system, and the envelopes were opened to allocate the teeth into different groups, according to the endodontic sealer: AH Plus; EndoFill and MTA Fillapex. Endodontic sealers were manipulated according to the manufacturer’s recommendations. The teeth were radiographed to test the gutta-percha cone and to determine if the entire canal should be filled. Then, the obturation material was cut with a heated instrument, the pulp chamber was cleaned with

| Endodontic sealer | Composition | Batch number |
|------------------|-------------|--------------|
| AH Plus (Dentsply, DeTrey, Konstanz, Germany) | Paste A: Bisphenol-A epoxy resin, Bisphenol-F epoxy resin, calcium tungstate, zirconium oxide, silica and iron oxide pigments. Paste B: Dibenzyldiamine, aminoadamantane, tricyclodecane diamine, calcium tungstate, zirconium oxide, silica and silicone oil. | 1609000660 |
| MTA Fillapex (Angelus, Londrina, Brazil) | Base Paste: Salicylate Resin, Natural Resin, Calcium Tungstate, Nanoparticulated Silica, Pigments; Catalyst Paste: Diluting Resin, Mineral Trioxide Aggregate, Nanoparticulated Silica, Pigments. | 42500 |
| EndoFill (Dentsply, Petrópolis Ind. e Com., Rio de Janeiro, Brazil) | Powder: Zinc oxide, hydrogenated resin, bismuth subcarbonate, barium sulfate and calcium borate. Liquid: Eugenol, almond oil and butylated hydroxytoluene. | 336206J |
alcohol, until the endodontic sealer was completely removed, and a composite resin restoration was made. The rubber dam was removed, and a final radiograph was taken.

No medication was prescribed for the patients; they were instructed to take only ibuprofen (600 mg every 8 hours) in the event of pain sensation.

**Postoperative pain evaluation**

Postoperative pain intensity was registered 24 h, 48 h and 7 days after obturation. Patients were instructed to record pain intensity as none, slight, moderate and severe. Scores from 1 to 4 (1-none, 2-slight, 3-moderate and 4-severe) were attributed to each level of pain at each timepoint. Patients were contacted by telephone at convenient and prescheduled times. Any need for analgesics was recorded.

**Statistical analysis**

Differences in the incidence of postoperative pain and the need for analgesic medication after 24 h and 48 h among the three groups were analyzed using the chi-square test. Differences in pain intensity among the groups, 24 h and 48 h following treatment were analyzed using the ordinal (linear) chi-square test. No statistical analysis was performed to assess differences in the incidence, intensity or analgesic intake among the groups 7 days after treatment, since no incidence of postoperative pain or analgesic consumption was reported for any of the different groups.

A logistic regression was also used to assess the incidence of postoperative pain 24 h and 48 h after treatment among the groups, and to control other possible confounding factors. Apart from the sealer used for obturation (AH Plus/EndoFill/MTA Fillapex), patient gender, tooth position (anterior or posterior) and arch (maxillary or mandibular) were also included in the analysis to ensure a correct estimation. A stepwise protocol was used to statistically enter and exclude factors from the logistic regression model, to obtain a better global fit.

**Results**

The study included 60 teeth of 57 patients (30 anterior and 30 premolars), 40 women and 17 men, having a mean age of 41 years (18–80 years) (Figure). Table 2 shows the demographic and clinical features of the patients in the study groups.

Overall, postoperative pain occurred in 11.6% of the cases (7 patients), at different intensities, after 24 h, dropping to 8.3% (5 patients) after 48 h. The results (n) for the incidence and intensity of postoperative pain in each group 24 h and 48 h after treatment are shown in Table 3. No pain was reported after 7 days in any of the groups.

No significant differences were detected among the groups either in incidence or intensity of postoperative pain, or in analgesic intake, at any of the timepoints. Moreover, no significant association of patient- or tooth-related factors composing the regression analysis was found (p > 0.05).

**Discussion**

The aim of this randomized, controlled and prospective clinical trial was to assess the occurrence and intensity of postoperative pain and analgesic intake after endodontic treatment performed with different root canal sealers used for filling root canals: AH Plus, EndoFill and MTA Fillapex. The results of the study suggest that the root canal sealers used in the present study had no influence on postoperative pain and analgesic intake during endodontic treatment procedures. Therefore, all three root canal sealers used in the study are predictable concerning short-term follow-up of postoperative pain. Given the present results, the tested null hypothesis was accepted. In *vitro* studies reported differences among the tested root canal sealers regarding cytotoxicity and inflammatory response. In addition, a previously published study demonstrated that root canal sealers can directly activate trigeminal nociceptors, leading to a robust release of calcitonin gene-related peptide, and may therefore lead to pain and neurogenic inflammation. However, these differences and findings did not seem to have a clinical impact, since the different sealers tested did not influence the postoperative pain in the present study. This result corroborates the findings of previously published studies, which also found no difference in postoperative pain when different sealers were used to fill root canals.
The incidence of postoperative pain was low in this randomized clinical trial (11.6% in 24 h and 8.3% in 48 h). The literature indicates a great variability of postoperative pain results that can range from 3–58%. This great variability can be explained by striking differences observed among the studies in regard to the postoperative evaluation.

