Journal of Craniomaxillofacial Research

Vol. 6, No. 2 Spring 2019

Comparison of the clinical efficacy of celebrex and celecoxib for pain relief after periodontal surgeries

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ARTICLE INFO

Article Type:
Original Article

Received: 2 Oct. 2018
Revised: 8 Dec. 2018
Accepted: 15 Jan. 2019

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ABSTRACT

Background: Currently one of the most common problems in dentistry is effective pain management after dental surgeries. Celecoxib is the only specific COX-2 inhibitor used in Iran.

Aim: The aim of this study was to determine the effectiveness of Celecoxib (an Iranian product) and Celebrex in pain relief after periodontal surgery.

Materials and Methods: This randomized double-blind cross-over clinical trial was conducted on 30 patients with chronic periodontitis. The patients underwent surgical procedures on two posterior symmetric sextant with a 4-week interval. The patients were assigned to 2 groups: Group A: 200mg of Celebrex under the brand name, (bid) and group B:200 mg of Celecoxib (bid). The patients reported their pain level using VAS (visual analog scale) 1, 3, 6, 12, 24 and 48 hours after periodontal surgery. Data were analyzed with SPSS 15, using Mann-Whitney and Freidman's tests.

Results: Statistical analysis of data showed significant differences between Celecoxib and Celebrex 1, 3, 6, 12 and 24 hours after surgery ($P<0.05$). In each group there were significant differences between different postoperative intervals ($P<0.05$).

Conclusion: Considering the lower rate of side effects of COX-2 specific inhibitors, if the patients have no financial problems, Celebrex can be a proper choice for pain management after periodontal surgeries.

Keywords: Celecoxib; Cyclooxygenase-2 inhibitors; Pain management.

Introduction

Approximately 80% of patients experience acute pain after periodontal surgeries, ranging from moderate to severe and very severe in 86% of these patients [1]. Postoperative pain might occur as a result of an extensive and long surgical procedure. Other factors affecting pain might be related to infection control, trauma during surgery, the surgical technique and the tools used, the patient's personal and psychological characteristics such as stress and anxiety, and factors affecting tissue healing (cigarette smoking, uncontrolled diabetes, compromised immune system, bisphosphates, etc.) [1-3]. Pain is very common during the first 24 hours after surgery [2-4]. Different antiinflammatory medications are available, including non-steroidal anti inflammatory drugs

(NSAIDs) and steroidal anti inflammatory drugs (SAIDs), which have been shown to be effective in relieving pain and are necessary as adjunctive analgesics after surgery [4]. Celecoxib is a member of the NSAID family, which selectively inhibits the activity of COX-2 (cyclooxygenase-2) activity [2,5,6]. This medicine was approved by the American Food and Drug Administration in 1998. It is more effective than other drugs in the NSAID family, which have an approximate half-life of 4–6 hours, in relieving odontogenic pain because it has a long plasma half-life of 11 hours [7]. No reports are available on an increase in the side effects of this medication, including hematologic and alimentary tract disturbances [5,8,9]. The alimentary tract's reaction to this medication is better than that to other NSAID drugs [4]. Therefore, celecoxib might be the drug of choice to minimize the complications resulting from the effect of oxidative stress on different organs [5,8,9].

It is a relatively new medication and has been marketed in the United States and Europe for almost a decade. Considering the fact that it has been marketed by pharmaceutical companies in Iran in recent years at a price much lower than the foreign products, the present study was designed to compare the efficacy of celecoxib (an Iranian product) and Celebrex (a foreign product) in relieving pain after periodontal surgery because very limited data are available on the effects of specific inhibitors of COX-2 after periodontal treatment.

