Effectiveness of Pregabalin in Reducing Early Postoperative Complications following Third Molar Surgery

Dr. Gaurav Karna[1], Dr. Sandhya Joshi[2], Dr. Asmita Koju[3], Dr. Kishor Bhandari[4], Dr. Ishfa Banu Haque[4], Prof. Dr. Bandana Khanal[6]

[1-2,4-6]Oral and Maxillofacial Surgery Unit, Department of Dental Surgery, National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal
[3]Periodontology and Oral Implantology Unit, Department of Dental Surgery, National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal

Correspondence: Dr Gaurav Karna. Email: brucella.gaurav@gmail.com

ABSTRACT

Background: Surgical removal of impacted mandibular third molars is a common procedure in oral and maxillofacial surgery, often associated with postoperative pain, facial swelling, and trismus. While standard analgesics provide relief, multimodal analgesia using pregabalin has shown promise in mitigating these complications.

Objective: The study was done to compare postoperative pain, facial swelling and interincisal distance following third molar extraction in patients with or without pregabalin.

Materials and Methods: A prospective, comparative study was conducted on 136 patients requiring bilateral mandibular third molar extractions. Each patient served as their own control, receiving pregabalin with standard analgesia for one extraction and only standard analgesia for the other. Pain was assessed using the Visual Analogue Scale (VAS) at various intervals, while facial swelling and interincisal distance were measured on postoperative days 1, 3, 7, and 14.

Results: Visual Analogue Scale **(**VAS) scores were consistently lower in the pregabalin group ($p = 0.000$), though differences were not statistically significant. Percentage facial swelling was significantly reduced in the pregabalin group on postoperative days 1 ($p = 0.009$) and 3 ($p = 0.004$). However, no significant differences were observed on days 7 and 14. Similarly, there was no statistically significant improvement in interincisal distance between groups.

Conclusion: Pregabalin demonstrates efficacy as an adjuvant therapy for reducing early postoperative pain and swelling following third molar extraction. Further multicenter, randomized, double-blinded trials are recommended to validate these findings and optimize pregabalin use in oral surgical care.

Keywords: Pain; pregabalin; swelling; third molar surgery; trismus.

INTRODUCTION

The mandibular third molars, or wisdom teeth, are present in approximately 90% of the population, with one-third exhibiting at least one impacted third molar. Due to their high prevalence, the surgical removal of impacted mandibular third molars is one of the most frequently performed procedures in oral and maxillofacial surgery.[1, 2]

Postoperative complications such as pain, swelling, and trismus typically occur within the first 24 to 48 hours after surgery. These symptoms often disrupt daily activities, affecting patients' work and social lives, with an average absence from work of 1.6 days following the procedure.[2]

Although conventional pain management involves the use of Non-Steroidal Anti-Inflammatory Drugs (NSAID), opioids, and local anaesthetics, many patients still experience significant postoperative pain. Approximately 50% of patients report pain one week after surgery, despite receiving analgesic therapy.[3] This has led to the development of multimodal analgesia, combining different drugs to enhance pain relief and reduce side effects.[4]

Pregabalin, a promising candidate in multimodal analgesia, functions by binding to the alpha-2-delta subunit of voltage-gated calcium channels, reducing the release of neurotransmitters and preventing central sensitization.[5, 6] It has shown efficacy in controlling postoperative pain and swelling across various surgical procedures, including maxillofacial surgeries.[7]

This study aimed to evaluate the effectiveness of pregabalin as an adjunct therapy to standard analgesics in reducing postoperative pain, facial swelling, and trismus following mandibular third molar extraction. By addressing these postoperative challenges, we sought to contribute to the optimization of analgesic regimens in oral surgery.

METHODOLOGY

This prospective comparative study was conducted over 15 months, from April 2019 to July 2020, at the Oral and Maxillofacial Surgery Unit, Department of Dental Surgery, National Academy of Medical Sciences (NAMS), Bir Hospital, Kathmandu, Nepal. The study included 136 patients requiring bilateral mandibular third molar extractions. Each patient acted as their own control, with one side serving as the test group (receiving pregabalin) and the contralateral side as the control group (without pregabalin). Non-probability convenience sampling was used to select participants.

Patients aged 18–40 years with bilaterally impacted mandibular third molars of comparable technical difficulty were included. Indications for extraction included pericoronitis, unrestorable decay, or severe periodontitis. Eligible patients were classified as ASA I or II under the American Society of Anesthesiologists guidelines and had to be capable of self-assessing pain using the Visual Analogue Scale (VAS). Excluded from the study were patients with impaired renal or liver function, pregnant patients, those with psychiatric illnesses, allergies to pregabalin, or those currently using it. Patients requiring inpatient care or parenteral medications post-extraction were also excluded.

