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Research Article

Pain Management after Single-visit Root Canal Treatment Using Different Non-Steroidal Anti-Inflammatory Drugs

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Received: June 18, 2018; **Published:** July 19, 2018

Abstract

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently used as pain killers during most dental procedures. The aim of this study was to evaluate the effectiveness of Celecoxib compared to Naproxen in the management of post-endodontic pain in anterior and premolar teeth with irreversible pulpitis.

Material and methods: Sixty anterior and premolar teeth with irreversible pulpitis were included in this study. Patients were randomly allocated into three groups according to the administered medicament: naproxen group (n = 20), celecoxib group (n = 20), and placebo group (n = 20). Naproxen group received naproxen 500 mg tablets, celecoxib group received celecoxib 100 mg capsules, and placebo group received placebo (starch containing capsules). All patients were given one tablet/capsule at the following time intervals: 1 hour preoperatively, 12, 24, 36, 48, hours postoperatively. A single operator performed a single-visit endodontic treatment for all patients. Visual analogue scale (VAS) was used to record pain at 6, 12, 24, 48 hours and 1 week after obturation. Data were statistically analyzed using Kruskal-Wallis and Mann-Whitney U tests. The significance level was set at $p < 0.05$.

Results: There were no statistically significant differences in VAS pain values between the studied groups 6, 12, 48 hours, and 1 week after obturation ($p > 0.05$). At 24 hours after obturation, there were no statistically significant differences between naproxen and celecoxib groups ($p > 0.05$). However, there were statistically significant differences between placebo group and both naproxen and celecoxib groups at that time ($p < 0.05$).

Conclusions: Naproxen and celecoxib were found to be effective in reducing post-endodontic pain in anterior and premolar teeth with irreversible pulpitis. The effectiveness of naproxen was similar to celecoxib.

Keywords: *Post-Obturation Pain; Non-Steroidal Anti-Inflammatory Drugs (NSAIDs); Celecoxib; Naproxen*

Introduction

Postoperative pain continues to be a relatively common sequela of endodontic treatment, in spite of the recent technical advances in modern endodontics. It has been reported that 3 - 58% of all endodontic patients experience post-endodontic pain with varying degrees of intensity [1]. This painful situation occurs because of acute inflammation within the peri-radicular tissues secondary to microbial, physical and chemical irritation coming from the root canal. Of these irritants, microbial infection was considered as the main causative factor of post-endodontic pain. This microbial infection may happen due to apical extrusion of infected debris, leaking rubber dam, contaminated endodontic instruments, leaking temporary restoration, etc [2,3].

Because successful pain control is one of the most important aspects of endodontic practice, numerous studies have focused on determining the predictors and ways of prevention and management of post-endodontic pain. Studies that tried to identify the predictive factors of post-endodontic pain agreed that the presence of preoperative pain or mechanical allodynia was the main predictor [4]. Also, several studies demonstrated that the severity of preoperative pain predict the severity of post-endodontic pain [5-7]. However, these studies have shown conflicting results with regard to other predictive factors, due to differences in their methodologies. Some of these factors are: presence and size of a periapical lesion, gender of patient, generalized swelling [8], occlusal contacts, pulp status, teeth with previous emergency treatment, teeth with three or more canals, molars, mandibular arc [5], number of treatment visits [5,8,9], number of days in the past week kept from usual activities due to pain, pain made worse with stress [6].

When the patient demonstrates preoperatively several risk factors for post-endodontic pain, the practitioner should take preventive measures to minimize the pain [6]. The suggested pain prevention and management strategies include pharmacologic and non-pharmacologic methods. The non-pharmacologic methods that proved to be effective in reducing post-endodontic pain include occlusal reduction [10], intracanal cryotherapy [11], simultaneous working length control during root canal preparation [12] etc. The pharmacologic methods include administering long-acting anesthetics [13] and medication with nonsteroidal anti-inflammatory drugs (NSAIDs) [14-19], corticosteroids [18,20,21], narcotic analgesics [14,19,22], or a combination of two medications (like combining ibuprofen with paracetamol) [14,23]. Despite the effectiveness of corticosteroids and narcotic analgesics that have been reported by several researchers, NSAIDs are considered as the first choice drugs for the management of post-endodontic pain [24]. This is because of the relative safety of NSAIDs compared to corticosteroids and narcotic analgesics [4,25].

