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The Outcome of Preoperative Administration of Single-Dose Ketorolac, Ibuprofen 400mg and Placebo on Postoperative Pain in Teeth with Irreversible Pulpitis and Apical Periodontitis

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Research Article

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Abstract

Aim: To compare the outcome of preoperative administration of single-dose ketorolac, ibuprofen 400mg and placebo on postoperative pain in teeth with irreversible pulpitis and apical periodontitis.

Methodology: A total of 54 patients (29 women and 25 men), 18 to 60 years of age with 54 eligible teeth consented to participate in the study, were divided into three groups (n = 18) according to the type of preoperative drug administrated, as follows: Group A: ketorolac 10mg, Group B: Ibuprofen 400mg, and Group C: A placebo (capsule filled with sugar). The data were analyzed with chi square test, one-way ANOVA. The Kruskal-Wallis nonparametric test was applied to compare the incidence of postoperative pain. The level of significance adopted was 5% (p= 0.05).

Results: At Days 1 and 3, preoperative administration of analgesic resulted in lower pain levels than the placebo. At Days 5 and 7, however, while preoperative administration of analgesic still resulted in less pain than the placebo, there was no significant difference between the analgesic and placebo (p= 0 .05). Ketorolac and Ibuprofen 400mg showed clinically significant relief in pain for the next three days compared with the placebo. In addition, no significant differences were demonstrated between ketorolac and ibuprofen 400mg (Table 3).

Conclusion: A single dose of ketorolac was as effective or as safe as NSAID for the relief of pain after operations on postoperative pain in teeth with symptomatic apical periodontitis.

Keywords: Post-operative pain; Flare-up; Apical healing

Abbreviations: NSAIDs: Non-Steroid Anti-Inflammatory Drugs; NRS: Numerical Rating Scale; VRS: Visual Rating Scale; VAS: Visual Analogue Scale.

Introduction

Dental pain is a multifaceted process that is partially comprised of biological, biochemical, environmental, and

psychogenic multi factors. Several factors can influence clinicians' decisions to recommend analgesics in helping combat their patients' postoperative pain. It is well recognized that, in general, preoperative pain is the principal factor in determining the level of postoperative pain [1]. Prevention and control of pain in endodontic therapy is an important issue [2].

Pain is conceptualized as a complex sensation and odontogenic pain is a multidimensional experience that involves sensory responses and cognitive, emotional, conceptual, cultural and motivational aspects [1]. The occurrence of postoperative pain of mild intensity is not an occasional event even when endodontic treatment has followed suitable standards [3]. This usually involves acute pain, meaning the correct treatment can be rapidly applied. Mild pain after chemo mechanical preparation can progress in about 10–30% of the cases [4], and in most cases the patient can suffer the discomfort or can make use of common analgesics, which are usually efficient in relieving symptoms. Development of severe pain, accompanied or not by swelling has been determined to be an unusual happening. However, these cases usually constitute a real emergency and frequently demand unscheduled visit for treatment [5]. Managing of postoperative pain has been the matter of many research studies, involving preoperative explanations and instructions [6], long-acting anesthesia [7], the glide path [8], occlusal reduction [9], treatment using salicylic acid [10], non-steroid anti-inflammatory drugs (NSAIDs) [11], combination of ibuprofen and acetaminophen [12], narcotic analgesics [13], a combination of narcotic analgesics with aspirin [14] or acetaminophen [15], and steroidal anti-inflammatory drugs [16].

Pain perception is a highly idiosyncratic and variable occurrence moderated by multiple physical and psychological aspects, and pain reporting is influenced by factors other than the experimental process [17]. The extrusion of microbes or debris during endodontic therapy ends in inflammatory reaction and inflammation [18]. A latest systematic evaluation revealed that among 3% and 58% of patients were reported to have experienced endodontic postoperative pain [6].

Stimulation of nociceptive nerve fibers may also be related to concentrations of inflammatory mediators like histamine [19]. Also, histamine, is capable of sensitizing and activating nociceptive nerve fibers [20]. Managing of pain is a serious part of medicine and dentistry, as pain is a main postoperative symptom after numerous dental procedures. There are various analgesics and procedures; patients want the best for control their pain, and clinicians need to know them. Knowing how well an analgesic and procedure works and its associated adverse effects is essential to clinical decision-making [2]. The occurrence and severity of postoperative pain are related with specific dental proedures; the highest is with root canal therapy [21]. Post-endodontic pain, especially after primary endodontic therapy, should ideally be eliminated by the treatment; however, analgesics are frequently required to reduce pain [2]. There is a solid association among pulp status and postoperative pain, influencing the capability of pain, which may undermine the patient's confidence in the procedure and the clinician [3]. Ketorolac is an excellent acting analgesic used widely in surgery and medicine [22].