Materials and Methods

In the present double-blind clinical trial, 30 patients were selected from those referring to a private office of a periodontist in Qazvin in 2010–2011, who had moderate generalized periodontitis, based on inclusion criteria. The subjects were selected randomly and sequentially using simple random sampling technique. The exclusion criteria consisted of any allergy to the two drugs used in the study and any other NSAID drug, asthma, cardiac conditions, pregnancy, a history of angioedema, alimentary tract conditions such as peptic ulcers, renal or hepatic diseases, coagulative disorders, systemic lupus erythematous, any history of periodontal surgery during the previous 6-month period, stress and anxiety related to dental treatments environments, and use of any analgesic during the previous 6-hour period. The patients were randomly assigned to Celecoxib and Celebrex groups. A total of 300 identical gelatin capsules were prepared. The contents of 150 Celecoxib capsules (200mg of the drug for each dose) were transferred into 150 new capsules and the contents of 150 Celebrex capsules were transferred into 150 new capsules (200mg of the drug for each dose) from the Sajjad and Pfizer Pharmaceutical Companies, respectively. The capsules were prepared by a third operator and coded and delivered to the operating researcher who was a periodontist.

The patients were included in the study after completing a questionnaire, signing an informed consent form and after receiving explanations about the study procedures by the operator. The patients were treated under local anesthesia with the use of 0.2% lidocaine with 1:100,000 concentration of epinephrine (one cartridge for each patient) in each sextant using the conventional undisplaced full thickness flap procedure without osseous surgery. To homogenize the results and decrease bias and eliminate he possible differences in the surgery in different parts of the oral cavity, all the surgical procedures were carried out symmetrically in two posterior sextants.

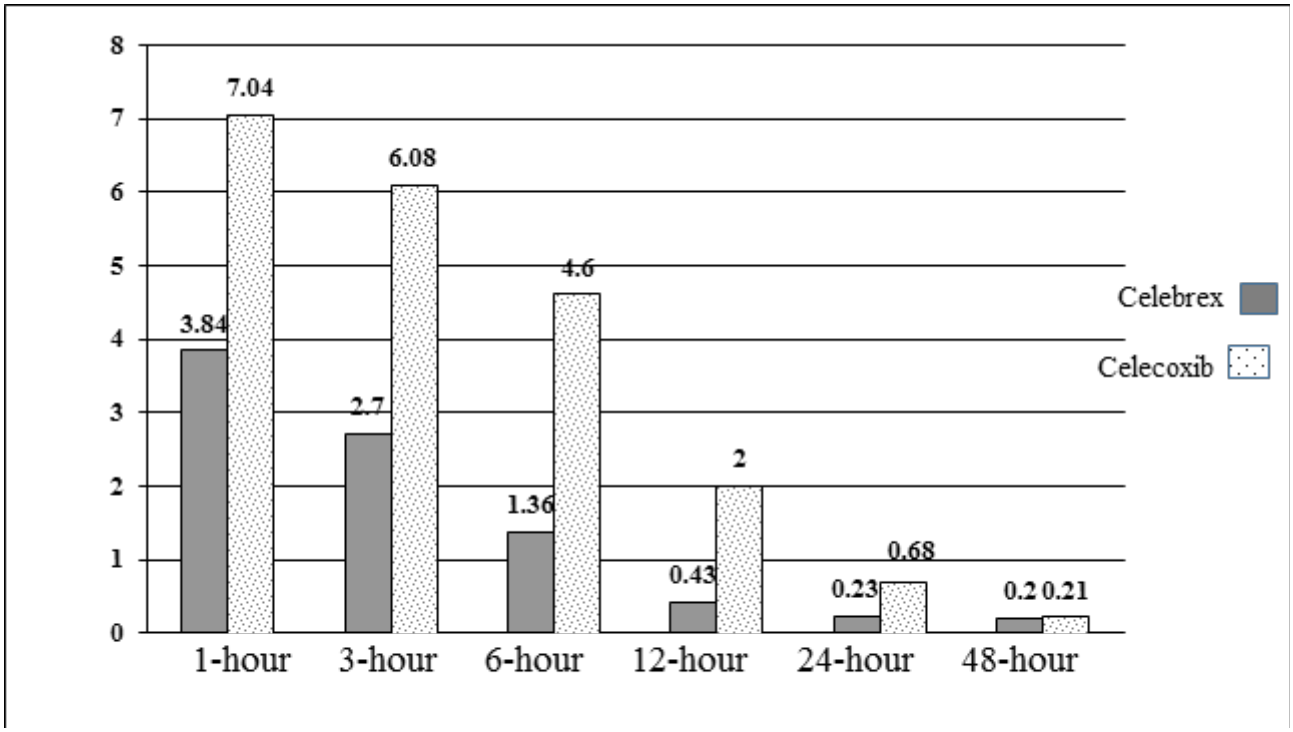
Each sextant was selected randomly for each medication regimen in order to manage postoperative pain. Four weeks of the surgery in the first sextant, the second sextant underwent surgery and the second drug regimen was prescribed. Considering the time required by the drugs to begin their effect (1 hour), the patients were asked to take the drugs 1 hour before the surgery and take the drugs every 12 hours after surgery for 48 hours. VAS was used by the patients to recorded the severity of their pain at 1-, 3-, 6-, 12-, 24 and 48-hour postoperative intervals. Data were analyzed with SPSS 15. Descriptive statistics were collected and normality of data was assessed. Since data were not distributed normally non-parametric tests were used. Mann-Whitney test was used to compare the two drug groups. Friedman's that was used to compare pain severity at different time intervals.

