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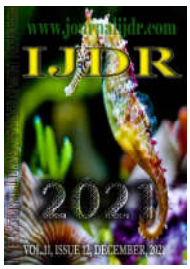

RESEARCH ARTICLE OPEN ACCESS

SUBMUCOSAL INJECTION OF DEXAMETHASONE OR BETAMETHASONE FOR POSTOPERATIVE PAIN MANAGEMENT IN PATIENTS WITH SYMPTOMATIC IRREVERSIBLE PULPITIS: A RANDOMIZED CONTROLLED CLINICAL TRIAL

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ABSTRACT

Introduction: We evaluated the effect of apical submucosal infiltration of dexamethasone or betamethasone for postoperative pain management in symptomatic irreversible pulpitis. **Methods:**Ninety patients with symptomatic irreversible pulpitis in mandibular molars were randomly divided into three groups after single-visit endodontic treatment (n=30): control group (CG) received a sham injection, while dexamethasone (DG) and betamethasone (BG) groups received apical submucosal infiltration of 0.7 mL (4 mg/mL) dexamethasone or betamethasone. Patients rated pain intensity on a visual analog scale at 6, 12, 24, 48, and 72 hours after treatment. Patient sex and age were also evaluated. **Results:**Pain scores did not differ between men and women in any group orany time point. Age was correlated with pain in DG only at 72 hours, indicating that older participants had a lower perception of pain. At 6 and 12 hours, dexamethasone and betamethasone had similar effects on pain reduction, but at 24 hours, betamethasone was more effective. At 48 and 72 hours, DG and BG were both associated with significantly lower pain scores than CG, with no significant difference between the two steroids. **Conclusion**: Submucosal infiltration of dexamethasone or betamethasone reduced postoperative pain in patients with symptomatic irreversible pulpitis after single-visit endodontic treatment.

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INTRODUCTION

Postoperative pain management is an essential part of endodontic practice. This symptom is to be expected, especially in teeth which were already painful before treatment. The biphasic pulp blood-flow response (vasodilation, increased blood flow, extravasation of intravascular fluid leading to increased pressure and decreased pulp blood flow) leads to the development of irreversible pulpitis or pulp necrosis, a condition that can extend to the periapical tissues, thus triggering the development of symptomatic apical periodontitis (VERA *et al*., 2018). Postoperative pain, which begins a few hours or days after treatment, is always an unpleasant experience for patient and clinician alike (ELKHADEM *et al*., 2018).

Patients still associate endodontic treatment with pain, even though practitioners frequently prescribe appropriate analgesia (ARIAS *et al*., 2015). In an attempt to contain postoperative pain, various classes of medication are often prescribed injudiciously. Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most prescribed drug classes in dentistry (SMITH *et al*., 2017). Although dentists are able to manage pain at the time of treatment with a variety of anesthetic, analgesic, and sedative techniques, post-treatment pain management remains a significant issue (CHINNI *et al*., 2018). Pain reduction has been achieved with the use of systemic agents such as analgesics and anti-inflammatory drugs. Dexamethasone is a corticosteroid with excellent anti-inflammatory efficacy and has long been used in endodontics. According to experimental and clinical research, it is effective before, during, and after the procedure, and can be

administered via the oral, intraligamentary, periapical, intracanal, or intramuscular routes (WALNUT *et al*., 2018). Betamethasone, in turn, has been the subject of increasing clinical research interest. Its efficacy has been demonstrated in single-visit and multiple-visit settings when administered orally. Gyanani *et al*. (2016) studied the effect of a combination of betamethasone 0.5 mg and 1.0 mg in a single preoperative dose plus antibiotic paste as an intracanal medicament and between visits in patients with asymptomatic apical periodontitis. Yavari *et al*. (2019) evaluated the effects of postoperative local submucosal infiltration of betamethasone 4 mg and dexamethasone 4 mg on pain perception and quality of life after single-visit root canal treatment in teeth with symptomatic irreversible pulpitis. Studies have shown that patient quality of life can be affected by pain after endodontic treatment, interfering with their mood and performance of the activities of daily living (LOPES et al., 2019; YAVARI et al., 2019). As a single submucosal injection administered in the apical region of the treated tooth, corticosteroids can be an option to reduce reliance on oral medications, preventing gastric discomfort and other adverse effects common with courses of analgesia that extend for days. Within this context, the present study was design to evaluate postoperative pain scores after endodontic treatment of mandibular molars with symptomatic irreversible pulpitis, comparing the use of two corticosteroids (betamethasone 4 mg and dexamethasone 4 mg) injected submucosally in the apical region. The null hypothesis was that the study groups would exhibit equivalent results.