The use of NSAIDs for post-endodontic pain management is based on the fact that they reduce the inflammation within the periradicular tissues. NSAIDs block inflammatory mediator prostaglandin synthesis from arachidonic acid by inhibiting the cyclooxygenase (COX) enzymes [25-27], thus they prevent inflammation and sensitization of the peripheral nociceptors [17].

COX enzymes have two major isotypes: COX-1 and COX-2 [26,28]. COX-1 is a constitutively expressed enzyme that regulates normal cell activities in the stomach, kidneys, and platelets. COX-2 is an inducible enzyme, expressed when tissue injury and inflammation occurs [25,28]. Based upon their preference for inhibiting COX-1 or COX-2, NSAIDs can be classified into: non-selective NSAIDs, and selective COX-2 inhibitors [26,28].

The non-selective NSAIDs (like ibuprofen, piroxicam, and ketorolac) block both COX-1 and COX-2 enzymes. Several studies have shown that this category of NSAIDs provide significant analgesia for post-endodontic pain [14,16,17,23]. However, the use of these medications is associated with gastrointestinal side effects such as stomach ulcers [26]. Thus, to overcome this problem, selective COX-2 inhibitors (like rofecoxib, meloxicam, and etodolac) were developed with significantly less gastrointestinal side effects compared with non-selective NSAIDs [29]. Yet, this advantage was challenged by concerns regarding increased cardiovascular risk [30]. Studies have shown that this risk differs, to some degree, across agents [31]. While rofecoxib and valdecoxib were withdrawn from the market because of cardiovascular toxicity [29], other selective COX-2 inhibitors can be used for brief periods of time among patients who are at low risk for cardiovascular events [31]. The efficacy of selective COX-2 inhibitors in controlling post-endodontic pain has been the focus of only a few studies. These studies found that some of selective COX-2 inhibitors are more effective than non-selective NSAIDs (rofecoxib vs. ibuprofen) [28], some are similar to them (meloxicam vs. piroxicam, etoricoxib vs ibuprofen) [15,32], and some are less effective than them (etodolac vs. ketorolac) [19].

Naproxen is a non-selective NSAID of the propionic acid class (the same class as ibuprofen). A meta-analysis by Trelle., *et al.* found that naproxen is the safest NSAID for use in people with cardiovascular complications, due to its relatively low risk of causing such complications, followed by celecoxib as an alternative in patients with stomach ulcers [33]. Naproxen has an intermediate risk of causing stomach ulcers compared with ibuprofen (low risk) and ketorolac (high risk) [34]. Mehrvarzfar., *et al.* compared the efficacy of naproxen (500

mg), novafen (325 mg of paracetamol, 200 mg ibuprofen and 40 mg caffeine anhydrous) and the opioid analgesic tramadol (100 mg) in the management of post-endodontic pain [14]. They found that naproxen and novafen provided similar analgesic effects, whereas the effect of tramadol was inferior to them. However, no other study has evaluated the effectiveness of naproxen in the management of post-endodontic pain.

Celecoxib is a selective COX-2 inhibitor. No study has evaluated the efficacy of celecoxib in reducing post-endodontic pain. Hence, the purpose of the present study was to evaluate the efficacy of celecoxib compared to naproxen in the management of post-endodontic pain.

Material and Methods

This prospective, double-blinded, placebo-controlled, randomized clinical trial was conducted in the outpatient clinic of the Department of Endodontics and Operative Dentistry, Faculty of Dentistry, Syrian Private University. The participants were selected from patients attending the aforementioned clinic after making sure that they meet the inclusion/exclusion criteria.