In dentistry, there have been numerous studies that used a single dose of ketorolac associated with tramadol for control of pain mainly in operations on the third molars. However, its analgesic efficacy is controversial, with reports that its effect is similar [23] or less good [24] that of non-steroidal anti- inflammatory drugs (NSAID). According to these findings a single dose of tramadol has some relatively usual unfavorable effects [25]. The purpose of this study was to compare the outcome of preoperative administration of single-dose ketorolac, ibuprofen 400mg and placebo on postoperative pain in teeth with irreversible pulpitis and apical periodontitis.

Materials and Methods

The institutional review board of the Facultad de Odontología Tijuana México approved the study protocol and all the participants were treated in accordance with the Helsinki Declaration (www.cirp.org/library/ethics/helsinki). The main inclusion criteria were: a) A diagnosis of pulpitis confirmed by positive response to hot and cold tests and b) Clinical and radiographic evidence of symptomatic apical periodontitis. It was determined based on the clinical symptoms severe preoperative pain (VAS > 60) and severe percussion pain (VAS > 60). Confirmed by positive response to hot and cold tests. Thermal pulp testing was performed by the author, and radiographic interpretation was verified by one certified oral surgeon.

Patient Selection

Fifty-four of sixty-five patients (29 women and 25 men), 18 to 60 years of age with 54 eligible teeth consented to participate in the study. The patients were randomly divided into three groups using a web program. The patient number and group number were recorded.

Informed consent was obtained from each patient and the possible discomforts and risks were fully explained.

A total of 54 patients were divided into three groups (n = 18) according to the type of preoperative drug administrated, as follows: Group A: ketorolac 10mg (Siegfried Rhein S.A. de C.V, Mexico, DF), Group B: Ibuprofen 400 mg (Pfizer, SA de CV, Mexico), and Group C: A placebo (capsule filled with sugar). A registered pharmacist compounded identical-appearing capsules of the ketorolac, Ibuprofen and the placebo (opaque yellow size ''0'' capsules). All medications were placed in identical bottles so that they were indistinguishable to the investigator.

The administration of drugs and root canal treatment were performed by two different researchers. One assistant knew the allocation and the drug type in the capsules, but the operator and the patient did not know which drug type was administered.

Patient selection was based on the following criteria: 1) The aims and requirements of the study were freely accepted; 2) Treatment was limited to patients in good health; 3) Patients with symptomatic or asymptomatic teeth with vital pulps and apical periodontitis; 4) A positive response to hot and cold pulp sensitivity tests; 5) Presence of sufficient coronal tooth structure for rubber dam isolation; 6) No prior endodontic treatment on the involved tooth and 7) No analgesics or antibiotics were used five days before the clinical procedures began.

Exclusion criteria included the following: 1) Patients who did not meet inclusion requirements; 2) Patients who did not provide authorization for participation; 3) Patients who were younger than 16 years old; 4) Patients who were pregnant; 5) Patients who were diabetic; 6) Patients with a positive history of antibiotic use within the past month; 7) Patients whose tooth had been previously accessed or endodontically treated; 8) Teeth with root resorption, and 9) Immature/open apex, or a root canal in which patency of the apical foramen could not be established were all excluded from the study. Teeth with periodontal pockets deeper than 4 mm, or the presence of a periapical radiolucency more than 2 cm diameter also were excluded of the study.

Also excluded were patients whose affected tooth and related work had any of the following issues: curved canals, problems in determining working length, broken files, over-instrumentation, and over or incomplete filling. Once eligibility was confirmed, the study was explained to the patient by the authors, and the patient was invited to participate. After explaining the clinical procedures and risks and clarifying all questions raised, each patient signed a written informed consent form and was randomly assigned to either the three groups by using a block of random numbers generated by one of the investigators.