MATERIALS AND METHODS

After approval by the local research ethics committee (4,214,669), patients from a private dental practice in São Paulo were recruited for this study. A total of90 mandibular molars were selected and, after endodontic treatment, randomly distributed into three experimental groups (n=30) according to the medication administered. The sample size was based on prior studies (LOPES*et al*., 2019; YAZDAN*et al*., 2012; NABI *et al*., 2018; BIDAR *et al*., 2017). Sample calculation was performed in the G*Power 3.1.9.4 software environment, based on pain severity at 12 hours as measured in a pilot study conducted with 10 patients in each group. For an effect size of 0.411 at the 5% significance level, with 90% statistical power and accounting for a 10% rate of loss to follow-up, the minimum sample size was calculated as 90 patients, i.e., 30 in each group. All procedures were carried out by a single practitioner specializing in endodontics. All patients were informed of the purpose of the trial and provided written informed consent for participation. Patients were selected according to the following inclusion criteria: low anesthetic risk (ASA I or II), aged 18 to 50 years, with indication for endodontic treatment of mandibular first or second molars with a diagnosis of symptomatic irreversible pulpitis; not on any systemic medication; absence of internal or external resorptions; absence of lacerations; absence of canal calcifications (confirmed radiographically); no contraindication for administration of corticosteroids. The exclusion criteria were: current intake of analgesics, anti-inflammatory drugs, antibiotics, or immunosuppressants; age <18 years; pregnancy or lactation; advanced periodontal disease; periapical lesion, abscess, or fistula; leakage of obturating material or unsatisfactory obturation of canal; calcifications; internal or external resorption; dental perforations or fractures; multiple-visit treatment; refusal to provide information on postoperative pain; known allergy to the medications used in the study.

Prior to treatment, patients were given a visual analogue scale (VAS) ranging from 0 to 10 and instructed to rate their pretreatment pain intensity. Pain perception was classified as none, mild (1-3), moderate (4-7), or severe (8-10). Diagnostic confirmation was obtained after analysis of radiographic and clinical examinations. For clinical examination, sensitivity testing was performed with EndoFrost™ refrigerant gas (Coltene; Whaledent, Langenau, Germany). All treatments were performed in a single visit by the same practitioner (a specialist endodontist) in the same private dental practice.

Treatment protocol: Anesthesia consisted of an inferior alveolar nerve block with 2% mepivacaine with 1:100,000 epinephrine (Alphacaine™; DFL Indústria e ComércioLtda, Rio de Janeiro, Brazil), administered with a long needle, supplemented by intrapulpal injection with a short gingival needle (Unoject™, Nova DFL, Rio de Janeiro, Brazil). After anesthesia, the teeth was isolated with a rubber dam (Madeitex, São José dos Campos, Brazil) secured by a JON folding frame (Vila Esperança, SP, Brazil) and clamps (Hu-Friedy, Rio de Janeiro, Brazil). Depending on the tooth, a light-cured resin barrier (Top Dam™, FGM, Joinville, Brazil) was used to achieve superior isolation. The tooth and surgical field were prepared with 2% chlorhexidine. The pulp chamber was accessed with a 1013/1015 long-shank ball-shaped diamond bur (KG Sorensen, Cotia, Brazil). Localization and exploration of the root canal system was carried out with the aid of a straight explorer (Golgran, São Caetano do Sul, Brazil) for wide canals and manual endodontic instruments (#8, #10, and #15) for more atresic canals (VDW, Munich, Germany). Cervical preflaring was performed with flexmaster intro™ rotary files (VDW, Munich, Germany) driven by a X-Smart Plus endodontic engine (Dentsply Maillefer; Ballaigues, Switzerland; speed 250 rpm, torque 3.0 Ncm). The working length was then determined with the aid of a GnatusEndus™ apex locator (Fabril de Portáteis, Barretos, Brazil), and apical patency was determined in all canals. All root canals were instrumented 0.5 mm short of the apical foramen (Wu et al. 2000). Glide paths were established with R-Pilot reciprocating files (VDW, Munich, Germany) after using C-Pilot #8, #10, and #15 hand files. The canals were then instrumented with WaveOne Gold system files (Dentsply Maillefer; Ballaigues, Switzerland), in WaveOne Gold programming mode, selected according to the volume of the anatomical diameter of each canal. Instrumentation was performed with a pecking motion in the apical direction until the working length was reached and with brush-stroke movements when exiting the canal. Each instrument was used to prepare 3 teeth (BUENO *et al*., 2017).