Inclusion/exclusion criteria

The inclusion criteria were: (I) Patient suffering from irreversible pulpitis in anterior and premolar teeth, with normal periapical appearance on radiographs; (II) Patient elects endodontic therapy; (III) Teeth that could be endodontically treated in a single visit; (IV) Patient who can read, understand and answer questionnaires; (V) Patient who provides informed consent; (VI) Patient with an ASA-I or ASA-II medical history [17,23,35].

The exclusion criteria were: (I) History of allergy to NSAIDs or local anesthetics; (II) History of asthma, gastrointestinal disorders, esophageal reflux, decreased hepatic or renal function, uncontrolled diabetes mellitus, bleeding problems; (III) Patient currently taking anticoagulants, diuretics, or any drugs contraindicated with NSAIDs; (IV) Pregnancy or lactation; (V) Patient younger than 18 or older than 65; (VI) Patient who had taken analgesics within the last 12 hours; (VII) Patient with periapical swelling [14,17,23,28,35-37].

Preparation of NSAIDs and randomization method

Prior to initiation of the study, the second author (who was not directly involved in the clinical steps of the study) packed the medicaments in 60 identical opaque packs, labeled with an unreal brand name, each pack containing 5 capsules/tablets. 20 packs contained naproxen 500 mg tablets (Xenarsyr; Pharmasyr, Damascus, Syria), 20 packs contained celecoxib 100 mg capsules (Celex; Alpha, Aleppo, Syria), and 20 packs contained placebo (starch containing capsules). The packs were coded numerically, and the code details were not revealed to the principal investigator until completion of the study. The packs were randomly assigned to the patients. Neither the operator (principal investigator) nor the patient knew the medicament that was given to the patient. Thus, the study was kept prospective, randomized and double-blinded.

Intervention

All endodontic treatments in this study were performed by the same clinician (principal investigator) in a single-visit approach using a standardized treatment protocol. After explaining the treatment procedures to the patients, consent forms were signed, and participants were asked to randomly pick up their packs. Participants were asked to take one capsule/tablet from their packs one hour before initiating the endodontic treatment.

The treated tooth was anesthetized using one cartridge (1.8 mL) of Adrecain Dental (2% lidocaine with 1:80000 epinephrine; Avenzor, Damascus, Syria). After rubber dam placement and disinfection, an access cavity was created using a sterile diamond bur. Glide path was established using a size #10 k-file (Mani, Japan), followed by PathFile rotary files (Dentsply Maillefer, Ballaigues, Switzerland) sizes 1,2, and 3. The root canal(s) was then prepared using ProTaper Universal (Dentsply, Maillefer, Switzerland) rotary files up to size F3. Thorough irrigation of the canal(s) with NaOCl 5.25% was done using a 30-gauge NaviTip needles (Ultradent, South Jordan, UT). After that, the

canal(s) was dried and filled with gutta-percha (Dentsply, Maillefer, Switzerland) and a resin-based sealer (AH Plus; Dentsply, Konstanz, Germany), using a lateral compaction technique. After obturation, a dry cotton pellet was placed in the chamber, and the cavity was sealed with a temporary filling material (Cavit; 3M ESPE Dental AG, Seefeld/Oberbay, Germany).

Finally, participants were asked to take one tablet/capsule from their packs at 12, 24, 36, and 48 hours after obturation (4 capsules/tablets). Also, they were asked to evaluate the intensity of post-endodontic pain after 6, 12, 24, 48 hours and one week (starting from the time of canal obturation) using a visual analogue scale (VAS) that was given to every patient. The VAS that was used in this study starts from 0 (no pain) to 100 (extreme pain) [38]. The pain records were then returned to the first author.

Statistical Analysis

A statistical analysis was performed on the collected data using SPSS 13 (SPSS inc., Chicago, IL, USA). The Kolmogorov-Smirnov test for normality was used to analyze data distribution. Because the data didn't show normal distribution, nonparametric tests were used to determine the differences between groups. Kruskal-Wallis test was applied to know if there were significant differences in VAS pain values between naproxen group, celecoxib group, and placebo group. Mann-Whitney U test was applied to know if there were significant pairwise differences between studied groups. The significance level was set at $p < 0.05$.

