Original Article – Comparative Study

Efficacy of Lornoxicam as a Pre-emptive Analgesic in Mandibular Third Molar Surgery – A Comparative Study

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Abstract

Introduction: The most common complication following third molar surgery is pain. The purpose of the study is to determine the efficacy of lornoxicam as a preventive analgesic in patients undergoing surgical removal of impacted mandibular third molars. **Materials and Methods:** This study included 26 participants aged 18–28 years with bilateral symmetrical third molars. Group A, the control group, received lornoxicam 8 mg 1 h after surgery, whereas Group B, the study group, received lornoxicam 8 mg 1 h before surgery. All patients were evaluated for pain at the 1st, 2nd, 4th, 6th, 8th and 12th post-operative hours. The number of rescue analgesics taken within 24 h of the procedure, as well as the first occurrence of pain postoperatively, was recorded and analysed. **Results:** Using the Mann–Whitney *U*-test and Friedman's analysis, the resulting data were statistically analysed. When Group B was compared to Group A, there was a significant difference in pain reduction levels in the immediate post-operative hours. When compared to Group A, Group B had a lower need for rescue analgesics within the first 24 h postoperatively. **Discussion:** Following mandibular third molar surgery, pre-emptive use of lornoxicam is effective in reducing post-operative pain and reducing the need for rescue analgesic consumption.

Keywords: Impacted mandibular third molar, lornoxicam, pre-emptive analgesia

Introduction

Pain is a complex natural protective phenomenon mediated by the central nervous system that serves to protect the body from potentially harmful stimuli. The surgical removal of an impacted third molar is a common procedure that causes post-operative complications such as pain and swelling, which are inconvenient for the patient.[1] Crile pioneered the concept of 'pre-emptive analgesia' to treat post-operative pain.[2] The goal of pre-emptive analgesia is to prevent peripheral and central sensitisation and to reduce post-operative pain amplification.[3]

Lornoxicam, an oxicam class non-steroidal anti-inflammatory drug (NSAID), is a powerful analgesic and anti-inflammatory NSAID. It is highly ionised at physiological pH and has a low lipophilicity, preventing the distribution of fatty tissues. It differs from other oxicam compounds in its potent inhibition of prostaglandin biosynthesis, which explains the drug's high efficacy.[4,5] It may exert peripheral analgesic effects through the NO–cGMP pathway and the opening of potassium channels, as well as by inhibiting spinal nociceptive processing and increasing plasma levels of dynorphin and ß-endorphin after intravenous administration. Peak plasma concentration is reached in 2.5 h and is rapidly and almost completely absorbed from the gastrointestinal tract. The bioavailability is 90%–100%, with nearly 99% bound to protein, i.e., albumin. There is no first-pass metabolism observed, and it is found in the plasma as its hydroxylated metabolite in its unchanged form. Approximately two-thirds of the drug is eliminated as inactive substances by the liver and one-third by the kidneys. The drug's plasma half-life is 3–5 h. Because of its rapid onset of action and short half-life, it is frequently used to treat post-operative pain for various surgical procedures. It has a low risk of causing adverse reactions and is well tolerated by

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the gastrointestinal tract.[6-8] The purpose of this study was to see if lornoxicam could be used as a preventive analgesic after surgical removal of the mandibular third molar.