Irrigation was performed at each file change with 2.5% sodium hypochlorite (NaOCl) solution (Asfer, São Caetano do Sul, Brazil) in a 10-mL hypodermic syringe (BD, New Jersey, USA) with Endo-Eze™ irrigator tips (Ultradent, Indaiatuba, Brazil), to a depth of 2 mm short of the working length. A total volume of 30 mL of irrigant solution was used for the preparation of each canal. After preparation, mechanical agitation of the irrigating solutions was performed with an Easy Clean™ instrument *(Easy, Belo Horizonte, Brazil), to enhance cleaning and increase dentin permeability. The canals were filled with irrigant solution and* three 20-second agitation cycles were performed in each canal, with fresh solution added every cycle (KATO *et al*., 2016). The instrument was driven by a X-Smart Plus™ engine (Dentsply Maillefer; Ballaigues, Switzerland) in reciprocating motion. Irrigation was performed initially with 17% EDTA (Formula e Ação, São Paulo, Brazil), and then with 2.5% NaOCl as described (Asfer, São Caetano do Sul, Brazil). The canals were dried with the aid of capillary suction tips (Ultradent, Indaiatuba, Brazil) and WaveOne absorbent paper points (Dentsply Maillefer; Ballaigues, Switzerland). The canals were filled using the single-cone technique and vertical compaction, with AH Plus endodontic cement (Dentsply Maillefer; Ballaigues, Switzerland) and WaveOne Gold gutta-percha cones (Dentsply Maillefer; Ballaigues, Switzerland), according to the diameter of the master file. The cement was prepared in accordance with the manufacturer's instructions. The cone was cut with a heated Paiva plugger (Paiva, Rio de Janeiro, Brazil), and the cavity was cleaned with a sterile cotton ball soaked in 70% alcohol. Coronal sealing was achieved with 1 to 2 mm of Coltosol™ temporary sealer (Coltene, Rio de Janeiro, Brazil) plus Maxxion R™ restorative glass ionomer cement (FGM, São Paulo, Brazil). After endodontic treatment, patients were randomly divided (www.random.org) into three groups (n=30): in the control group (CG), the operator performed sham submucosal injection with an empty 1-mL ultrafine syringe and needle (BD, New Jersey, USA), merely touching the gingival mucosa without penetration; in the dexamethasone group (DG) and betamethasone group (BG), submucosal infiltration of 0.7 mL (4 mg/mL) dexamethasone or betamethasone, respectively, was performed. The administered volume was selected according to

previous work by Yavari *et al*. (2019). The operator was not aware of which medication was being administered, as he received the syringes prefilled and ready for infiltration. Patients were instructed to contact the investigator at any time if they had any questions. In case of severe pain, patients were instructed to take paracetamol 750 mg every 6 hours (Figure 1).