Results

Sixty single-visit root canal treatments of 60 anterior and premolar teeth were performed. The ages of the participants ranged from 19 - 54 years. There were not any patient losses. Teeth were randomly allocated into three groups: naproxen group (n = 20), celecoxib group (n = 20), and placebo group (n = 20).

The distribution of the sample in the three groups according to patient and tooth characteristics is presented in table 1. There were no statistically significant differences in VAS pain values according to patients' characteristics (gender, age category, and smoking habit) at the confidence level of 95% ($p > 0.05$) (see table 2).

Studied variable	Category	Number of teeth				Percentage			
		Naproxen	Celecoxib	Placebo	Total	Naproxen	Celecoxib	Placebo	Total
Gender	Male	10	13	17	40	50.0	65.0	85.0	66.7
	Female	10	7	3	20	50.0	35.0	15.0	33.3
Age category	< 30 years	8	12	9	29	40.0	60.0	45.0	48.3
	> = 30 years	12	8	11	31	60.0	40.0	55.0	51.7
Smoking habit	Non-smoker	12	10	18	40	60.0	50.0	90.0	66.7
	Smoker	8	10	2	20	40.0	50.0	10.0	33.3
Tooth type	Central incisor	10	2	4	16	50.0	10.0	20.0	26.7
	Lateral incisor	2	7	3	12	10.0	35.0	15.0	20.0
	Canine	0	5	0	5	0.0	25.0	0.0	8.3
	First premolar	4	0	4	8	20.0	0.0	20.0	13.3
	Second premolar	4	6	9	19	20.0	30.0	45.0	31.7
Tooth location and side	Upper right	8	11	9	28	40.0	55.0	45.0	46.7
	Upper left	6	0	3	9	30.0	0.0	15.0	15.0
	Lower left	6	7	5	18	30.0	35.0	25.0	30.0
	Lower right	0	2	3	5	0.0	10.0	15.0	8.3

Table 1: *Sample distribution in the study groups according to patient and tooth characteristics.*

Studied variable	P-value	Significant difference?
Gender	0.663	No
Age category	0.102	No
Smoking habit	0.151	No

Table 2: *The results of Kruskal-Wallis and Mann-Whiteny U tests that were applied to know if there were significant differences in VAS pain values according to patients' characteristics.*

The intensity of post-endodontic pain in the three groups of the study at each time interval is shown in figure 1. Statistically, there were no significant differences in VAS pain values between the studied groups 6, 12, 48 hours, and 1 week after obturation ($p > 0.05$) (see table 3). At 24 hours after obturation, there were no statistically significant differences between naproxen and celecoxib groups ($p > 0.05$) (see table 4). However, there were statistically significant differences between placebo group and both naproxen and celecoxib groups at that time ($p < 0.05$).

