Evaluating the effect of oral premedication with nonsteroidal anti-inflammatory drugs on the anesthetic success of inferior alveolar nerve block in treatment of irreversible pulpitis

Kriti Shrestha,[1] Sageer Ahmed,[1] Snigdha Shubham,[2] Gyanendra Jha,[1] Vanita Gautam,[1] Narayan Gautam[3]

ABSTRACT

INTRODUCTION

Achieving profound anesthesia in mandibular molars with symptomatic irreversible pulpitis is often difficult, with high failure rates reported for inferior alveolar nerve block (IANB). Preoperative use of nonsteroidal anti-inflammatory drugs (NSAIDs) may improve anesthetic efficacy by reducing inflammation and nociceptor sensitization. Objective of the study is to compare the effect of oral premedication with ketorolac, piroxicam, and etorocoxib on the anesthetic success of IANB in patients with symptomatic irreversible pulpitis.

MATERIAL AND METHODS

This cross-sectional, observational study included 120 patients aged 18–60 years with symptomatic irreversible pulpitis in mandibular molars. Participants were randomly allocated into four groups (n=30 each): etorocoxib (90 mg), ketorolac (10 mg), piroxicam (20 mg) and placebo. Premedication was administered 45 minutes prior to IANB using 2% lidocaine with 1:200,000 epinephrine. Pain was assessed using the Visual Analog Scale (VAS) before medication, after 45 minutes, and during access opening and instrumentation. Anesthetic success was defined as absence of pain during the procedure. Data were analyzed using ANOVA and post hoc Tukey tests.

RESULTS

NSAID premedication significantly reduced VAS scores compared to placebo (p<0.001). Piroxicam showed the greatest reduction in intraoperative pain, followed by etorocoxib and ketorolac. Post hoc analysis demonstrated significant differences between placebo and all NSAID groups, while no significant difference was observed between piroxicam and etorocoxib during instrumentation.

CONCLUSION

Oral premedication with NSAIDs significantly improves the success of IANB in symptomatic irreversible pulpitis, with piroxicam showing the most favorable outcome.

KEYWORDS

Etorocoxib, Inferior alveolar nerve block, Irreversible pulpitis, Ketorolac, NSAIDs, Piroxicam

AUTHORS' AFFILIATIONS

1. Department of Conservative Dentistry and Endodontics, Universal college of Medical Sciences, Bhairahawa, Nepal.
2. Department of Conservative Dentistry and Endodontics, NAMS, Kathmandu, Nepal.
3. Department of Biochemistry, Universal College of Medical Sciences, Bhairahawa, Nepal.

https://doi.org/10.3126/jucms.v14i02.99666

For Correspondence
Dr. Kriti Shrestha
Department of Conservative Dentistry and Endodonitcs
Universal College of Medical Sciences
Bhairahawa, Nepal
E-mail: drkritishrestha@gmail.com

INTRODUCTION

Mandibular posterior teeth especially with irreversible pulpitis are commonly known to be extremely challenging to anesthetize. Patient comfort is a major concern for both individuals receiving care and dental professionals, leading to numerous studies aimed at enhancing the effectiveness of anesthesia during and after endodontic procedures.[1]The inferior alveolar nerve block (IANB) is the most commonly employed injection technique to achieve mandibular anesthesia for endodontic procedures. However, failure rates associated with IANB have been reported to range from 44% to 81%. [2, 3]

The increased sensitization of nociceptors as a result of pulpal inflammation adversely affects the effect of anesthetics.[4] Pain during access opening and instrumentation caused by the anesthetic failure was even recorded in patients who had demonstrated positive signs of anesthesia such as numbness in the lower lip and the tip of the tongue.[5] Thus, lip numbness was shown not to be always related to successful pulpal anesthesia. Therefore, it is paramount to increase the success rate of the IANB block during root canal treatment.

Previous studies have indicated that administering medication before treatment may enhance the success of the IANB. Therefore, preoperative analgesics could potentially improve its effectiveness in patients with irreversible pulpitis.[3]

Despite evidence supporting NSAID premedication for improving IANB success, there is limited direct comparison among commonly used agents with different pharmacological profiles. Therefore, the purpose of this study was to compare the efficacy oforal pre-medication with ketorolac, piroxicam, etorocoxib and placebo (neurobion forte) on the anesthetic efficacy of IANB with 2% lidocaine with 1:2,00,000 epinephrine in patients with irreversible pulpitis.