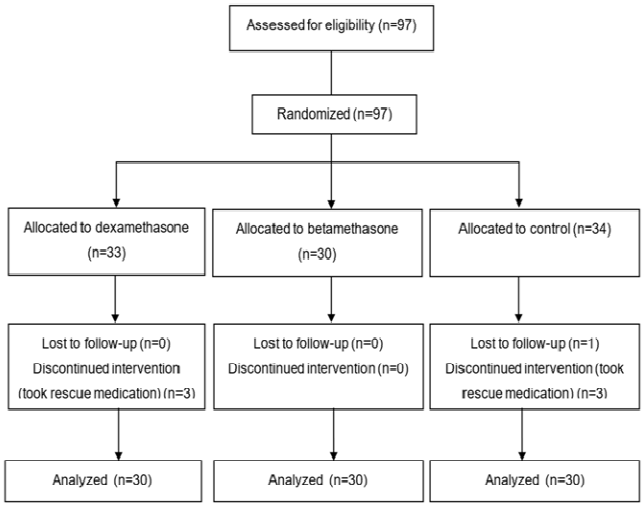

Figure 1. Flow diagram of patient progression through the clinical trial

Postoperative pain assessment and statistical analysis: After completion of endodontic treatment, the patients were asked to self-assess their perceived pain on a visual analogue scale (VAS) from 0 to 10. Pain was recorded at 6 hours, 12 hours, 24 hours, 48 hours, and 72 hours postoperatively. Pain perception was classified as none, mild (1-2), moderate (3-7), or severe (8-10). Patients were instructed to return their completed scales at the end of the 72-hour period or send them via WhatsApp, and to contact the practitioner if further pain relief was needed. The study sample was characterized in terms of sex, age, and endodontically treated mandibular molar using absolute (n) and relative (%) frequencies. Analysis of variance (ANOVA) was performed to test for a difference in age between participants in each group. The chi-square and Spearman tests were used to evaluate potential associations of sex and age with the type of local submucosal infiltration (dexamethasone, betamethasone, or none). The Mann–Whitney test was used to verify whether, at different time points, postoperative pain in the dexamethasone, betamethasone, and control groups was affected by sex. Comparisons across groups regarding postoperative pain, regardless of sex and age, were performed using the Kruskal–Wallis test. The Friedman test was used to assess postoperative pain at different time points, also disregarding sex and age. Multiple comparisons were conducted by means of Dunn's tests. All calculations were performed in SPSS 23 (SPSS Inc., Chicago, IL, USA) and BioEstat 5.0 (FundaçãoMamirauá, Belém, PA, Brazil). The level of significance was set at 5%.

RESULTS

Of the 90 trial participants, 31 (34.3%) were male and 59 (65.6%) female. In the control, dexamethasone, and betamethasone groups, 40.0%, 36.7%, and 26.7% of the participants were male, respectively, while 60.0%, 73.3%, and 63.3% were female, respectively (Table 1). Age ranged from 18 to 50 years (mean, 33.6 years). Participants in the dexamethasone, betamethasone, and control groups had a mean age of 31.8 years (standard deviation: 8.7 years), 33.8 years (standard deviation: 9.4 years), and 35.1 years (standard deviation: 8.6 years), respectively. ANOVA showed no statistically significant difference in age across the three groups (p=0.370). Figure 2 shows the proportion of mandibular molars (#36, #37, #46, and #47) that were treated endodontically and subsequently received local submucosal infiltration of dexamethasone, betamethasone, or sham injection. Chi-square tests indicated that there were no statistically significant differences in the proportion of men and women and in the distribution of participants across the three groups (Table 1) when considering the median age.