Table 2. Baseline demographic and clinical features of patients in the study groups.

| Variable       | AH Plus | EndoFill | MTA Fillapex |
|----------------|---------|----------|--------------|
| Gender         |         |          |              |
| Male           | 4       | 8        | 7            |
| Female         | 16      | 12       | 13           |
| Age (year)     |         |          |              |
| < 30           | 1       | 7        | 8            |
| 30–50          | 11      | 8        | 8            |
| > 50           | 8       | 5        | 4            |
| Teeth          |         |          |              |
| Anterior       | 10      | 10       | 10           |
| Premolar       | 10      | 10       | 10           |
| Arch           |         |          |              |
| Upper teeth    | 14      | 13       | 17           |
| Lower teeth    | 6       | 7        | 3            |

Table 3. Incidence and intensity of postoperative pain in each group 24h and 48h after treatment.

| Sealer       | 24h  | 48h  |
|--------------|------|------|
|              | No pain | Slight | Moderate | No pain | Slight | Moderate |
| AHPlus       | 17    | 2     | 1       | 19      | 1      | 0        |
| EndoFill     | 19    | 0     | 1       | 19      | 1      | 0        |
| MTA Fillapex | 17    | 2     | 1       | 17      | 2      | 1        |

Figure. Flow diagram of the progress of the patients at each stage of the clinical trial, according to CONSORT.
method, the pulp and the periradicular condition during treatment, as well as the treatment protocol performed. Among the studies evaluating the influence of root canal sealers on postoperative pain, that by Graunaite et al.\textsuperscript{14} (2018) conducted a split-mouth randomized clinical trial in patients with asymptomatic apical periodontitis in previously endodontically treated single-rooted teeth, and found that 35\% of the patients perceived pain. Ates et al.\textsuperscript{13} included vital and non-vital mandibular premolars and molars in a randomized controlled clinical trial, and detected a 68\% and 59\% prevalence of patients with pain in teeth filled with AH Plus and iRoot, respectively. Shashirekha et al.\textsuperscript{15} evaluated pain in apically extruded sealers in vital and non-vital teeth, but did not report the percentage of patients with postoperative pain. Pain is expected after root canal treatment, and includes slight discomfort referred to as sensitivity, caused either by clamp placement or by physical trauma caused by instrumentation and chemical solutions.\textsuperscript{1} In the present study, an electronic apex locator was used to determine the apical constriction precisely, and thus avoid overinstrumentation and overfilling. Intentional sealer extrusion was not performed in any of the cases. However, it occurred unintentionally in 2 of them, but these few cases could not have influenced the outcome of postoperative pain.\textsuperscript{23,24}

Contrastingly, the root canal filling technique used in this study was different from that used in others, and might have influenced the low incidence of postoperative pain reported in this study. Therefore, it is more likely that post-obturation pain is related to the root canal filling technique rather than the root canal sealer. At the same time, immunological responses that might be linked to postoperative reactions to sealers were minimized, since the presence of systemic diseases was considered an exclusion criteria for ethical purposes.

In the present study, a notable decrease in the incidence of postoperative pain was also observed. Moreover, after 7 days no patient presented pain and no participants scheduled reinsertion during the observation period. Both outcomes are commonly observed in most postoperative pain studies.\textsuperscript{14,25,26,27}

Postendodontic pain is multifactorial in nature, and is influenced by factors inherent to patients and tooth conditions.\textsuperscript{7,28,30} In the present study, molars were not included intentionally, since it is already known that this group of teeth presents a higher incidence of postoperative pain.\textsuperscript{7,29,30} In addition, only asymptomatic patients were enrolled in the present study, since preoperative pain is known to be a strong predictor of postoperative pain.\textsuperscript{2,23,30} Moreover, stratified randomization was performed so that all groups would present the same number of anterior and premolar teeth, to avoid interference of this factor. Randomization also ensured similar distribution of demographic variables among the root canal sealer groups. This similarity, associated to the adequate sample size, resulted in the high internal and external validity of the present study. Even so, a logistic regression was applied to control any other possible confounding factor caused by the complexity of the pain process.

Some studies have shown that men and women differ in their responses to pain, and point out that women are at a substantially greater risk for many clinical pain conditions, such as tooth pain.\textsuperscript{32,33} In terms of postendodontic pain, data are controversial; whereas some studies have reported a higher incidence and longer duration of postoperative pain in women,\textsuperscript{7,23} others\textsuperscript{31} have found that the duration of the pain was significantly longer for males than for females. In the present study, no significant association of patient-related factors was found with postoperative pain, including gender, as also observed by Ates et al.\textsuperscript{13}

One of the main concerns about studying pain is the subjectivity of the evaluation. Each person’s pain threshold is unique, and heavily dependent on his cultural, individual, and economic background. Several endodontic postoperative pain studies have used the Visual Analogue Scale (VAS) as an instrument to evaluate pain;\textsuperscript{13,14,15,24,25,34,35} however, in the present study the occurrence and intensity of postoperative pain was measured using a simple descriptive scale. It is noteworthy to mention that both VAS and the method used herein are comparable, as evaluated earlier.\textsuperscript{35} In addition,
the scale used herein was very responsive, and averted patient loss to follow-up, probably because it allowed patients to be contacted by phone, an advantage recognized by this study and others found in the literature.\textsuperscript{17,31}

**Conclusion**

Root canal filling using AH Plus, MTA Fillapex and EndoFill resulted in the same postoperative pain occurrence and intensity, and need for analgesic intake.

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