MATERIAL AND METHODS

The present study was done after obtaining clearance from the Institutional Review Committee with IRC number UCMS/IRC/159/21. In this cross-sectional, observational study, the total 120 patients were enrolled with the age group of 18-60 years with acute pain in mandibular molar teeth (first or second molar) diagnosed as symptomatic irreversible pulpitis. The written informed consent was obtained from all human subjects who participated in the investigation after they were explained fully about the nature of the procedure, possible discomforts and risks. Patient allergy to any medication; history of significant medical problem; pregnancy; lactating; or inability to give informed consent; periodontal disease; pulp necrosis;calcified root canals; root resorption; open apex or unrestorable teeth; patients who had used analgesic or anti-inflammatory drugs within 24 hours before the treatment were excluded.

Each patient was asked to rate the intensity of pain that he or she was feeling on the pain score rating scale chart at the baseline adapted from Hatipoğlu FP[6] by Visual Analogue Scores (VAS) in 0-10 cm scale. The 0 coded as no symptoms, 1-3 mild symptoms, 4-6 moderate symptoms, 7-10 severe symptoms. The score wasrecorded as the 1st VAS score.

Patients underwent treatment allocation who had given premedications and root canal procedure done by different Endodontist based on the four groups with each group comprising 30 patients. Group I was administered erozox (etorocoxib 90 mg), Group II ketorolac (ketorol 10 mg, Dr Reddy), Group III piroxicam (dolonex DT 20mg), and Group IV as placebo with tablet neurobion forte and recording was done by the main supervisor of study.

Patient of all groups were asked to wait for 45 minutes after which the patients were again asked to score pain on the pain chart (2nd VAS score). All patients received conventional IANB with 1.5 ml of 2% lidocaine having 1:200,000 adrenaline and were asked to wait for 15 minutes. After 15 minutes, teeth were again cold tested to confirm pulp anesthesia as only lip numbness doesn't confirm complete pulp anesthesia. If the patient did not feel any pain or discomfort, the offending teeth of premedicated group were isolated with rubber dam. Then endodontic access was opened and the patients were again instructed to rate their score during the time of access opening and instrumentation (3rd VAS score). If the patient experienced pain during access opening and instrumentation the outcome was recorded as failure while if there was no pain the IAN was recorded as a success.

The demographic and pain score were recorded for all the groups. The categorical data were represented by frequency and percentage. The continuous data of Pain Score was compared for their Mean/SD among all groups using one way Analysis of Variance (ANOVA). The intra group comparison was made by post hoc multiple tests using Tukey'stest. The *p*-value was set at <0.05 for statistical significance.

RESULTS

Table 1. Gender wise distribution of premedications and placebo in irreversible pulpitis (N=120)

Group	Female	Male	Total
Etorocoxib	16	14	30
	53.33	46.67	100.00
Ketorolac	17	13	30
	56.67	43.33	100.00
Piroxicam	18	12	30
	60.00	40.00	100.00
Placebo	13	17	30
	43.33	56.67	100.00
Total	64	56	120
	53.33	46.67	100.00

The total distributions of the subjects with premeditations were 120 comprising 30 in each group. The maximum frequency (%) of female distribution of 60%, 56.67% and 53.33% were observed in piroxicam, ketorolac, and etorocoxib respectively.

Table 2. Distribution of age wise category in premedications and placebo group (N=120)

	Age category				
Group	18-25	26-35	36-45	46-55	>55
Etorocoxib	8	11	4	5	2
	26.67	36.67	13.33	16.67	6.67
Ketorolac	7	6	9	6	2
	23.33	20.00	30.00	20.00	6.67
Piroxicam	5	9	7	8	1
	16.67	30.00	23.33	26.67	3.33
Placebo	9	7	3	8	3
	30.00	23.33	10.00	26.67	10.00
Total	29	33	23	27	8
	24.17	27.50	19.17	22.50	6.67

The maximum distribution of age group 26-35 years were observed in etorocoxib and piroxicam group with frequency of 36.67% and 30% respectively while in ketorolac the maximum distribution of age was 36-45 years with frequency 30%.

Table 3. Distribution of age wise (Mean±SD) of premedication and placebo groups

Group	Mean	SD	Min	Max	*p*- value (ANOVA)
Etorocoxib	34.63	11.94	18	59	0.749
Ketorolac	37.83	12.02	19	56	
Piroxicam	37.4	12.16	18	59	
Placebo	37.2	13.57	19	58	
Total	36.77	12.35	18	59	

The maximum age of 37.83±12.02 years was seen in ketorolac group and age groups were comparable with others with no statistical significance difference (p=0.749).