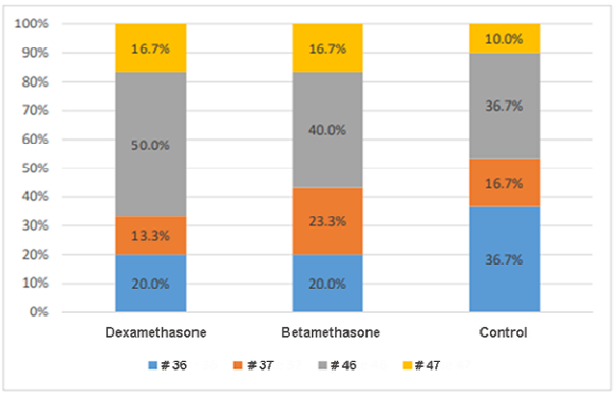

Figure 2. Bar chart of the proportion (%) of endodontically treated mandibular molars that did or did not receive local submucosal infiltration of corticosteroids

As shown by the Mann–Whitney test, there no difference in pain scores reported by male and female participants in any of the groups (dexamethasone, betamethasone, or control) at any of the time points of evaluation (Table 2). Spearman tests showed a weak correlation between age and pain in the dexamethasone group only at 72 hours, which indicates that increasing age was associated with decreasing pain perception. At other time points, no statistically significant correlation was identified between age and postoperative pain in the dexamethasone group (Table 3). On the other hand, in the betamethasone group, only at the 24- and 72-hour time points there was no statistically significant correlation between age and pain. At the other time points, there was a moderate (baseline, 6 hours, and 48 hours) or weak (12 hours) correlation, and, again, increasing age was associated with decreasing pain (Table 3). In the control group, at all time points, there was a statistically significant correlation between age and pain, which was moderate (baseline up to 24 hours) or weak (48 and 72 hours), again suggesting that, with advancing age, there was a reduction of pain perception (Table 3). Comparison of the three groups at each time point (Table 2), regardless of gender and age, revealed that, at baseline, the control group had significantly lower pain scores than the group randomized to receive betamethasone, while the pain scores initially reported by participants randomized to receive dexamethasone did not differ from those of any of the other groups. At 6 and 12 hours, participants in the dexamethasone and betamethasone groups endorsed significantly less pain than controls. At 24 hours, treatment with betamethasone continued to result in significantly lower pain scores than in the control group; dexamethasone, however, was associated with moderate pain scores, which did not differ significantly from either the betamethasone or the control group. However, at 48 and 72 hours, participants in the dexamethasone group reported significantly less pain than those in the control group, while those in the betamethasone group reported moderate pain scores, not significantly different from either the dexamethasone or the control group. Friedman tests showed that, regardless of group, the pain reported by the participants decreased significantly and progressively over time. In the betamethasone and control groups, pain scores at 6 hours did not differ significantly from baseline, while in the dexamethasone group, there was a statistically significant reduction in pain as early as the 6-hour time point (Table 2). Specifically in the dexamethasone group, pain scores at 6 and 12 hours were significantly higher than those reported at 48 and 72 hours. At 24 hours, the pain reported by participants who received dexamethasone infiltration did not differ significantly from that seen at 6, 12, 48, and 72 hours (Table 2); whereas in the betamethasone group, there was no difference between pain scores at 6 and 12 hours, with a statistically significant reduction at 24 hours, persisting at the same level at 48 hours. The results found from the baseline to the 48-hour time point in the betamethasone group were also seen in the control group.

Table 1. Distribution of absolute (n) and relative (%) frequencies by sex and median age of participants who did or did not receive local submucosal infiltration of corticosteroids after endodontic treatment

Variable	Dexamethasone	Betamethasone	Control	Total	P-value
Sex					
Female	22 (73.3%)	19 (63.3%)	18 (60.0%)	59	0.528**
Male	8 (26.7%)	11 (36.7%)	12 (40.0%)	31	
Total	30	30	30		
Age*					
Up to 33 years	18 (60.0%)	16 (53.3%)	12 (40.0%)	46	0.288**
34 or more	12 (40.0%)	14 (46.7%)	18 (60.0%)	44	
Total	30	30	30		

* Stratified by median age (33 years)
** Chi-square test

Table 2. Median and minimum/maximum pain scores at different time points of assessment, according to local submucosal infiltration with dexamethasone or betamethasone after endodontic treatment and sex