A medical history was obtained and a clinical examination performed. All teeth were 11 asymptomatic and 43 symptomatic with a diagnosis of pulpitis determined by hot and cold sensitivity tests and radiographically all teeth showed a small and irregular radiolucency at the tooth apex (Schick Technologies, Long Island City, NY, USA). The diagnostic findings were checked by comparing the tooth's response against that of an adjacent tooth with a vital pulp. Periodontal probing revealed no increased probing depth (> 3 mm) around any of the teeth. The author performed all the clinical procedures.

Treatment Protocol

All treatment sessions were approximately 45 minutes in length to allow for acceptable time for completion of treatment in one visit. The author performed all the clinical procedures. The standard procedure for the three groups included local anesthesia with 2% lidocaine with 1:100,000 epinephrine (Septodont Saint-Maur des Fossés, France) and rubber dam isolation the tooth was disinfected with 2.5% NaOCl (Ultra bleach, Bentonville, AR, USA).

Infected dentine was completely removed and endodontic access cavities prepared with sterile high-speed carbide burs # 331 (SS White. Lakewood, NJ, USA). After gaining access, the canals were explored with #06, #08, and #10 K-type hand files (Flex-R files, Moyco/Union Broach, York PA, USA) according to the initial diameter of the foramen, its degree of flattening, and its canal curvature using a watch-winding motion. Working Length (WL) was established by introducing a #10 K-file up to the apical foramen as determined by a Root ZX (J Morita, Irvine, CA, USA). The WL was confirmed radiographically (Schick Technologies, Long Island City, NY, USA).

The root canals were negotiated and enlarged with hand instruments (Flex-R files, Moyco/Union Broach, York PA, USA) until reaching an ISO size #20 at WL. The coronal portions of the root canals were flared with sizes 2-3 Gates-Glidden burs (Dentsply Maillefer). Irrigation with 2mL 2.5% sodium hypochlorite (NaOCl) was performed using a 24-G needle (Max-I-Probe; Dentsply Tulsa Dental, York, PA) during access and a 31-G NaviTip

needle (Ultradent Products Inc., South Jordan, UT) when reaching the WL after each file insertion. Reciprocating files (VDW, Munich Germany) were used to complete root canal preparation. 17% EDTA (Roth International Ltd, Chicago, IL, USA) served as a lubricant.

All Reciprocating files were driven by an electric micro motor with limited torque (VDW Silver Reciproc Motor, VDW). R25 files (25.08) were used in narrow and curved canals, and R40 files (40.06) were used in large canals. Three in-and-out (pecking) motions were applied with stroke lengths not exceeding 3 mm in the cervical, middle, and apical thirds until attaining the established WL. All the files were used in only 1 tooth (single use) and then discarded. Patency of the apical foramen was maintained during all the techniques by introducing a #10 K-type file at WL. The preparations for all the groups were finished using a #45 file for narrow or curved canals and a #60 file for wide canals.

Each tooth received a final irrigation with cold (6oC) 17% EDTA gently delivered to the working length using a cold (6oC) sterile metallic micro cannula attached to the Endovac negative pressure irrigation system (Kerr Endo) for three minutes to eliminate the smear layer and reduce post-endodontic pain. Caution was taken to ensure that the micro cannula would suction correctly by detecting the system's transparent evacuation tube. In case there was any obstruction, the micro cannula was instantly substituted.

The root canals were dried with sterile paper points and obturated at the same appointment using lateral condensation of gutta-percha and Sealapex sealer (SybronEndo). Access cavities of anterior teeth were etched and restored with Fuji IX (GC Corp, Tokyo, Japan). For posterior teeth, a buildup restoration was placed using the same etching technique and Fuji IX.

After concluding the endodontic treatment procedure, all patients were given postoperative advices to take analgesics (acetaminophen 325 mg) in the event of pain at a dosage of 1 tablet every 6 hours. The level of discomfort was valued as follows: no pain; mild pain, which was recognizable but not discomforting; moderate pain, which was discomforting but bearable (analgesics, if used, were effective in relieving pain); flare-up, which was difficult to bear (analgesics, if used, were ineffective in relieving pain). Cases with severe postoperative pain and/or the occurrence of swelling were categorized as flare-ups and treated accordingly. After completion of RCT, patients were instructed to return to their referring dentist for definitive restoration as soon as possible.

