

Effect of Preoperative Oral Celecoxib on Pain Reduction in Elective Patients for Leg Surgery

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Abstract

Background: Acute pain intensity after surgical operation is an important predictor of the chronic post-operation pain. Thus, controlling acute pain can play an important role during the convalescence of the patient after surgery. Preemptive analgesia indicates that if controlling the pain process starts before onset of the painful process, it will be more effective than after onset of the painful process. This study was designated with regard to the importance of controlling pain and special properties of celecoxibs.

Materials and Methods: As a double-blind clinical trial, the study was conducted on 80 people who have undergone leg surgery. Patients were divided into two 40-member groups and were treated with 200 mg celecoxib or placebo two hours before surgery. The statistical blocks were used for randomization purposes. Both the patient and the person who was responsible for checking the pain intensity and opioid intake were not informed on the prescribed medicine. After the surgery was wrapped up, the patient's pain intensity was estimated based on Visual Analog Scale (VAS) 2, 6, 12 and 24 hours after surgery. After 24 hours, the uptake amount of the consumed opioid was recorded in the information form.

Results: The difference in VAS of patients two hours after surgery was not significant statistically ($p=0.2$); while in celecoxib group it became significantly lower than placebo group in the hours 6 ($p=0.038$), 12 ($p=0.037$) and 24 ($p=0.038$) after surgery. Also pethidine intake has been significantly decreased ($p=0.042$) in celecoxib group compared to the placebo group.

Conclusion: Taking 200 mg celecoxib two hours before operation will decrease significantly pain intensity and opioid intake after surgery.

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Introduction

Acute pain management after operation has experienced many developments during the two recent decades. Surgeries usually cause tissue damage and subsequently releasing of histamine and inflammatory mediators such as bradykinin, prostaglandins and neurotransmitters [1, 2]. Acute pain intensity after surgical operation is an important predictor of the chronic post-operation pain. Thus, controlling the acute post-operation pain including preemptive analgesia can play an important role in streamlining patient's short-term or long-term convalescence after surgery [3, 4]. The uncontrolled pain after the surgery activates the sympathetic system which in turn increases morbidity and mortality rates, because it enhances oxygen intake in myocardia on the one hand and decreases oxygenation process in myocardia through coronary vasoconstriction on the other hand. Similarly, it delays movements of the digestive tract [1, 3]. After surgery, the patient's respiratory performance is declined considerably because of severe pains. Generally, opioids act through mu receptor across the central nervous system (CNS). Theoretically, their analgesic property is not limited, but practically their

analgesic properties will be limited due drug tolerance or opioid intake complications such as drowsiness, nausea, vomiting or respiratory suppression. Recent studies have underlined the effect of non-steroidal anti-inflammatory drug (NSAIDs). As a part of the multimodal strategy, they are particularly helpful, because in contrast to opioids and local anesthetic drugs they follow a different mechanism; thus, they halve the intake dose of opioid hence the potential complications are decreased and patient's recovery is facilitated as well. It also saves some hospital costs. Using NSAIDs facilitates the digestive tract recovery, decreases nausea and respiratory suppression and increases patient's satisfaction [1, 5-7]. Digestive complications, homeostasis, and negative effects on bone repairing will be improved by taking selective inhibitors of Cox-2 in comparison to ordinary NSAID but it is ineffective for the renal complications [1, 2, 8, 9]. Preventing from establishment of such changes in the central processes through analgesic treatments may bring about several short-term (e.g. decreased post-operation pain and facilitated recovery) and long-term (e.g. decreased chronic pain and improved life quality)

advantages. Here, prevention refers to Preemptive Analgesia which is very useful than alleviating after it was felt [1, 3, 4, 10, 11]. Therefore, we started this study regarding the importance of pain control and few studies on celecoxibs in Iran.

Materials and Methods

Our study was conducted based on principles of a double-blind clinical trial. Each group included a total of 40 subjects. After the study was approved and verified by the ethics committee of Medical Sciences University of Zahedan, initially 80 uniform capsules were prepared, out of which 40 capsules contained 200 mg celecoxib and 40 capsules contained placebo. Eighty patients who have undertaken leg surgery were selected. The inclusion requirements for the study were age between 20 to 50 year old, Iranian race and ASA class 1 and 2. After being justified and signing the written consent, the patients were trained on how to express and set their pain intensity using a ruler and how to measure the visual analog scale. The patients were treated with 200 mgr. celecoxib or placebo depending on their group, two hours before the selective surgery which was taken with 100 ml or a half glass of water. The randomized statistical blocks method was used for sampling. A uniform surgical method (implantation) was conducted by a single surgeon for all patients. Both the patient and the person who was responsible for checking the pain intensity and opioid intake were not informed on the prescribed medicine. The exclusion condition were sensitivity to aspirin, a history of peptic ulcer, History of myocardial infarction in a past year, lithium intake, renal disorders, history of neurological diseases, drug abuse and also body weight lower than 45 kg or more than 100 kg. If a patient who has accepted to take part in the study was failed to take capsule two hours before surgery for any reason or was transfused with more than two units of blood, he/she was excluded from the study. Also, operations which lasted more than 3 hours and leaving the hospital before completing 24 hours post-operation period for any reason were the other exclusion condition of this study. The limiting procedure was used to control confounding variables and participants were not different significantly in terms of demographic features. All patients were submitted to the general anesthesia for surgery and 1-2 mg/kg fentanyl and 1-2 mg/kg midazolam were used for premedication and 5 mg/kg thiopental sodium and 0.5 mg/kg atracurium were used for induction. The anesthesia state was maintained using 100-200 µg/kg/min propofol along with 40% oxygen and 60% nitrous oxide. After the surgery was finished, patients' pain intensity was appraised based on VAS 2, 6, 12, and 24 hours after surgery and the results were recorded in the information form of each patient. After 24 hours since operation, the consumed opioid amount to alleviate unbearable possible pains was measured and recorded in the form. Then the collected information was processed by SPSS-17 software and the results including the mean value, standard deviation were measured. Then variance analysis was