Time point	Dexamethasone		Betamethasone		Control	
	Men	Women	Men	Women	Men	Women
Baseline	9* (7.10) p = 0.527** 8^{ABc} (7.10) p = 0.020¥	8* (7.10)	8* (7.9) p = 0.897** 8^{Bd} (7.9)	8* (8.9)	8* (7.10) p = 0.927** 8^{Ad} (6.10)	8* (6.9)
6 hours	5* (4.5) p = 0.870** 5^{Ab} (4.6) p < 0.001¥	5* (4.6)	5* (4.6) p = 0.747** 5^{Acd} (4.6)	5* (4.6)	6* (5.7) p = 0.054** 6^{Bcd} (4.7)	5* (4.7)
12 hours	4* (4.5) p = 0.251** 5^{Ab} (4.6) p < 0.001¥	5* (4.6)	4* (4.5) p = 0.914** 4^{Ac} (3.5)	4* (3.5)	6* (4.7) p = 0.244** 5^{Bc} (3.7)	5* (3.7)
24 hours	3* (0.5) p = 0.336** 3^{ABab} (0.6) p < 0.001¥	3* (1.6)	2* (2.4) p = 0.683** 3^{Ab} (0.4)	3* (0.4)	4* (2.6) p = 0.553** 4^{Bb} (0.6)	4* (0.6)
48 hours	2* (0.3) p = 0.606** 2^{Aa} (0.5) p = 0.004¥	2* (0.5)	2* (0.4) p = 0.931** 2^{ABb} (0.4)	2* (0.4)	3* (0.4) p = 0.751** 3^{Bab} (0.5)	3* (0.5)
72 hours	1* (0.2) p = 0.590** 1^{Aa} (0.2) p < 0.001¥	1* (0.2)	1* (0.3) p = 0.863** 2^{ABa} (0.3)	2* (0.2)	2* (0.4) p = 0.409** 2^{Ba} (0.4)	2* (0.3)
Friedman test	p < 0.001Ψ		p < 0.001Ψ		p < 0.001Ψ	

Asterisks denote no statistically significant difference (Mann–Whitney test; p-values identified by **). Under the median and minimum and maximum scores for each sex, in each group and at each time point, the median, minimum, and maximum overall scores (i.e., disregarding sex) are given. Medians followed by different uppercase letters indicate a statistically significant difference between groups, considering each time point separately (Kruskal–Wallis test; p-values identified by ¥). Medians followed by different lowercase letters denote a statistically significant difference in pain scores between time points, considering each group separately (Friedman test; p-values identified by Ψ).

Table 3. Spearman correlation between age and pain, according to the type of local submucosal infiltration and the time point of assessment

Pain–age correlation	Dexamethasone	methasone	Control
Baseline	p = 0.563	p < 0.001	p = 0.001
	r = -0.110	r = -0.664	r = -0.584
6 hours	p = 0.105	p = 0.011	p = 0.001
	r = -0.302	r = -0.456	r = -0.554
12 hours	p = 0.529	p = 0.051	p < 0.001
	r = -0.120	r = -0.359	r = -0.599
24 hours	p = 0.709	p = 0.287	p < 0.001
	r = 0.071	r = -0.201	r = -0.618
48 hours	p = 0.486	p = 0.007	p = 0.041
	r = -0.132	r = -0.483	r = -0.376
72 hours	p = 0.047	p = 0.098	p = 0.038
	r = -0.366	r = -0.308	r = -0.380

r = correlation coefficient.

The only difference between these two groups was that, while the betamethasone group experienced significantly less pain at 72 hours than at 48 hours, in the control group, there was no significant difference in pain between the 48- and 72-hour time points (Table 2).

DISCUSSION

Dental practitioners often find their confidence shaken by some patients' belief that postoperative pain is directly related to the dentist's skills as a professional.