Table 4. Distribution of pain by VAS (Mean±SD) of premedication and placebo groups

Group	Before LA	*p*-value	After 45 minutes	*p*-value	During procedure	*p*- value
Etorocoxib	6.53 ± 1.71		2.23 ±1.61		1.03±1.45	
Ketorolac	6.60 ± 1.65		2.40 ± 1.81		2.30 ± 1.64	
Piroxicam	6.03 ± 2.04	0.012	1.53 ± 1.35	<0.001	0.60 ±1.00	
Placebo	5.17 ± 2.00		4.20 ± 1.75		3.70±2.09	<0.001
Total	6.08 ± 1.92		2.59 ± 1.90		1.91±1.99	

Before LA, the maximum mean VAS recorded was observed in ketoralac group as compared to other groups (p=0.012). After 45 minutes of premedication the lowest mean VAS was observed in piroxicam as compared to other groups (p<0.001). During procedure of premedication the lowest VAS was observed for piroxicam as compared to other groups (p<0.001).

Table 5. Mean± SD distribution of Post hoc analysis before premedication

	Tukey Tukey					
Before	Contrast	Std. Error	t	P>(t)	[95% Conf.	Interval]
Group						
Ketorolac vs Piroxicam	0.57	0.48	1.18	0.64	-6.86	1.82
Etorocoxib vs Piroxicam	0.50	0.48	1.04	0.73	-0.75	1.75
Etorocoxib vs Ketorolac	-0.07	0.48	-0.14	1.00	-1.32	1.18
Placebo vs Ketorolac	-1.43	0.48	-2.98	**0.02**	-2.68	-0.18
Placebo vs Etorocoxib	-1.37	0.48	-2.84	**0.03**	-2.62	-0.11
Placebo vs Piroxicam	-0.87	0.48	-1.80	0.28	-2.12	0.38

Post hoc analysis of various groups shown in the table 5 had significant difference in placebo and ketorolac (p=0.02) and etorocoxib (p=0.03) respectively. Others were found to be statistically non-significant difference.

Table 6. Mean± SD distribution of post hoc analysis after 45 minutes under premedication

	TukeyTukey					
After 45 minutes	Contrast	Std. Error	t	P>(t)	{95% Conf.	Interval}
Group						
Ketorolac vs Piroxicam	0.87	0.42	2.04	0.18	-0.24	1.97
Etorocoxib vs Piroxicam	0.70	0.42	1.65	0.35	-0.40	1.80
Etorocoxib vs Ketorolac	-0.17	0.42	-0.39	0.98	-1.27	0.94
Placebo vs Ketorolac	1.80	0.42	4.25	**<0.001**	0.69	2.90
Placebo vs Etorocoxib	1.97	0.42	4.64	**<0.001**	0.86	3.07
Placebo vs Piroxicam	2.67	0.42	6.29	**<0.001**	1.56	3.77

Post hoc analysis of various groups shown in the table 6 had significant difference in placebo and piroxicam (p<0.001), ketorolac (p<0.001) and etorocoxib (p<0.001) respectively. Others were found to be statistically non-significant difference.

Table 7. Mean± SD distribution of post hoc analysis during procedure

	Tukey Tukey					
During procedure	Contrast	Std. Error	t	P>(t)	{95% Conf.	Interval}
Group						
Ketorolac vs Piroxicam	1.70	0.41	4.13	**<0.001**	0.62	277
Etorocoxib vs Piroxicam	-0.43	0.41	1.05	0.71	-0.64	1.51
Etorocoxib vs Ketorolac	-1.27	0.41	- 3.08	**0.01**	-2.34	-0.19
Placebo vs Ketorolac	1.40	0.41	3.40	**<0.001**	0.69	2.47
Placebo vs Etorocoxib	2.67	0.41	6.48	**< 0.001**	0.86	3.74
Placebo vs Piroxicam	3.10	0.41	7.53	**< 0.001**	2.03	4.17

Post hoc analysis of various groups shown in the table 7 had significant difference in ketorolac and piroxicam (p<0.001), placebo and piroxicam (p<0.001), etorocoxib and ketorolac (p=0.01) respectively. While comparing placebo and ketorolac (p<0.001), etorocoxib (p<0.001) respectively. Remaining found to be statistically non-significant difference.