Patients were contacted by telephone by the clinical assistant after 24 hours, 48 hours, 72 hours, and 7 days and asked to provide the following information: their perceived pain score and whether they had taken the analgesic medication prescribed and, if so, the quantity of tablets and the number of days needed to control the pain. All the patients were instructed to contact the clinic or the dentist in charge of their treatment if the analgesic medication failed to provide pain release or in the event of any other type of emergency. The data were analyzed with chi square test, one-way ANOVA.

The Kruskal-Wallis nonparametric test was applied to compare the incidence of postoperative pain. The level of significance adopted was 5% (p= 0.05).

The final scale was as follows:
None: 0-6.0, Faint: >6.0-17.0, Weak: > 17.0-27.0, Mild: >27.0-42.3, Moderate: >42.3-60.3, Strong: >60.3-74.7, Intense: >74.7-90.6 and Maximum: > 90.6 - 100

Results

There were no statistically significant differences among the groups in terms of demographic data (Table 1) or pulp and periapical status (Table 2) (P > .05). Ketorolac and ibuprofen 400mg showed clinically significant relief in pain for the next three days compared with the placebo group. In addition, no significant differences were demonstrated between ketorolac and ibuprofen 400mg (Table 3). Similarly, there were no significant differences among the groups in terms of preoperative pain levels and percussion pain levels, but there was a difference in post-operative pain in placebo group. Results from this study indicated that pre-operative pain with the diagnoses of irreversible pulpitis with apical periodontitis were the most common for respondents to choose analgesics to relieve their patients' pain.

A total of 7 patients needed analgesics postoperatively: five of these were in the placebo group, one in the ketorolac group, and one in the ibuprofen group. Table 3 shows lower pain levels in all groups. In the present study, two patients experienced a flare-up. Two cases of flare-up were from the placebo group. Both required an intra-appointment visit. The flare-up from the patient in the placebo group showed no signs of swelling, but caused extreme pain. Upon opening the tooth, inflammatory drainage was established.

Ibuprofen	(n)	Ketorolac	Ibuprofen	Placebo
Age		30.69 ±7.35	28.12 ±5.99	31.87 ±7.35
Gender				
Male	25	8	9	8
Female	29	10	9	10
Tooth number				
Tooth 3	13	4	5	4
Tooth 14	10	3	4	3
Tooth 18	7	2	3	2
Tooth 29	8	3	2	3
Tooth 13	7	2	2	3
Tooth 7	9	4	2	3
Total:	54	18	18	18

p= 0.05
Table 1: Demographic data.

	(n)	Ketorolac	Ibuprofen	Placebo
Pulp Status				
Vital	54	18	18	18
Periapical Status				
Score 1	44	16	14	14
Score 2	10	2	4	4
Presence of:				
Preoperative palpation		0	0	1
Preoperative swelling		0	0	0
Preoperative Sinus Tract		0	0	0
Postoperative palpation		0	0	1
Postoperative swelling		0	0	0
Postoperative sinus tract		0	0	0

Table 2: Pulp and periapical status of teeth and postoperative pain.

	Ketorolac	Ibuprofen	Placebo
Preoperative percussion	13 (I)	15 (I)	14 (I)
Preoperative pain	16 (I)	15 (I)	12 (I)
Postoperative one-day pain	1(M)	3 (M)	7 (I)
Postoperative two-day pain	0(W)	1 (W)	4 (Mi)
Postoperative three-day pain	0(N)	0 (F)	1 (F)

p= 0.05
Scale: I: Intense, M: moderate, Mi: Mild, W: Weak, F: Faint and N: None
Table 3: Pain levels according to the groups.

Discussion

The purpose of this study was to evaluate the outcome of preoperative administration of single-dose ketorolac, ibuprofen 400mg and placebo on postoperative pain in teeth with irreversible pulpitis and apical periodontitis. Practice background was significant for analgesic preferences relating to severe pain with an endodontic diagnosis of irreversible pulpitis with acute periradicular periodontitis [26]. Our findings agree with Nusstein [27] relating to prescribe analgesic in teeth with irreversible pulpitis and symptomatic apical periodontitis.