applied in order to test the difference between average values of groups.

Results

The visual analog scale for 40 patients of celecoxib group after two hours was equal to 2.45 ± 0.6 . The scale of this group after 6, 12 and 24 hours was set as 2.25 ± 0.38 , 2.3 ± 0.43 , and 2.2 ± 0.32 , respectively. While the VAS for placebo group after 2, 6, 12, and 24 hours was determined as 2.75 ± 0.78 , 2.67 ± 0.74 , 2.8 ± 0.72 and 2.57 ± 0.71 respectively (Table 1).

It is necessary to say that 33.25 ± 1.16 mg and 51.5 ± 6.6 mg pethidine was consumed 24 hours after surgery by celecoxib and placebo groups, respectively; thus pethidine intake has been decreased significantly in celecoxib group compared to the placebo group ($p=0.042$). The different VASs two hours after surgery ($p=0.2$) was not statistically significant; While VAS measured after 6 hours ($p=0.038$), 12 hours ($p=0.035$) and 24 hours ($p=0.038$) since operation in celecoxib group was significantly lower than that in placebo group.

Table 1. VAS statistical indicators during leg surgery based on the group receiving celecoxib or placebo

VAS	Celecoxib Mean±SD	Placebo Mean±SD	p-Value
2 h After surgery	2.45±0.6	2.75±0.78	0.2
6 h After surgery	2.25±0.38	2.67±0.74	0.038
12 h After surgery	2.3±0.43	2.8±0.72	0.035
24 h After surgery	2.2±0.32	2.57±0.71	0.038

Discussion

Results and evidence of our study show that taking 200 mg celecoxib only two hours before operation by the adult patients who are permitted to take celecoxib can be considered as a part of the temporal multimodal strategy which alleviates post-operation pain and decreases pethidine intake hence decreases complication of bearing pain and complications caused by taking opioids.

Qeshlaqi et al. studied 120 patients with periodontitis in Shahid Beheshti Medical Sciences University. They divided the patients into two groups and the treated a group with celecoxib and another group with ibuprofen, and finally they concluded that the celecoxib group experienced lesser pain than the other group [2]. Phinchantrap et al. conducted a study in Obstetrics and Gynecology group of Bangkok in 2004 in which the acute pain after infertility diagnostic laparoscopy was decreased significantly after taking 200 mg celecoxib two hours before surgery and the need to consume opioids during 24 hours after surgery was decreased considerably [3]. Pilatti et al. conducted the fixed jaw surgery on 20 patients, according to VAS the acute post-operation pain for patients who have been treated with celecoxib was lesser than that in patients who have been treated with dexamethasone [4]. Dorr et al. have indicated that the patients who have taken celecoxib before knee joint replacing surgery showed lower VAS than the control group during the first 24 hours hence the need to intake

opioid during this period was lesser in this group as well [5]. Barden et al. conducted a study in Pain Studies Center of Oxford University, Britain, in 2003. 418 patients were enrolled in this study. Finally they concluded that taking 200 mg celecoxib, which is half of necessary dose to control the acute pain, two hours before surgery is significantly effective in controlling the acute pain after operation and no certain detrimental effect has been reported for the substance [6]. Salo et al. studied 105 patients and they showed that there is no significant difference in controlling the acute post-operation pain for patients treated by 200 mg or 400 mg celecoxib and patients treated by 600 mg ibuprofen [7].

As mentioned in this article, all studies have emphasized the effective role of celecoxib as the multimodal strategy or pre-treatment on post-operation pain; however, some studies showed opposite results. Certainly, as our studied shows taking 200 mg celecoxib two hours before surgery

can alleviate the post-operation pain and opioid intake considerably, hence pain, opioid intake complications and hospital costs will be decreased. Therefore, taking this drug as a pre-treatment in selective surgical operations would be very helpful.

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This study was coded as IRCT201010284947N2 and has been registered in Clinical Trials Registration Center.

Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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