Ethical clearance was obtained from the Institutional Review Board (IRB) of NAMS, Bir Hospital, and written informed consent was obtained from all participants prior to enrollment. Each patient underwent two separate extractions with a minimum washout period of three weeks. For the test group, a 75 mg dose of pregabalin was administered orally every 12 hours for three days, starting one-hour post-surgery, alongside a standard ibuprofen-paracetamol regimen. The control group received only the standard ibuprofen-paracetamol regimen. Randomization was achieved using sealed envelopes, and both patients and surgeons were blinded to group assignments.

Preoperative and postoperative data (on days 1, 3, 7 & 14) were meticulously recorded. VAS (Visual Analogue Scale) was used to compare pain levels. Horizontal facial measurement was taken as the distance between the corner of the mouth and the ear lobe, while vertical measurement spanned from the outer canthus of the eye to the angle of the mandible. The difference in postoperative & preoperative facial measurement was expressed as % Facial Swelling. Similarly, interincisal distance was recorded as the vertical gap between the incisal edges of maxillary and mandibular central incisors during maximum mouth opening.

All surgeries were performed by the same surgeon following a standardized protocol. Modified Ward's incisions were used, and mucoperiosteal flaps were elevated. Necessary osteotomies and odontectomies were carried out, and wounds were closed with 3-0 silk sutures.

SPSS version 20.0 was used for statistical analysis, with normality tested using the Shapiro-Wilk test. The Non-Parametric Wilcoxon Signed-Rank test was applied for non-normally distributed data, with significance set at $p<0.05$.

Figure 1**:** Horizontal facial measurement

Figure 2**:** Vertical facial measurement

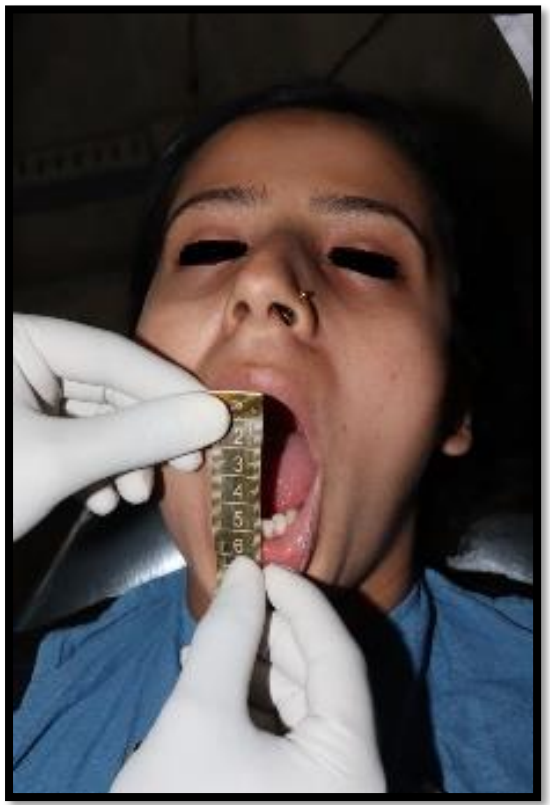

Figure 3**:** Interincisal distance measurement

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RESULTS

The study enrolled a total of 136 patients with a mean age of 27.87 ± 6.54 years (age range: 16–48 years), with equal gender distribution. The mean weight of the participants was 59.35 ± 7.94 kg, and the median washout period between extractions was 34 days (Q1–Q3: 32–40 days). Surgical difficulty index and surgery duration did not significantly differ between the two groups.

Visual Analogue Scale (VAS) Scores

The VAS scores were consistently higher in the control group compared to the test group at all time points, with statistically significant differences ($p = 0.000$). The median VAS scores at 2, 4, 8, 12, 24, 48, and 72 hours post-surgery for both groups are presented in Table 1 and Figure 4.

Facial Swelling and Mouth Opening Measurements

Percentage facial swelling was significantly lower in the pregabalin group on postoperative Day 1 (2.32 [1.77–2.95] vs. 2.32 [1.82–3.60], $p = 0.009$) and Day 3 (6.67 [5.17–8.44] vs. 7.49 [5.77–9.43], $p = 0.004$) compared to the control group. No significant differences were observed in facial swelling on Days 7 and 14.