DISCUSSION

Irreversible pulpitis is characterized by recurrent episodes of severe, sharp pain that may persist from minutes to hours. The associated pulpal inflammation is typically severe, which frequently compromises the effectiveness of local anesthesia.[7] The likelihood of local anesthetic failure is reported to be nearly eight times greater in patients with irreversible pulpitis than in healthy control individuals. There are different hypothesis for failure of local anesthesia but the main hypothesisis that inflammation evokes an increase in the anesthetic-resistant subpopulation of sodium channels that exist on pain neurons.[8]

Prostaglandins are key chemical mediators that contribute to inflammation and enhance the sensitivity to pain. These medications act by blocking cyclooxygenase enzymes (COX-1 and COX-2), which are responsible for generating prostaglandins. NSAIDs decrease the formation of prostaglandins, which helps control the pain associated with pulpitis while also minimizing vasodilation and tissue edema. These changes promote improved blood flow and allow anesthetic agents to reach the target area more effectively. Consequently, their anti-inflammatory properties can enhance the success of inferior alveolar nerve block (IANB), as inflammation can otherwise impair anesthetic spread and reduce its effectiveness. Thus, premedicated with NSAIDs before the anesthetic procedure can enhance the nerve block, promoting a more prolonged and complete response to local anesthesia and reducing the risk of anesthetic failure in patients with Irreversible pulpitis.[9]

Due to this proven efficacy in decreasing pain and inflammation,NSAID are commonly used analgesics for reducing pulpal inflammation.[10] However, there is still a controversy about the superiority of different types of NSAID when compared to each other as NSAIDs vary in time of onset; the longer half-life of the analgesic, the slower the onset of effect.

The result of the present study showed that premedication with ketorolac, piroxicam and etorocoxib given before 45 minutes significantly reduced Visual Analog Scale (VAS) scores during access opening and canal instrumentation compared to placebo (p<0.001) thus enhancing the success of inferior alveolar nerve block. This finding aligns with a systematic review and meta-analysis by Nagendra babu et al[5], which concluded that NSAID premedication significantly improves the anesthetic success of IANB in symptomatic irreversible pulpitis, with an overall relative risk of success approximately 1.5 times greater than placebo. Similarly, Shirvani et al[10] in their meta-analysis of 13 randomized controlled trials and Kazandag et al[11] reported that oral NSAIDs reduced intraoperative pain and improved pulpal anesthesia rates when administered preoperatively. Further, the age of the patients were not significantly different (p=0.749) in all groups, subsequently did not affect the success of the study results.

Success of inferior alveolar nerve block was significantly greater in patients premeditated with piroxicam when compared to etorocoxib and ketorolac. There were significant differences in distribution of pain after 45 minutes and during procedure (p-value <0.001). This result is similar to the study done by Wali et al[7] where piroxicam has shown 90% success rate compared to diclofenac potassium and naproxen sodium and Riaz M et al[12] with success rate of piroxicam 93% followed by tramadol and diclofenac sodium.

The post-hoc Tukey analysis revealed no statistically significant difference between etorocoxib and piroxicam during the instrumentation phase (p=0.71), suggesting clinical equivalence between the two agents in this setting despite their mechanistic differences. Piroxicam's pharmacokinetic advantage stems from its prolonged half-life of approximately 50 hours, the longest among conventional NSAIDs, combined with near-complete protein binding (99%) and low systemic clearance.[13] Additionally, piroxicam's inhibition of both COX-1 and COX-2 isoforms provides a broader anti-inflammatory profile, which may be particularly advantageous in the acutely inflamed pulpal environment[14] while etorocoxib a selective COX-2 reduces the synthesis of pro-inflammatory prostaglandin there by alleviating pain and inflammation associated with pulpal inflammation and has a half-life of 22 hours.

Ketorolac, a potent non-selective NSAID with notable analgesic rather than purely anti-inflammatory properties, demonstrated significant superiority over placebo in this study, consistent with previous investigations by Ganguly Saha et al[2] and Jena Aet al.[3]

Piroxicam and etorocoxib are mainly used for relieving postoperative pain after endodontic therapy[12,15,16] or after any surgical procedure, it has shown the efficacy of this drug as premedication.

This present study signifies the importance of premedication with oral analgesics on the success of inferior alveolar nerve block in patients with symptomatic irreversible pulpitis. These drugs have been shown as beneficial in providing relief in pain and inflammation in irreversible pulpitis and low side effect profile at the therapeutic doses which helps in providing effectiveness of inferior alveolar nerve block. Moreover, they have a short half-life, which would make them ideal for a single dosage prior to the management of severe pain.

CONCLUSION

From this present study, it can be concluded that in most of the cases there is difficulty in attaining profound local anesthesia in mandibular posterior teeth with symptomatic irreversible pulpitis by sole injection of conventional IANB. Oral premedication with ketorolac, piroxicam and etorocoxib decreases the pain sensation during access opening and instrumentation of canal in teeth with symptomatic irreversible pulpitis, among which piroxicam showed significant pain reduction with non-significant difference between piroxicam and etorocoxib.