Materials and Methods

The current randomised controlled trial study was approved by the institutional review board, and the reference number is VDC/IEC/2018/53. The sample size was determined using the previous study's standard deviation of 594.93 min and the expected difference of 500 min. With a 20% dropout rate, a sample size of 26 was determined. The study included 26 healthy individuals with bilateral similarly impacted mandibular third molars aged 18–28 years who had reported to the Department of Oral and Maxillofacial Surgery, Vishnu Dental College, between January 2019 and December 2019. Patients suffering from an acute infection or inflammation at the surgical site, as well as medically compromised conditions such as pregnancy, hypertension, diabetes, gastrointestinal disorders, renal impairment, bleeding disorders and clotting and those allergic to NSAIDs and/or had taken NSAIDs within 72 h before the procedure were all excluded from the study. Bilaterally similarly impacted third molars were extracted in two separate appointments at seven day intervals using a split-mouth study design. The intraoral sites were randomly assigned to either the A or B groups using a coin toss. Lornoxicam 8 mg tablets were given to Group A 1 h after surgery. Lornoxicam 8 mg tablets were given to Group B 1 hour before surgery. The investigator was blinded regarding the drug being given preoperatively or post-operatively. Under local anaesthesia, the standard surgical extraction of impacted mandibular third molars was performed. All patients were given standardised post-operative medication, which included capsule amoxicillin 500 mg oral every 8th h for five days or tablet erythromycin 500 mg oral every 6th h for five days if they were allergic to penicillin. As a rescue analgesic, tablet aceclofenac 100 mg was prescribed. Patients were instructed to take the rescue analgesic at the first sign of pain in the post-operative period and to keep a record of it, as well as the number of rescue analgesics taken within 24 h. The Visual Analogue Scale (VAS) questionnaire was used to assess pain at the 1st, 2nd, 4th, 6th, 8th and 12th h post-operatively.

The resulting data were statistically analysed using the Mann–Whitney *U*-test and Friedman's analysis in SPSS version 21 (IBM SPSS Statistics, Chicago, USA).

Results

The study included 26 patients, 11 were male and 15 were female. The patients' ages ranged from 18 to 28 years old. Out of 26 bilaterally symmetrically impacted mandibular third molars, eight (30.7%) were mesioangular, nine (34.6%) were vertical, five (19.2%) were horizontal and four (15.3%) were distoangular. From the 1st post-operative hour to the 8th post-operative hour, there was a significant increase in the mean VAS score in Group A [Table 1], followed by a decrease in the 12th post-operative hour. There was a significant increase in the mean VAS score in Group B [Table 2] from the 1st to the 12th post-operative hour. The VAS score of the 1st post-operative hour was compared to that of the 2nd and 4th and was found to be statistically insignificant within Group A [Table 3]. The VAS score of the 1st post-operative hour was compared to that of the 2nd, 4th, 6^{h}, 8th and 12th and was found to be statistically significant within Group B for 8th and 12th h [Table 4]. The VAS scores recorded at the 1st post-operative hour in both Groups A (0.1923) and B (0.00) were not statistically significant [Table 5]. At 2nd, 4th, 6th, 8th and 12th h post-operatively, a statistically significant difference (P = 0.01) was observed in both groups [Table 5]. In terms of the first incidence of pain after the procedure, the results revealed a statistically significant difference (P = 0.001) between Groups A and B [Table 6]. The first incidence of pain after the procedure was 2.692 ± 0.970 (h) (mean ± standard deviation [SD]) in Group A and 7.038 ± 1.341 (h) in Group B. The number of rescue analgesics consumed within 24 h post-operatively showed a statistically significant difference between the two groups [Table 7]. The mean SD in Group A was (3.50 ± 0.54), whereas the mean SD in Group B was (2.69 ± 0.54).

Discussion

Third molar surgery for pain studies meets the majority of the requirements of a good pain model, including a predictable development of inflammation and a homogeneous study population of young, healthy individuals who can understand the information provided. Furthermore, this type of surgery is localised, uses a standardised technique, takes 10–20 min and is performed under local anaesthesia.[9] Coulthard *et al*. concluded that the majority of patients with third molar surgery experienced the most pain during the first 24–48 post-operative hours.[10]

Table 1: Mean Visual Analogue Scale score in Group A

Time interval (h)	Mean±SD	Test value	*P*
1	0.1923±0.69393	108.728	0.000*
2	2.0385±2.34061		
4	5.1538±1.43366		
6	5.7692±0.90808		
8	6.1923±0.84943		
12	6.0000±0.63246		

*Statistically significant, SD: Standard deviation

Table 2: Mean Visual Analogue Scale score in Group B

Time interval (h)	Mean±SD	Test value	*P*
1	0.0000±0.00000	112.601	0.000*
2	0.0000±0.00000		
4	0.3462±1.23101		
6	1.4615±2.15835		
8	3.8077±1.44275		
12	4.5385±0.85934		