Similarly, Mouth opening measurements (Interincisal Distance - IID) did not show significant differences between the two groups at any of the postoperative time points ($p > 0.05$).

Table 1: Comparison of median Visual Analogue Scale scores between test & control

Variables	Test	Control	*p-value*
VAS score at 2h	7 (6 – 8)	8 (6 – 8)	0.000
VAS score at 4h	5 (4 – 6)	6 (4.25 – 7)	0.000
VAS score at 8h	4 (3 – 5)	6 (4 – 6)	0.000
VAS score at 12h	4 (2 – 4)	5 (4 – 6)	0.000
VAS score at 24h	2 (2 – 4)	4 (3 – 5)	0.000
VAS score at 48h	2 (1 – 3)	3 (2 – 4)	0.000
VAS score at 72h	1 (1 – 2)	2 (2 – 3)	0.000

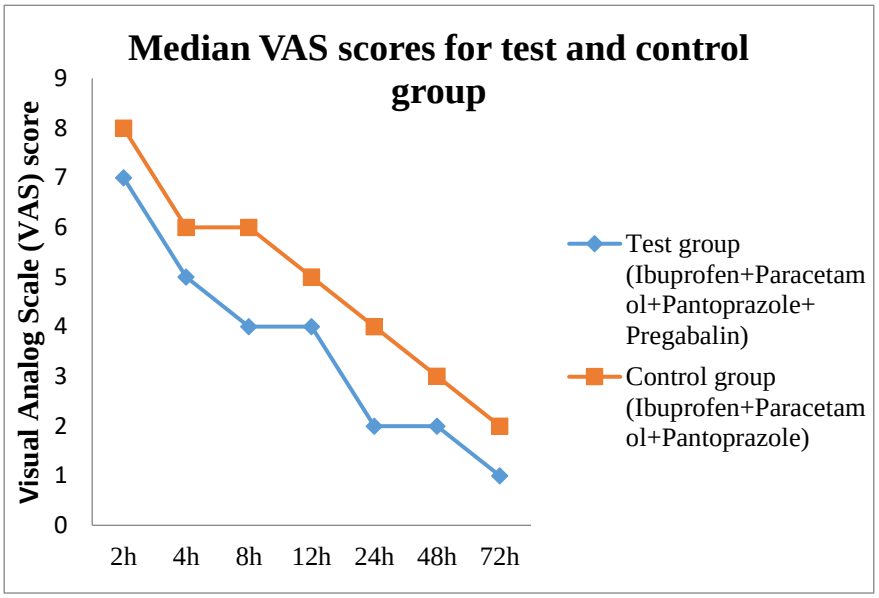

Figure 4: Graph showing median VAS scores for test & control group

Table 2: Comparison of Percentage Facial Swelling (% FS) and mouth opening measurements (IID- Interincisal Distance) between test & control groups

	Variables	Test	Control	*p-value*
Day 1	% FS	2.32 (1.77 – 2.95)	2.32 (1.82 – 3.60)	**0.009***
	IID	22 (18 – 25)	20 (18 – 25)	0.743
	% IID	52.63 (44.04 – 59.45)	55.44 (45.43 – 60.41)	0.817
Day 3	% FS	6.67 (5.17 – 8.44)	7.49 (5.77 – 9.43)	**0.004***
	IID	28 (25 – 32)	28 (24 – 30)	0.384
	% IID	38.15 (29.45 – 44.44)	40.00 (30.95 – 46.11)	0.351
Day 7	% FS	0.95 (0.46 – 1.86)	0.98 (0.47 – 2.00)	0.279
	IID	35 (32 – 38)	34 (32 – 38)	0.632
	% IID	22.95 (12.66 – 29.73)	24.16 (13.60 – 29.95)	0.757
Day 14	% FS	0.00 (0.00 – 0.00)	0.00 (0.00 – 0.00)	0.575
	IID	42 (40 – 45)	42 (40 – 45)	0.873
	% IID	5.33 (2.15 – 10.61)	5.94 (0.53 – 10.81)	0.902

DISCUSSION

Third molar extraction is one of the most common procedures performed by oral and maxillofacial surgeons worldwide, frequently resulting in postoperative pain, facial swelling, and trismus.[8] The management of postoperative pain generally involves local anaesthetics, opioids, and cyclooxygenase inhibitors. However, studies indicate that postoperative pain remains under-managed, particularly after third molar extractions.[2]

Evans et al.[5] emphasized that early identification of patients at risk for severe postoperative pain, combined with a multidisciplinary approach and multimodal analgesia can reduce complications, patient distress, and the risk of chronic pain development. Pregabalin, initially developed as an anticonvulsant, has shown efficacy in postoperative pain management by inhibiting central sensitization associated with surgical tissue damage.[3] This ability makes it a promising addition to multimodal analgesia strategies.