REFERENCES

1. Parirokh M, Hatami N, Nakhaee N, Abbott P. Comparing the Efficacy of Premedication with Ibuprofen in Combination with an Inferior Alveolar Nerve Block and Primary Buccal Infiltration in Mandibular Molars with Irreversible Pulpitis: A Triple-blinded Randomized Clinical Trial. Iranian Endodontic Journal. 2022;17(4):165.

2. Saha SG, Jain S, Dubey S, Kala S, Misuriya A, Kataria D. Effect of oral premedication on the efficacy of inferior alveolar nerve block in patients with symptomatic irreversible pulpitis: a prospective, double-blind, randomized controlled clinical trial. Journal of clinical and diagnostic research: JCDR. 2016 Feb 1;10(2):ZC25.

3. Jena A, Shashirekha G. Effect of preoperative medications on the efficacy of inferior alveolar nerve block in patients with irreversible pulpitis: A placebo-controlled clinical study. Journal of Conservative Dentistry and Endodontics. 2013 Mar 1;16(2):171-4.

4. Henry MA, Hargreaves KM. Peripheral mechanisms of odontogenic pain. Dent Clin North Am 2007;51:19–44

5. Nagendrababu V, Pulikkotil SJ, Veettil SK, Teerawattanapong N, Setzer FC. Effect of nonsteroidal anti-inflammatory drug as an oral premedication on the anesthetic success of inferior alveolar nerve block in treatment of irreversible pulpitis: a systematic review with meta-analysis and trial sequential analysis. Journal of endodontics. 2018 Jun 1;44(6):914-22.

6. Hatipoğlu FP. Assessment of pain scales used in endodontic postoperative pain evaluation: frequency, advantages, and limitations. Journal of Endodontics and Restorative Dentistry. 2025 Mar 1;3(1):2-5.

7. Wali A, Siddiqui TM, Qamar N, Khan R, Jawaid N. Effectiveness of premedication with analgesics vs placebo for success of inferior alveolar nerve block in irreversible pulpitis. International Journal of Prosthodontics and Restorative Dentistry. 2012 Mar 1;2(1):5-9.

8. Hargreaves KM, Keiser K. Local anesthetic failure in endodontics: mechanisms and management. Endodontic topics. 2002 Mar;1(1):26-39.

9. Inchingolo AD, Marinelli G, Zaminga LP, Savino A, Dell'Anna FE, Inchingolo F, Tartaglia GM, Del Fabbro M, Palermo A, Di Venere D, Inchingolo AM. Effectiveness of anti-inflammatory premedication on inferior alveolar nerve block success in acute irreversible pulpitis: a systematic review. Exploration of Medicine. 2026 Feb 3;7:1001381.

10. Shirvani A, Shamszadeh S, Eghbal MJ, Marvasti LA, Asgary S. Effect of preoperative oral analgesics on pulpal anesthesia in patients with irreversible pulpitis—a systematic review and meta-analysis. Clinical oral investigations. 2017 Jan;21(1):43-52.

11. Karapinar-Kazandag M, Tanalp J, Ersev H. Effect of premedication on the success of inferior alveolar nerve block in patients with irreversible pulpitis: a systematic review of the literature. BioMed research international. 2019;2019(1):6587429.

12. Riaz M, Zafar F, Khalid Z, Sultan T, Wali A, Siddiqui TM. Comparison of Preoperative Analgesics on the Efficacy of Inferior Alveolar Nerve Block with Patients Having Symptomatic Irreversible Pulpitis: A Double-Blinded, Randomized Controlled Trial. EurEndod J. 2023;8:246–52.

13. Mohamed AF, El-Asfouri HA, Amin SA. Effect of sublingual fast-dissolving piroxicam premedication on postoperative pain experience in mandibular molars with non-vital pulp: a randomized double-blind controlled trial. Head & Face Medicine. 2024 Sep 21;20(1):52.

14. Kaushal, A., Verma, P., Singh, A. P., & Singh, A. P. (n.d.). A critical review of piroxicam: From mechanism to adverse effects in clinical use. International Journal of Innovative Research and Technology. Retrieved April 5, 2026

15. KrishnaprasadaL JM. A Comparative evaluation of the Efficacay of two oral medication on post operative pain following single visit root canal therapy–An in vivo study. Int J Med Sci. 2013;5(2):01-4.

16. Krishna A, Vedavathi B, Uppin V, Swapna DV. Effectiveness of Prophylactic use of Etoricoxib in Comparison with Ibuprofen on Postendodontic Pain-randomized Double-Blind, Placebo-controlled Study: An in vivo Study. World Journal of Dentistry. 2012 Dec 1;2(3):243-7.