OriginalArticle

Sublingual Piroxicam - A Painless Way In The Management Of Lower Third Molar Extraction

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Abstract

Background: This study was conducted with the need to evaluate and compare the efficacy of oral piroxicam with sublingual piroxicam in regulating post operative pain after third molar surgery

Objectives: The objectives of this study were to evaluate the efficacy of oral and sublingual piroxicam in controlling pain after third molar extraction at 4 and 6 hours with the help of VAS and time taken for ingesting the first rescue medication post operatively.

Methodology: A total of 27 participants, with 52 sites which met the inclusion and exclusion criteria were selected for this study. These were then divided into two groups; one was oral piroxicam group and the other was sublingual group. The intensity of pain was recorded at 4th and 6th post operative hour using a VAS analogue scale. The time when the participant first complained of pain was recorded and the participant was given 20mg of piroxicam as a rescue medication.

Results: It was observed that both the drugs were equally effective at 4th post operative hour and the pain intensity at 6th post operative hour was found to be less in the sublingual piroxicam group than the oral group. The mean time for taking the first rescue medication was greater in the sublingual piroxicam group as compared to the oral group.

Conclusion: It was concluded that sublingual piroxicam has better efficacy in terms of postoperative pain control than oral piroxicam in mandibular third molar surgery.

Keywords: Sublingual piroxicam, postoperative pain management, oral piroxicam.

INTRODUCTION

One of the most common procedures in oral surgery is the extraction of an impacted third molar[1]. During the postoperative phase, participants endure oedema and pain as a result of the inflammatory response, which has a variety of effects on their quality of life. The release and manufacture of various biochemical mediators involved in the pain process, including histamine, bradykinin, and prostaglandins, is triggered by the removal of the impacted third molar[2]. The production and action of prostaglandins, a group of biologically active fatty acids generated from arachidonic acid and linoleic acid, appear to be intimately linked to the longer periods of pain and inflammation.[3]

Third molar surgery commonly results in pain, oedema, and restricted jaw movements.[4] It is critical to reduce the occurrence of these postoperative problems, and many strategies have been proposed including the use of low level laser therapy (LLLT)[5], kinesio tapes[6], photo biomodulation therapy[7], application of external cold dressing[8] , modulating the closure technique, varying the dressing agents, open vs closed dressing (with drain vs without drain)[9], modulating extent of surgical trauma which includes the surgeon's competence, surgical technique, and altering the flap design, among other things. Then there are the pharmacological therapies which include the use of NSAID's[10], analgesics[11], topical gels[12], antibacterial mouthwashes[13] and steroid therapy.[14]

Piroxicam, a nonsteroidal anti-inflammatory drug, has been shown to be effective in reducing the pain effects after third molar surgery. It is the oxicam family member with the most clinical use as a nonsteroidal anti-inflammatory drug (NSAID) which works by inhibiting the cyclooxygenase (COX) enzyme, thus, ultimately resulting in inhibition of prostaglandin production. Piroxicam has a 50-hour plasma half-life and reaches peak blood levels 3 to 5 hours after oral dosing. It can be used topically or systemically, and its once-daily administration has made it useful for chronic conditions that require NSAID's treatment. Hepatic metabolism accounts for a significant amount of piroxicam elimination. As a result, participants with hepatic illness may require lower piroxicam doses than those with normal hepatic function**[15]**. Piroxicam are not entirely devoid of side effects. It can cause allergic responses in certain people and hence should be avoided by participants who are at risk for hepatic failure, gastrointestinal inflammation or peptic ulcers[16]. The most prevalent side effects are minor and include flatulence, abdominal discomfort, diarrhoea, constipation, abdominal pain, epigastric distress and nausea in about 30% of all participants receiving daily doses of 20 mg of piroxicam.[17]. Some of the more uncommon side effects, such as gastrointestinal bleeding and peptic ulcers, are more serious, and in a few of these isolated cases, these side effects were severe enough to result in death. [18]

Hence, due to these reasons there was a need to give immediate start of pharmacological effect that led to the development of systemic drug delivery via the sublingual route. Sublingual drug delivery involves placement of a drug under the tongue, where it enters the bloodstream directly through the ventral surface of the tongue and the floor of the mouth. The medication solutes are absorbed quickly into the reticulated vein beneath the tongue mucosa, transmitted through the facial vein, internal jugular vein, and brachiocephalic vein, and finally released into systemic circulation.[19]. Passive diffusion into the lipoidal membrane is the principal method for drug absorption into the oral mucosa[20]. The medicine is absorbed 3 to 10 times faster through the sublingual route than through the oral route, and just a tiny amount of saliva is normally required for tablet disintegration in the oral cavity.