The present study evaluated the effectiveness of a 75 mg dose of pregabalin as an adjunct to standard analgesic therapy following bilateral mandibular third molar

extraction. This dose was selected to minimize adverse effects, as higher doses (e.g., 300 mg) are associated with dizziness and somnolence.[4] The study targeted patients predominantly in their second decade of life, as individuals aged between 17 and 27 years are the most likely to require surgical intervention for impacted mandibular third molars.[9]

Consistent with previous studies, patients in the pregabalin group reported lower VAS scores at all postoperative time points. Although the differences in pain scores between the test and control groups were not statistically significant, they reflect a clinically relevant trend in favour of pregabalin administration. Zhang et al.[6] reported similar findings, where cumulative opioid consumption was significantly reduced in patients treated with pregabalin, highlighting its opioid-sparing potential.

Facial swelling was significantly lower in the pregabalin group on postoperative Days 1 and 3, but no differences were noted on Days 7 and 14. These results suggest that pregabalin effectively reduces early-stage inflammation, aiding in the initial recovery phase.[7] However, no significant differences in mouth opening measurements (IID) were observed between the two groups, indicating that pregabalin might not substantially impact trismus reduction.[10]

CONCLUSION

Pregabalin effectively reduces postoperative pain and swelling following mandibular third molar extraction, as evidenced by lower VAS scores and reduced swelling. While these findings support the inclusion of pregabalin in postoperative protocols, further research through multicentre, randomized trials are recommended to confirm its benefits, optimize dosing, and explore its potential to reduce opioid consumption.

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Conflict of Interest: None

REFERENCES

1. Yolcu Ü, Acar A. Comparison of a new flap design with the routinely used triangular flap design in third molar surgery. Int J Oral Maxillofac Surg. 2015;44(11):1390-7. [PubMed | Full Text | DOI]

2. Olmedo-Gaya MV, Manzano-Moreno FJ, Galvez-Mateos R, et al. Oral pregabalin for postoperative pain relief after third molar extraction: a randomized controlled clinical trial. Clin Oral Investig. 2016;20(7):1819-26. [PubMed | Full Text | DOI]
3. Mishriky B, Waldron N, Habib A. Impact of pregabalin on acute and persistent postoperative pain: a systematic review and meta-analysis. Br J Anaesth. 2015;114(1):10-31. [PubMed | Full Text | DOI]
4. Sbirkova TI, Neychev DZ, Raycheva RD, et al. Factors which Influence Postoperative Pain Intensity after Surgical Removal of Impacted Mandibular Third Molars. J of IMAB. 2019;25(4):2793-9. [Full Text | DOI]
5. Evans S, McCahon R. Management of postoperative pain in maxillofacial surgery. Br J Oral Maxillofac Surg. 2019;57(1):4-11. [PubMed | Full Text | DOI]
6. Zhang Y, Wang Y, Zhang X. Effect of pre-emptive pregabalin on pain management in patients undergoing laparoscopic cholecystectomy: a systematic review and meta-analysis. Int J Surg. 2017;44:122-7. [PubMed | Full Text | DOI]
7. Ahiskalioglu A, İnce İ, Aksoy M, et al. Effects of a single-dose of pre-emptive pregabalin on postoperative pain and opioid consumption after double-jaw surgery: a randomized controlled trial. J Oral Maxillofac Surg. 2016;74(1):53. e1-. e7. [PubMed | Full Text | DOI]
8. Colorado-Bonnin M, Valmaseda-Castellón E, Berini-Aytés L, et al. Quality of life following lower third molar removal. Int J Oral Maxillofac Surg. 2006;35(4):343-7. [PubMed | Full Text | DOI]
9. Contar C, Kanegusuku K, Berticelli R, et al. Complications in third molar removal: a retrospective study of 588 patients. Med Oral Patol Oral Cir Bucal. 2010;15(1):e74-8. [PubMed | Full Text | DOI]
10. Li H, Yao Q, Huang X, et al. Therapeutic effect of pregabalin on radiotherapy-induced trismus in nasopharyngeal carcinoma patients. Eur Ann Otorhinolaryngol Head Neck Dis. 2019;136(4):251-5. [PubMed | Full Text | DOI]