In this context, it is worth noting that several etiological factors are implicated in the process of pain, i.e., its cause cannot be defined with absolute precision; however, several lesions and, indeed, procedural errors may contribute to pain after endodontic treatment (SIQUEIRA *et al*., 2005). Pain compromises quality of life and psychological status (YAVARI *et al*., 2019). Therefore, this study evaluated local submucosal infiltration of 0.7 mL (4 g/mL) dexamethasone or betamethasone in the apical region of mandibular molars as an adjunct for management of postoperative pain in patients with known symptomatic irreversible pulpitis. Wayman *et al*. (1994) infiltrated dexamethasone into the buccal region of the mandibular teeth of

laboratory rats and found that the steroid was rapidly absorbed from the injection site and distributed to the entire extension of the ipsilateral mandible, including the contralateral muscle and bone, which suggests systemic distribution and particular affinity of bone for dexamethasone uptake; these characteristics may be beneficial in relieving the pain of acute endodontic trauma. Inflammation is induced by several chemical mediators and is initiated by a tissue injury process. This injury leads to the conversion of cell membrane phospholipids into arachidonic acid, catalyzed by the phospholipase A2 enzyme, which is inhibited by corticosteroids. Arachidonic acid can then enter two pathways, the lipoxygenase pathway or the cyclooxygenase (COX1, COX2) pathway, which is inhibited by non-steroidal anti-inflammatory drugs; this prevents the formation of prostaglandin and prostacyclin, which are the mediators of hyperalgesic pain (AGGARWAL *et al*., 2011; GOMES, 2002). Shahi *et al*. (2013) reported that premedication with non-steroidal anti-inflammatory drugs inhibits the COX2 pathway, blocking the formation of prostaglandin, which may explain the greater effectiveness of inferior alveolar nerve blockade in patients with irreversible pulpitis who were premedicated with 0.5 mg dexamethasone capsules. WaveOne Gold system files (Dentsply Maillefer; Ballaigues, Switzerland) were used for instrumentation of the root canal system in the present study, as in previous work by Bueno et al. (2017). Files were used three times, on three posterior teeth: the first use when brand new, removed from the original packaging; the second use after the first round of sterilization, with the silicone ring still attached; and the third use after a second round of sterilization, with the silicone ring removed. No instrument fractures occurred in the present study, which corroborates the work of BUENO *et al*. (2020). The aim of endodontic treatment is for the patient to be free of painful symptoms during and after the endodontic procedure. Bidar *et al*. (2017) evaluated the preoperative use of placebo versus two medications (ibuprofen 400 mg and dexamethasone 4 mg orally) to potentiate the anesthetic effect of inferior alveolar nerve block during treatment in patients with irreversible symptomatic pulpitis. Pain improved 38.5% with placebo, 73.1% with ibuprofen, and 80.8% with dexamethasone. This study provided evidence to further the search for patient comfort not only postoperatively, but also during endodontic treatment. Irrigation is a crucial step of any endodontic procedure (TAMBER *et al*., 2013). However, one of the factors that can lead to postoperative pain is extravasation of irrigant solution. In the present trial, irrigation was performed passively; the Endo-Eze™ irrigator needle does not catch on the walls of the canals and its lateral opening allows a depth of insertion closer to the foramen, facilitating backflow and reducing the risk of fluid extrusion. For subjective analysis of pre- and postoperative pain, a visual analogue scale (VAS) was used. This method has several advantages, including simplicity and ease of use (BODIAN *et al*., 2001).

Patients' preoperative pain scales were kept at the dental office, to prevent any influence of subjective preoperative scores on their postoperative perception of pain. Use of the VAS to assess pain is not exclusive to dental practice. Alghadir*et al*. (2018) used three types of scales to analyze pain in patients with knee osteoarthritis, and found that all had excellent reliability. However, the VAS was most reliable, with fewer errors in pain measurement. Single-visit endodontic treatment was selected for this trial because of its comfort, time, and convenience advantages for both patient and dentist (MANFREDINI *et al*., 2016). Several factors, such as preoperative diagnosis, ability to achieve infection control, and anatomy, are involved in the decision to indicate single-visit or multiple-visit endodontic treatment (VIEYRA, HENRIQUEZ *et al*., 2012). The medications evaluated in this trial promoted a significant reduction in postoperative pain as compared to placebo. Therefore, the null hypothesis was rejected. Of the 97 patients who started the trial, 7 were excluded: one did not return the completed VAS scale and 6 took rescue medication before the 72-hour time point. Of those excluded, 5 were women and 3 reported being in the menstrual period, which made them more susceptible to pain. Of the 90 remaining participants who were included in the analysis, 31 (34.3%) were male and 59 (65.6%) female.