Orally delivered drugs go through the bloodstream via the inferior vena cava, which takes longer than sublingual administration to reach all tissues. Piroxicam must travel through the caustic environment of the gastrointestinal tract if it is taken orally; sublingual administration eliminates this route and the accompanying side effects[21.] The participant can take the drug without water before or after surgery, which is one of the advantages of the sublingual route.[22] The role of sublingual piroxicam as compared to oral piroxicam needs to be assessed in minor oral surgery procedures. Thus, the purpose of this study was to compare the efficacy of oral versus sublingual piroxicam in relieving pain post extraction of mandibular third molars

MATERIALS AND METHODS

Trial Design

This was a prospective single blind study which was carried out in the department of Oral and Maxillofacial Surgery in our institute. This study was approved by the institutional review board (DYPDCH/IEC/124/140/19). No deviations from the original protocol were necessary or occurred during the course of the study.

Eligibility criteria

Participants with bilaterally impacted mandibular third molar who met the inclusion criteria were included in the study. The duration of the study was from December 2019 to August 2021. Participants willing to participate in the study of age 18 years and older with bilateral impacted mandibular third molars with a difficulty index within the range of 5-6 (Pederson Difficulty Indexed) along with the clinical and radiographic diagnosis of an impacted mandibular third molar. It also consisted of healthy participants with no systemic diseases like any hepatic diseases, uncontrolled diabetes and hypertension, bleeding disorders etc. The exclusion criteria consisted of participants unwilling to participate in the study and with a known history of allergic reaction to local anesthesia. It also excluded pregnant women and participants allergic to piroxicam or other NSAIDs.

Case selection

Three hundred and seventy participants requiring surgical removal of bilateral impacted third molar were assessed for eligibility. Two hundred and forty participants of these did not meet the selection criteria. 100 participants refused to participate in the study. Three of the remaining thirty did not report back for second surgery and therefore, had to be excluded from the study. So, 27 participants were ultimately selected for the study.

Sampling and Grouping

The sample size formula was calculated using G power software (3.1.9.2)
Effect size = 0.78
$\propto = 0.05$
Power = 0.30
Allocation ratio = 1:1
The sample size consisted of total 27 participants with bilaterally impacted mandibular third molars, i.e., 52 sites

Randomization

The right and left sites were randomly allocated into two groups using a coin toss method. The researcher who was responsible for the random allocation into two groups did not perform the surgical procedure or assessment of parameters.

Grouping

52 sites were divided into 2 groups
Group A – Oral piroxicam: 27 sites
Group B- Sublingual piroxicam: 27 sites

Procedure

A detailed case history was taken and consents were obtained before beginning the procedure. Radiographic investigation using orthopantomogram (OPG) was done to classify the impacted tooth, assess the difficulty level and to rule out any pathology. Participants with bilaterally impacted mandibular third molars having the same angulation/spatial relationship and same difficulty of operative procedure with Pederson difficulty index between 5-6 were included in the study. According to the group allocation, participant was prescribed oral or sublingual piroxicam.

Surgical technique for removal of impacted mandibular 3rd molar

The participants were painted with povidone iodine solution and draped with sterile drapes. Local anesthesia was achieved through inferior alveolar nerve block, lingual nerve block and long buccal nerve block. A wards or modified wards incision was taken according to the position and level of impacted tooth. A full thickness mucoperiosteal flap was reflected to expose the site. Buccal and distal gutter was created around the tooth with either a round or straight fissure bur. After sufficient amount of bone removal, the tooth was extracted from the socket using an elevator. Sharp bony edges were smoothened and the socket was irrigated with povidone iodine and saline to remove debris. The wound was closed using 3-0 silk suture using simple interrupted technique and every participant was given the same set of post operative instructions and antibiotics. After 2 weeks the other side third molar was extracted using the oral or sublingual route as per grouping. This time frame was decided to avoid wash over effect of the drug as well as participant's convenience.