*Statistically significant, SD: Standard deviation

Table 3: Mean Visual Analogue Scale score comparison between post-operative hours in Group A

Pair 1 (I) (h)	Pair 2 (J) (h)	Mean difference (I−J)	SE	*P*	95% CI for difference	
					Lower bound	Upper bound
1	2	−1.846*	0.436	0.004	−3.260	−0.433
	4	−4.962*	0.291	0.000	−5.905	−4.018
	6	−5.577*	0.216	0.000	−6.278	−4.876
	8	−6.000*	0.208	0.000	−6.673	−5.327
	12	−5.808*	0.167	0.000	−6.348	−5.267
2	4	−3.115*	0.365	0.000	−4.300	−1.931
	6	−3.731*	0.366	0.000	−4.918	−2.543
	8	−4.154*	0.391	0.000	−5.422	−2.885
	12	−3.962*	0.431	0.000	−5.361	−2.562
4	6	−0.615	0.201	0.077	−1.266	0.035
	8	−1.038*	0.245	0.004	−1.833	−0.244
	12	−0.846*	0.258	0.046	−1.684	−0.008
6	8	−0.423*	0.099	0.004	−0.744	−0.103
	12	−0.231	0.150	1.000	−0.717	0.256
8	12	0.192	0.124	1.000	−0.211	0.595

*Statistically insignificant, Pair 1 represents the post operative hour 1 , 2 , 4, 6 and 8, Pair 2 represent the subsequent post operative hours with which pair 1 is being compared. CI: Confidence interval, SE: Standard error

Table 4: Mean Visual Analogue Scale score comparison between post-operative hours in Group B

Pair 1 (I) (h)	Pair 2 (J) (h)	Mean difference (I−J)	SE	*P*	95% CI for difference	
					Lower bound	Upper bound
1	2	0.000	0.000	-	0.000	0.000
	4	−0.346	0.241	1.000	−1.129	0.437
	6	−1.462*	0.423	0.030	−2.835	−0.088
	8	−3.808*	0.283	0.000	−4.726	−2.890
	12	−4.538*	0.169	0.000	−5.085	−3.992
2	4	−0.346	0.241	1.000	−1.129	0.437
	6	−1.462*	0.423	0.030	−2.835	−0.088
	8	−3.808*	0.283	0.000	−4.726	−2.890
	12	−4.538*	0.169	0.000	−5.085	−3.992
4	6	−1.115	0.352	0.061	−2.258	0.027
	8	−3.462*	0.300	0.000	−4.434	−2.489
	12	−4.192*	0.208	0.000	−4.866	−3.519
6	8	−2.346*	0.337	0.000	−3.440	−1.252
	12	−3.077*	0.328	0.000	−4.140	−2.013
8	12	−0.731*	0.204	0.022	−1.393	−0.068

*Statistically insignificant, CI: Confidence interval, SE: Standard error

Lornoxicam, an oxicam group NSAID with analgesic, anti-inflammatory and antipyretic properties, is available in oral and parenteral forms. It differs from the other established oxicams in that it has a relatively short elimination half-life, which may have an advantage from the tolerability standpoint.[11] It has been shown to be as effective as opioids such as morphine, pethidine and tramadol in relieving post-operative pain after surgery, as well as other NSAIDs after oral surgery.[12]

Acute post-operative pain is a cause for concern because it can aggravate the patient's discomfort and turn into chronic pain by activating the peripheral and central pain pathways. The timing of NSAID administration is critical for analgesic efficacy.[13] Pre-emptive analgesia is a type of antinociceptive therapy that begins before surgery and prevents the establishment of transformed processing of afferent input after incisional and inflammatory injuries, which exacerbates post-operative pain.[14]

Crile introduced the concept of pain prevention into clinical practice in 1913, and it was further developed by Wall and Woolf, who proposed that 'simple changes in the timing of treatment can have profound effects on post-operative pain'.[2] Pre-emptive analgesia refers to the administration of analgesics before the onset of a noxious (i.e., surgical) stimulus in order to completely block nociception. This afferent blockade of nociceptive impulses is then maintained throughout the intra-operative period and even post-operatively.[15]