Results

Thirty patients (17 females and 13 males) were included in the preset study, with an age range of 22–45 years and mean age of 37.3 years. Surgeries were carried out on both posterior sextants in each patient, with each sextant randomly receiving one of the drug regimens: Celecoxib or Celebrex. This way all the subjects received the two medications. The results showed significant differences between the two groups at 1-, 3-, 6-, 12- and 24-hour intervals based on VAS ($P<0.05$). However, the difference was not significant at 48-hour interval ($P>0.05$). Graph 1 shows these changes and comparisons.

	Mean pain score at 1-hour postoperative interval	Mean pain score at 3-hour postoperative interval	Mean pain score at 6-hour postoperative interval	Mean pain score at 12-hour postoperative interval	Mean pain score at 24-hour postoperative interval	Mean pain score at 48-hour postoperative interval
Celebrex	3.8±1.7	2.7±1.5	1.5±1.3	1.3±0.4	1.1±0.2	0.9±0.2
Celecoxib	7.04±1.7	6.08±1.4	4.06±2.01	2±1.5	1.3±0.6	0.9±0.2

Table 1. Comparison of pain scores between the two groups at different time intervals.



Graph 1. Comparison of the mean pain scores after the use of drugs at different intervals after periodontal surgery.

Discussion

Postoperative pain is one of the problems and complications as an unpleasant experience for patients [3]. There is inflammation in tooth-supporting structures after surgery due to tissue trauma and the subsequent healing process. The tissue traumas damage the cell membranes [3], tearing it with the help of phospholiɵ pase enzyme and resulting in the release of membrane phospholipids, which in term results in pain through conversion of them to prostaglandins, thromboxane and other metabolites by COX-1 and COX-2 enzymes [3,8]. Previous studies have shown that specific drugs that inhibit COX-2 result in a significant decrease in the concentration of inflammatory cells, edema and vascular dilatation subsequent to inflammation. A decrease in inflammation and the concentration of inflammatory cells means that pain-inducting metabolites are released at a lower rate; therefore, during the early hours after tissue injury, they will result in a significant decrease in pain severity [10]. The majority of studies have applied the commonly used VAS, NRS-101 and VRS-4 techniques to record the severity of pain and have shown a positive and linear correlation between these three techniques [2].