Outcomes

After extraction, the participants were evaluated for pain on a 10-point facial visual analogue scale (VAS) with score 0 indicating no pain, whereas 10 indicating excessive pain. This evaluation was done at postoperative 4th and 6th hour. The number of rescue medication taken by each group was noted by the participant and reported to the assessor on post operative day 1.

Interventions

40mg oral piroxicam was given 2 hours preoperatively for group A whereas 40 mg sublingual piroxicam was given 15 minutes preoperatively for group B. This was difference in time prior to surgery for ingestion of the drug was planned due to difference in the onset of action of oral and sublingual route.

Blinding

In this study, the operator, assessor and statistician were blinded. The participants could not be blinded. The oral or sublingual piroxicam was given by different researcher and this was not known to the operator. The assessment of pain using VAS and number of rescue medication was done either by assessor who was not aware of the group allocation. The statistician too was not disclosed the information of group allocation prior to statistical analysis.

Statistical Analysis

Statistical analysis was done using paired and unpaired t-test. Paired t test was done to assess the difference between the VAS scores at 4 hours and 6 hours for oral piroxicam and sublingual groups. Chi square test was done to check the association of VAS scores and Time for 1st rescue medication with Gender and Age group.

RESULTS

Out of which 16 were male and 11 were female, in age range of15 to 36 with mean (SD) age was 26.63 years (±5.253). (Table 1)

Table 1: Demographic Characteristics Of The Patients

Sr. No.	Characteristics	Frequency(N)	Percentage (%)	Mean±SD
Age				
1	15-20	4	14.8	26.63±5.263
2	21-25	9	33.3	
3	26-30	7	25.9	
4	>31	7	25.9	
Gender				
1	Female	11	40.7	
2	Male	16	59.3	

VAS scores at 4 hours: Paired t test was done to assess the difference between the VAS scores at 4 hours for oral piroxicam and sublingual groups. At 4 hours, the mean value for oral piroxicam group was 1.48 and standard deviation was 1.805 and the mean value for sublingual piroxicam was 0.89 and standard deviation was 1.601. P-value was not significant. (Table 2)

VAS scores at 6 hours: Paired t test was done to assess the difference between the VAS scores at 6 hours for oral piroxicam and sublingual groups. At 6 hours, the mean value for oral piroxicam was 1.41 and standard deviation was 2.275 and the mean value for sublingual piroxicam was 1.04 and standard deviation was 1.506. P-value was significant (0.008). (Table 2)

Rescue medication: The mean time for 1st rescue medication in oral piroxicam group was 6.44 hours and standard deviation was 0.705 and in the sublingual group was 8.47 hours and standard deviation was 0.624. There was a statistically significant difference with p-value of 0.0001. (Table 2)

Safety: No significant harms or effects was observed in any of the groups but some participants had few side effects. Out of 27 participants in the oral piroxicam group, 5 participants suffered from gastrointestinal discomfort. 2 participants

had flatulence, 2 participants complained of constipation and 1 participant had nausea. None of the 27 participants of the sublingual piroxicam group had any complications.

Outcomes and Estimation: The estimated effect size was 0.78 and the confidence interval was 95%.

Table 2: Difference In VAS Scores And Time Taken For 1st Rescue Medication Between Oral And Sublingual Piroxicam Groups

	Mean	SD	Mean Diff	95% CI	t-value	p-value
VAS Score 4 hours						
OP	1.48	1.805	0.593	0.339 1.525	1.276	0.208
SP	0.89	1.601				
VAS Score 6 hours						
OP	1.41	2.275	0.370	0.683 1.424	0.705	0.008*
SP	1.04	1.506				
Time taken for 1st Rescue medication						
OP	6.44	0.705	-2.026	2.485 1.567	-8.982	0.0001*
SP	8.47	0.624				

DISCUSSION

In oral and maxillofacial surgery, surgical extraction of partially or completely impacted lower third molars are routinely carried out and is always accompanied with postoperative discomfort. Pain being the most impacting factor found postoperatively that affects the participant's quality of life.[23] Pain after third molar surgery is a routine sequela due to trauma induced inflammation. Therefore, third molar surgery is one of the most often used intervention to study acute analgesia and numerous studies have been published on this issue.[4,5,6,8,24] Drugs like analgesics and NSAIDs inhibit cyclo oxygenase activity which reduces the synthesis of prostaglandins thus help in curbing the pain[25]. Piroxicam is one such NSAID which has been widely used as a preemptive and postoperative analgesic to control the pain after third molar surgery.