This is consistent with previous work by Ferreira *et al*. (2020), who noted the predominance of women in endodontic treatment cohorts. At the 6-hour postoperative time point, local infiltration of dexamethasone was significantly more effective in controlling postoperative pain compared to either placebo or betamethasone. Glassman *et al*. (1989) reported similar findings, administering three 4-mg tablets of dexamethasone every 4 hours orally between appointments and obtaining the same result at 6 hours. The administration of 40 mg prednisolone tablets was also effective in controlling postoperative pain at 6, 12, and 24 hours after endodontic treatment in patients with symptomatic irreversible pulpitis (ELKHADEM *et al*., 2018). Local submucosal infiltration of dexamethasone 4 mg after endodontic treatment proved to be effective in decreasing pain in the first 12 hours compared to a sham control group. Similar results were reported by Pochapski*et al*. (2009) and Suresh *et al*. (2021), who administered dexamethasone 4 mg orally 1 hour before the endodontic procedure; Aksoy and Ege (2020), who performed local infiltration with 2 mL of dexamethasone (8 mg) before endodontic treatment; and Meharvarzfar*et al*. (2016), who performed intraligamentary infiltration of 2 mL dexamethasone (8 mg) before treatment. Conversely, Yavari et al. (2019) reported a significant increase in pain over the same period of time. Within 24 hours, local infiltration of betamethasone was more effective than either dexamethasone or sham control, a result that is in agreement with Pochapski*et al*. (2009).

Meanwhile, Moskow*et al*. (1984) reported different results, with dexamethasone providing far superior pain management than in the control group; however, their methodology also differed, consisting of intracanal infiltration of 4 mg dexamethasone after apical foramen enlargement, thus ensuring delivery of the medication to the periapical tissues. Yavari *et al*. (2019) compared betamethasone and dexamethasone and found similar results in relation to the control group, as the pain reported by the patients was more severe when comparing the other groups at all time points. However, their results diverged from the present study at the 24-hour time point, when betamethasone was superior to both the control group and to dexamethasone, and at 48 and 72 hours, with dexamethasone having a significantly greater effect than control, but not a significantly different one compared to betamethasone. One aspect of the present trial that is worth noting was the exclusion of three patients who were in the menstrual period and reported having taken rescue medication because they experienced severe postoperative pain, with or without infiltration of the tested medications. Alves (2017) showed that women are more sensitive to pain during the menstrual period due to hormonal changes. Her study, carried out with 39 women between the ages of 19 and 47, measured hormone levels in saliva specimens and found that, the higher the estrogen level, the lower the pain threshold and the more sensitive women were to pain. Two pain trials were performed, in the forearm and in the maxillary nerve; both found decreased sensitivity in the luteal period and heightened sensitivity in the menstrual period.

This may explain the aforementioned observations made in the present study. Garcia *et al*. (2018) evaluated postoperative pain after endodontic retreatment and also found that women were more susceptible to pain than men. Analgesia is necessary for pain management before, during, and after endodontic treatment. As a single submucosal injection administered in the apical region of the treated tooth, corticosteroids can be an option to reduce reliance on oral medications, preventing gastric discomfort and other adverse effects common with courses of analgesia that extend for days. This is advantageous both for patients, who experience greater comfort, and for dentists, who experience a feeling of accomplishment, having fulfilled their duty of care by relieving postoperative pain. At 6 and 12 hours postoperatively, apical submucosal infiltration of dexamethasone and betamethasone had similar effects on pain reduction, while at 24 hours, betamethasone was more effective. At 48 and 72 hours, dexamethasone and betamethasone were both associated with significantly lower pain scores than in the control group, with no significant difference between the two steroids. Submucosal infiltration of dexamethasone or betamethasone into the

apical region reduced postoperative pain in patients with symptomatic irreversible pulpitis after single-visit endodontic treatment.

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