Therefore, it is possible to compare the results of these three techniques to some extent. The severity of pain depends on many tractors, including the type of the dental procedure (surgery, endodontic treatment, periodontal treatment), the type of periodontal surgery (mucogingival surgery, periodontal flap, osseous surgery), the patient's emotional status, gender, duration of surgery, the extent of trauma inflicted on the tissues, duration of affliction with gingivitis, and the type of anesthetic agent used (anesthesia with a long, moderate and short effect) [1,2], making it difficult to properly compare the results of different studies in this respect. The most commonly used anesthetic agent in surgical procedures is 2% lidocaine with 1:100,000 concentration of epinephrine [11], which was also used in the present study. In the present study, Celebrex exhibited

better analgesic effects at all the postoperative intervals compared to Celecoxib and the difference in analgesic effects between the two groups were significant at all the intervals except the 40-hour interval. It might be claimed that an increase in the sample size or changing the surgical conditions might have resulted in a significant difference at this interval, too. Steffen et al (2011) compared the analgesic effects of Celecoxib, Etoricoxib and placebo. The results showed that Etoricoxib resulted in more pain relief compared to placebo at 2-, 3-, 4-, 5-, 6- and 7-hour postoperative intervals compared to placebo ($P<0.05$), with no significant difference between the Celecoxib an Etoricoxib groups. Pain and discomfort were significantly less severe in the Celecoxib group compared to the placebo group at 3-hour postoperative interval ($P=0.03$) [11].

In a study by Steffen et al (2010), the patients were divided into three groups: placebo, 8mg of dexamethasone, and 20mg of Etoricoxib in a single dose one hour before surgery. The results showed significant differences between the dexamethasone and Etoricoxib groups on one hand and the placebo group on the other hand at all the postoperative intervals [12]. In addition, in a study by Saatchi et al, one group received 2.5mg/kg of Celecoxib one hour before surgery and at 8-, 12- and 24-hour intervals. There were significant differences between this group and the three group not receiving any medication [13].

In a study by Popova et al (2008), at 8-hour postoperative interval ibuprofen exhibited higher analgesic effects compared to Aulin (a specific inhibitor of COX-2). At 1- and 2- day postoperative intervals, Aulin exhibited greater analgesic effects compared to Ibuprofen [14]. In a study by Pillati et al (2006), the results showed that in the Celecoxib group, based on VAS during first 4 hours and based on NRS-101 at 1-, 2-, 3-, 4-, 6- and 7-hour postoperative intervals and based on VRS4 at 1-, 3-, 4- and 7-hour postoperative intervals, pain was significantly less than that in the placebo groups. No significant difference were observed between the Celecoxib and dexamethasone groups [2].

Fricke et al (1999) evaluated the analgesic effects of sodium naproxen (550mg) and Refcoxib (25 and 50 mg) after oral surgeries. Refcoxib (a specific inhibitor of COX-2) exhibited greater analgesic effects compared to sodium naproxen; however, the difference was not significant [15]. In the present study, no gastrointestinal disturbances were observed in the study groups of ibuprofen, Naproxen and Celecoxib, which might be attributed to the fact that the subjects were followed for only 48 hours after taking the drugs. However, if the patients had ben followed for a longer period, it might have been possible for them to develop such problems. In a study by Azouble et al (2007), in addition to the comparison of the therapeutic effects of Etoricoxib and indomethacin on periodontitis, the gastrointestinal side effects of these two drugs were also compared after 11 days. Microscopic and histopathological studies on gastric and intestinal mucosa in rats showed that Etoricoxib resulted in less injuries compared to indomethacin. Rats receiving indomethacin exhibited weight loss from day 7; they also had a higher rate of mortality compared to the Etoricoxib group [16].

Conclusion

The results of the present study showed that Celebrex was more effective in relieving pain at 48-hour postoperative interval than Celecoxib. Celebrex is recommended for pain relief considering its analgesic, antiinflammatory and antipyretic effects, lower odds of gastrointestinal disturbances (gastric and intestinal irritation) and platelet problems. It is recommended that this dug be used in all the patients or at least in patients with gastrointestinal, coagulative or renal problems to relieve pain.

Conflict of Interest

There is no conflict of interest to declare.

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Please cite this paper as:
Naseh M, Mirkeshavarz M, Jafary Z; Comparison of the clinical efficacy of celebrex and celecoxib for pain relief after periodontal surgeries. J Craniomaxillofac Res 2019; 6(2): 55-59