This study design was developed to assess and compare the pain threshold of the participants administered either oral or sublingual piroxicam preoperatively before the surgery. The pain caused by surgical removal of bilateral third molar surgery was selected as model to assess the post operative pain, as it provides a unique setting of same biological response, similar pain threshold and same healing and inflammatory response. This reduces the confounding factors making it a unique way to assess the pain and has become a standard model for evaluating the efficacy of several pharmaceutical analgesics.[21] This pain is usually mild and only lasts a few days. Lower third molar extraction pain peaks 2–4 hours after the procedure is completed, and most participants require analgesic medication.[26]

Pain was assessed after 4 hours using visual analogue scale (VAS). The difference in the VAS scores at 4 hours for oral and sublingual piroxicam groups were found to be statistically insignificant as the drug plasma concentration of piroxicam usually peaks between 3 to 5 hours. The oral as well as sublingual piroxicam are both equally effective at 4 hours post-operatively. Studies conducted by Desjardins PJ[31] and Bhutani N[33] found piroxicam to be effective in reducing post operative pain after 4 hours.

Pain was assessed after 6 hours using visual analogue scale (VAS). Sublingual piroxicam was found to be effective as compared to the oral piroxicam. Sublingual administration of piroxicam avoids the first passage of the drug in the liver where the drug is metabolized. It is absorbed by the reticulated veins in the floor of the mouth, leading directly to the superior vena cava, thus resulting in faster distribution of the drug to all tissues through the bloodstream.[27] As in this route the drug does not go to the stomach so it is not destroyed by the enzymes and acids present in the stomach so that it is stable for a longer time.[28] Studies carried out by Sunshine A[30], Hans F Gramke[20], Desjardins PJ[31], Mohammad S[32], Bhutani N[33], Nappi G[34] also found that piroxicam was effective in reducing post operative pain when assessed after 6 hours.

There was a statistically significant difference in the meantime of taking the 1st rescue medication which was 6.44 hours for the oral piroxicam group and 8.47 hours for the sublingual group. Sublingual piroxicam bypasses the first pass effect and therefore, it lasts longer in the bloodstream making it more effective than the oral piroxicam[29]. In other studies, by F. Graziani[27], G L Hutchinson[35] similar effect of sublingual route was found.

Advantages of sublingual over oral route

1. In oral route because food there is delay in absorption of tablets, which is not a problem with the sublingual route
2. Only a part of the oral tablet is absorbed, but sublingual route does not present this problem.
3. Because of the first pass effect, the only a part of the oral piroxicam that is absorbed reaches the bloodstream. In the sublingual piroxicam, the entire amount of the drug reaches the bloodstream.
4. The absorption of the drug through the sublingual route is 3 to 10 times greater than the oral route
5. As it bypasses the digestive route, the side effects like nausea, vomiting, gastrointestinal discomfort are absent when sublingual is used.

Limitations of study

Blinding could not be done of the participant in this study design as the participant was aware of the medication. This limitation may influence VAS reading given by the participant.

Future implications

The result of this study suggests that sublingual piroxicam is better in post operative pain control than oral piroxicam. Hence, sublingual piroxicam is recommended to be used in post operative pain control in all extraction and minor oral surgical procedures.

CONCLUSION

This was a prospective study in which the efficacy of sublingual piroxicam was compared with oral piroxicam in post operative pain control after mandibular third molar surgery. It was found that sublingual piroxicam was more effective in controlling pain at 4 hours and 6 hours interval and also required rescue medication much later than the sublingual piroxicam group. It was also noted that sublingual piroxicam group reported no side effects in the participants as compared to the oral piroxicam group. Thus, it can be concluded that sublingual piroxicam is more efficient than oral piroxicam in controlling the post operative pain after mandibular third molar surgery.

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