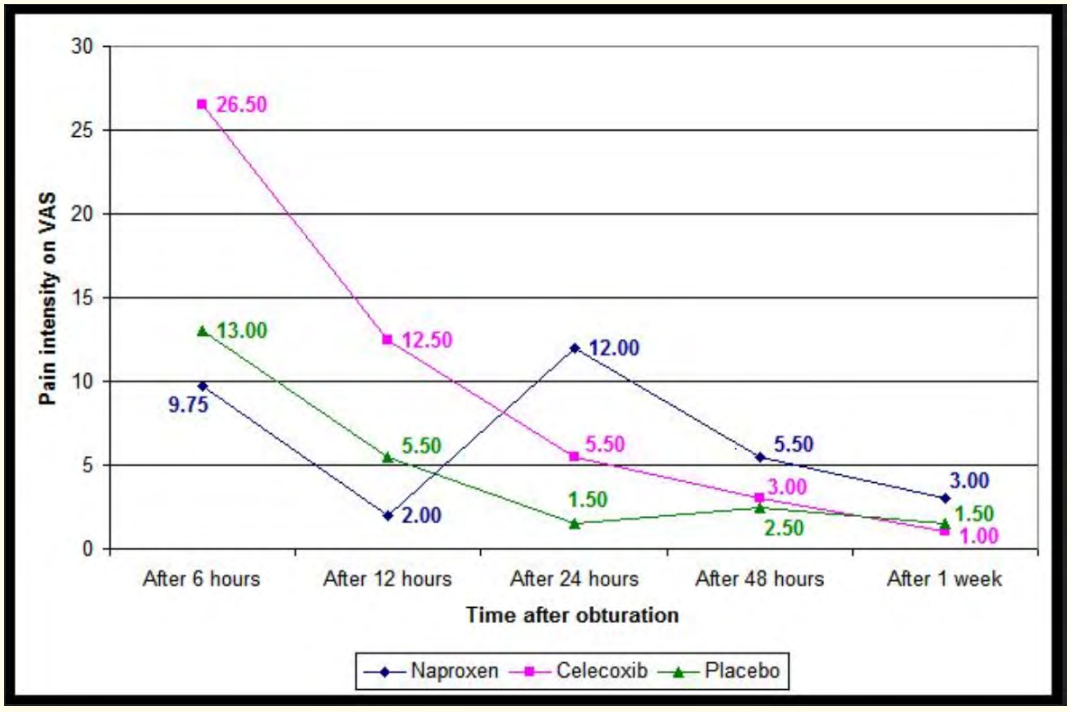

Figure 1: *Average of post-endodontic pain intensity in the three groups of the study rated on a 0-100 VAS at each time interval.*

Studied period	P-value	Significant difference?
After 6 hours	0.621	No
After 12 hours	0.237	No
After 24 hours	0.004	Yes
After 48 hours	0.083	No
After 1 week	0.344	No

Table 3: *The results of Kruskal-Wallis test that was applied to know if there were significant differences in VAS pain values between the studied groups according to the studied period.*

Treatment method 1	Treatment method 2	P-value	Significant difference?
Naproxen	Celecoxib	0.085	No
Naproxen	Placebo	0.001	Yes
Celecoxib	Placebo	0.046	Yes

Table 4: *The results of Mann-Whitney U test that was applied to know if there were significant pairwise differences in VAS pain values between the studied groups after 24 hours.*

In summary, these results have shown that naproxen and celecoxib were effective in reducing post-endodontic pain only at 24 hours after obturation. No adverse effects were reported.

Discussion

Until now, there are insufficient data to recommend the most effective NSAID, dose amount, or dose interval for post-endodontic pain relief [27]. Only one study has evaluated the efficacy of administering naproxen in reducing post-endodontic pain [14]. Moreover, no previous study has evaluated the efficacy of administering celecoxib in the management of post-endodontic pain.

The results of this study have shown that the first doses of both naproxen and celecoxib that was administered preoperatively were ineffective in reducing post-endodontic pain at 6 and 12 hours after obturation. This may indicate that a single preoperative dose does not provide sufficient analgesia postoperatively. Contrary to the present study, Mehrvarzfar., *et al*. found that a single preoperative dose of naproxen significantly reduced postoperative pain [14]. This contradiction may be attributed to an inherent problem in these types of studies which is relying on patients' answers to questionnaires.

24 hours after obturation, the analgesic effects of both naproxen and celecoxib were evident. This may be attributed to the effects of the second dose taken 12 hours after obturation. The absence of any significant differences between naproxen, celecoxib, and placebo at 48 hours and 1 week after obturation may be due to the normal decrease of post-endodontic pain at the mentioned time intervals.

Conclusion

Collectively, the results of the present study demonstrate that both naproxen and celecoxib are similarly effective in reducing post-endodontic pain. However, further studies are needed to replicate the findings of the present study.

Within the limitations of this study, the administration of both naproxen and celecoxib was found to be effective in reducing post-endodontic pain in anterior and premolar teeth with irreversible pulpitis. The effectiveness of naproxen was similar to celecoxib.

Acknowledgment

The Authors are thankful to Dr. Talaat Abu Hatab for his precious help regarding the preparation of the scientific subject of this research work.

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Volume 17 Issue 8 August 2018