Table 5: Mean comparison of Visual Analogue Scale scores in Group A and B at 1st, 2nd, 4th, 6th, 8th and 12th h interval

	Mean±SD	Test value	*P*
1st h			
Group A	0.1923±0.69393	−1.428	0.153
Group B	0.0000±0.00000		
2nd h			
Group A	2.0385±2.34061	−3.874	0.000*
Group B	0.0000±0.00000		
4th h			
Group A	5.1538±1.43366	−6.112	0.000*
Group B	0.3462±1.23101		
6th h			
Group A	5.7692±0.90808	−5.712	0.000*
Group B	1.4615±2.15835		
8th h			
Group A	6.1923±0.84943	−5.611	0.000*
Group B	3.8077±1.44275		
12th h			
Group A	6.0000±0.63246	−5.213	0.000*
Group B	4.5385±0.85934		

*Statistically significant, Mann–Whitney *U*-test. SD: Standard deviation

Table 6: Mean first incidence of pain postoperatively

Parameter	Group	Mean±SD	Mean difference	Test value	*P*
First incidence of pain	Group A	2.6923±0.97033	4.34615	6.000	0.000*
	Group B	7.0385±1.34107			

*Statistically significant, SD: Standard deviation

Table 7: Mean number of rescue analgesics consumed within 24 h

Parameter	Group	Mean±SD	Mean difference	Test value	*P*
Analgesics consumed within 24 h	Group A	3.5000±0.54913	−0.80769	123.500	0.000*
	Group B	2.6923±0.54913			

*Statistically significant, SD: Standard deviation

Pre-emptive analgesia has three objectives; (i) to reduce acute pain following tissue injury, both intra-operatively and post-operatively, (ii) prevent pain-related pathologic central nervous system modulation ('pain memory') and (iii) prevent the development of chronic pain and the persistence of post-operative pain.[16-19]

In this study, patients in Group B had a significant reduction in pain levels in the first seven post-operative hours (mean: 7.0385 h) when compared to patients in Group A (mean: 2.6923), and patients in Group B required fewer rescue analgesics within the first 24 h (mean: 2.6923 rescue analgesics) when compared to patients in Group A (mean: 3.5 rescue analgesics). These findings were consistent with the findings of a study conducted by Zor ZF *et al*.,[20] Pektas *et al*., compared the pre-emptive analgesic efficacy of diflunisal 1000 mg versus lornoxicam 16 mg at 2, 4, 6, 12 and 24 h post-operatively. According to their findings, there were no statistically significant differences between groups in terms of rescue analgesic consumption or postoperative pain scores.[21]

Mojsa *et al*. conducted a study in which Group A was given pre-emptive lornoxicam (16 mg) orally, Group B was given post-operative lornoxicam (16 mg) orally and Group C was given a placebo. They discovered that the efficacy of post-operative analgesia was higher in both lornoxicam groups when compared to the placebo groups, but there was no significant difference in the number of rescue analgesics in any of the three groups.[22] These findings contradicted the current study, which found a significant difference in pain reduction in Group B when compared to Group A in the first seven post-operative hours and a lower need for rescue analgesics within 24 h in Group B when compared to Group A. Nørholt *et al*. compared the dose–effect relationship of lornoxicam 4–32 mg with placebo and ketorolac 10 mg (KET). They reported 37 adverse events that were evenly distributed across six treatment groups.[13] Despite the fact that many studies have reported adverse events such as diarrhoea, induced intolerability, nausea, stomach pressure, gastric disturbance and vomiting with the use of lornoxicam, no adverse events were reported in our study. This could be due to the amount and dosage of the drug used.

Conclusion

The current study confirmed the pre-emptive analgesic effect of lornoxicam 8 mg, which provided a pain-free period of 7 h after mandibular third molar surgical extraction, with no adverse events and good patient acceptance, implying its safe use as a pre-emptive analgesic in mandibular third molar surgery. Furthermore, research is needed to determine the dosage efficacy of lornoxicam in the control of post-operative pain.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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