Many local and systemic factors such as age, gender, general health, group of teeth, pulp and periapical status, and occlusal contacts, amongst others, may interact and

modulate the occurrence of pain of endodontic origin [28]. Know those factors as predictors may contribute to define preventive oral health strategies to manage this undesirable condition, minimizing pain incidence and/or intensity and reducing patient suffering at the individual and population levels. Additionally, clinicians may use this information to advise patients about pain outcomes related to RCT [29]. The results of the present study indicated that some clinicians were more likely to choose medication before and after endodontic treatment to manage this painful clinical scenario, whereas other educators and residents were much more likely to prescribe combination drugs in addition to instrumentation [30]. Prescribe a drug before start root canal in patients with irreversible pulpitis will reduce postoperative pain or sensitivity.

The results from this present study are consistent with the findings of Law [29] that to avoid severe postoperative pain in endodontic therapy, preemptive analgesia strategies before initiation of treatment are necessary and with Krasner & Jackson [31] who noted from their study that although pulpectomy eliminates endodontic pain, postoperative pain and discomfort. Two previous investigations have reported that the prophylactic use of analgesics at the end of the treatment visit had a positive influence on postoperative pain felt by the patients [10,32]. Therefore, in the present study, all patients were instructed to take the first dose of the drug fifteen minutes before start the treatment visit. Considering the multifactorial nature of preoperative pain and postoperative pain, prevention and treatment strategies should depend on the identification and management of key predisposing factors [3,33].

Pain intensity is therefore influenced by various factors, including environmental, previous experience, mental health and attitude making it a challenge to measure. Numerous scales have been used for pain intensity evaluation. Of these, the numerical rating scale (NRS), which is a scale with end points of the extremes of no pain and as bad as it could be or the worst pain. There is also the visual rating scale (VRS), which is made up of a list of descriptors that represent the level of pain intensity. It is subjective, and its association with disease may be indirect; however, it is a personal qualitative judgment of patients' perception of pain strength [8]. In this study were used the visual analogue scale (VAS) that is a 10-cm line arrangement that relates to verbal parameters. Although its value as a measurement is well-documented and another form to evaluate the response of the patients' pain to the analgesics. To show the real amount/perception of postoperative pain felt by patients, it appears to be reasonable for researchers to provide two evaluation forms: one to include the conventional VAS and another form to evaluate the response of the patients' pain to the analgesics [34,35]. Additionally, visual analogue scales (VAS) and numeric rating scales (NRS) for assessment of pain intensity agree well, are equally sensitive in assessing acute pain, and are superior to a four-point verbal categorical rating scale [36]. Hence, in the present study, patients were given one such form, and the results showed that some patients reported severe pain that was unbearable and not interfered with the patient's daily activities with no significant difference between the groups A and B.

Our findings agree with Wells [37]. That reported the presenting initial moderate pain level is representative of emergency patients with symptomatic teeth, a pulpal diagnosis of necrosis, and a periapical radiolucency. Postoperative pain or sensitivity is often used to assess the quality of analgesics because of its consistency and intensity. Pre-operative examination, interpretation of symptoms and diagnosis are crucial factors in long-term success of endodontic therapy. No controversies exist regarding the fact that teeth diagnosed with irreversible pulpitis should be treated in one session, if no technical complications arise [38]. However, in cases of pulp necrosis with or without periradicular periodontitis the literature is more controversial. Although preoperative administration of analgesics has been found to be effective in reducing postoperative pain [29], there has been various studies related to the effect of the preoperative administration of antihistamines on postoperative pain.

Wells [37] found that there were decreases in postoperative pain levels with the preoperative administration use of ibuprofen, a finding in harmony with ours. The decreased pain levels in the analgesic group can be explained by the ability of analgesic to eliminate pain resulting in blocking of nociceptive sensory nerve fibers [19,20]. An interesting finding in the present study was that while the preoperative administration of ketorolac resulted in less pain than that of an ibuprofen 400mg there was no significant difference between ketorolac and ibuprofen 400mg administration. This finding suggests that the preoperative administration of ketorolac as a single dose before the treatment is beneficial in reducing postoperative pain. Pain of endodontic origin depends on the multidimensional interrelationship between host, pulp and periapical tissues, and the nature of endodontic procedures. The measurement of pain intensity is a reasonable way to evaluate treatment efficacy [39].

Conclusion

A single dose of ketorolac was as effective or as safe as NSAID for the relief of pain after root canal treatment on postoperative pain in teeth with symptomatic apical periodontitis. The incidence of post-operative pain is lower when pre-operative pain is absent. Any drug in endodontics is an aid to reduce symptoms caused by pain by itself, forces during instrumentation or reactions against the irrigants used.

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