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Effect of intravenous dexamethasone on post-operative inflammatory sequelae after third molar surgery: A split-mouth comparative study

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Abstract

Introduction: Postoperative inflammatory sequelae following surgical removal of third molars adversely affect the quality of life for patients. Dexamethasone is well known to suppress inflammation. As acute inflammation peaks around post-operative day 1 to 3, a single dose of parental dexamethasone (having long half-life long half-life of 36 to 72 hours) is effective. This comparative study aims to evaluate the effect of intravenous dexamethasone on post-operative inflammatory sequelae after third molar surgery.

Method: In a prospective comparative study at Nepal Medical College and Teaching Hospital, Kathmandu, Nepal, from Aug 2025 to Oct 2025, 51 patients underwent surgical extraction of bilaterally symmetrical mandibular third molars in two sessions on an outpatient basis following ethical approval. Fifty-one patients received a single dose of 8 mg intravenous dexamethasone 30 minutes before extraction at one site and normal saline as a placebo on the contralateral site. Post-operative pain, swelling, and trismus were evaluated on the first, third, and seventh post-operative days. The IBM SPSS was used to analyse data. For descriptive analysis, Mean±SD was used after confirming normality (Kolmogorov-Smirnov test) and a paired t-test for comparison of continuous variables. A $p \leq 0.05$ was considered significant.

Result: Dexamethasone injection group showed significantly less pain than the control group at postoperative day 1 and less swelling on day 3. There was no statistically significant difference in mean maximal mouth opening between the two groups on any day.

Conclusion: Prophylactic intravenous administration of dexamethasone was effective in reducing postoperative pain and swelling after third molar surgery.

How to cite

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Introduction

Postoperative inflammatory sequelae of pain, swelling and trismus following surgical removal of third molars affect the quality of life for patients.¹ Dexamethasone is a synthetic, long-acting corticosteroid (half-life, 36-72 hours) with high anti-inflammatory potency.² A single dose before surgery is rationale as acute inflammation peaks around post-operative day 1 to 3.³

Intravenous administration provides excellent and immediate plasma drug levels compared to intramuscular route which depends on blood flow to the site of administration, and oral route has a slowest onset of action and absorption.⁴ A meta-analysis suggested that dexamethasone may be more effective than methylprednisolone when administered preoperatively at comparable doses in lower third-molar surgery for swelling and trismus.⁵ A dose of 8 mg is widely used because it roughly approximates the maximum physiological cortisol release during physical stress. Studies showed that 8 mg was more effective than 4 mg at reducing facial swelling and trismus.^{6,7}

Bilaterally symmetrical impactions in same individual is less frequently reported.^{8,9} There is lack of common consensus among clinicians regarding routine use of parental dexamethasone in third molar surgeries. Hence this study was undertaken to evaluate the effects and efficacy of intravenous dexamethasone 8 mg given 30 minutes pre-operatively to observe postoperative inflammatory sequelae following surgical removal of third molars.

Method

This prospective split-mouth comparative study was conducted in the Department of Oral and Maxillofacial Surgery, Nepal Medical College and Teaching Hospital after prior approval from the institutional review committee, ref number: 03-082/083. A total of 51 participants fulfilling the inclusion criteria were selected consecutively for surgical removal of bilaterally symmetrical lower third molars in two sessions,

with at least a 2-week interval between sessions from Aug 2025 to Oct 2025 on outpatient basis after obtaining their written informed consent. This sample size was calculated by using two tailed tests, formula ' $n=(Z_{\alpha/2}+Z_{\beta})^2 \cdot 2\sigma^2/d^2$ ' reported in previous study.¹⁰ A power of 80 % with a 0.05 level of significance, the n =required sample size, σ =Population variance (standard deviation) and d =the difference in effect of two interventions which required $Z_{\alpha/2} = 1.96$, α =Significance level, $Z_{\beta}=0.84$ (Critical value for 80% power).

Inclusion criteria were healthy patients according to the American Society for Anaesthesiologists categorized (ASA) I and had bilaterally symmetrical lower third molars according to Pell and Gregory's classification assessed radiographically from their Orthopantomogram (OPG). Exclusion criteria were a clinically significant medical history (e.g., systemic infective disease, heart and vascular disease, liver disease, haematological disease, deficiency of coagulation, diabetes and neoplastic disease), active oral infection, recent anti-inflammatory treatment, chronic use of medications that would obscure assessment of the inflammatory response (e.g., antihistamines, NSAIDs, steroids and antidepressants) and pregnant or lactating women.

Each patient received a single dose of 8 mg intravenous dexamethasone via dorsal venous arch on the back of hand 30 minutes prior to extraction. In next session, intravenous normal saline as placebo was administered 30 minutes prior to extraction from the contralateral site. Computer-generated 2 digits randomized table and coin tossing technique were used to allocate the drug and extraction side on the first operation. One researcher was fixed for this allocation process and prepared identical unmarked syringes containing either dexamethasone or placebo before surgery. The same oral and maxillofacial surgeon operated on each participant. Another researcher assessed the clinical outcomes of all participants. The participants, surgeon and assessor were unknown for drug in use.

Local anaesthetic agent (2% lignocaine hydrochloride with 1:200000 epinephrine) was administered using inferior alveolar, lingual and long buccal nerve block. Standard Ward or modified Ward's incision with full thickness mucoperiosteal flap was routinely designed.¹¹ Then ostectomy and tooth sectioning if deemed necessary was done using slow-speed surgical hand-piece and tungsten-carbide bur. Following tooth extraction, the socket was carefully inspected, irrigated with normal saline and the flap sutured back with interrupted sutures using 3-0 silk suture. After all extractions, patients were given standard postoperative instructions, standard antibiotic therapy (amoxicillin and clavulanic acid, 625mg thrice a day) for 5 days or alternative (azithromycin 500 mg/day for 3 days) if allergic to penicillin and analgesic (acetaminophen 500 mg four times a day for 3 days).

Facial dimension, maximal mouth opening and pain were recorded pre-operatively then on post-operative day 1, 3 and 7. Facial oedema was evaluated by measuring the distance from the outer lateral canthus of eye to gonion, tragus to corner of mouth and tragus to

pogonion.¹² Trismus was evaluated as the difference in inter-incisal distance at maximum opening in millimetres using Vernier calliper before and after the operation.¹³ Severity of patient pain perception was assessed via a simplified visual analogue scale (VAS).¹⁴ The collected data was compiled, processed and analysed by IBM SPSS version 16. Descriptive data was analysed using mean and standard deviation. Normality test was confirmed with Kolmogorov-Smirnov test normality test and paired t-test was used for continuous variables to test significance at 5% level.

Result

Out of a total of 51 patients with bilaterally symmetrical impacted mandibular third molars, 14(27.5%) were males and 37(72.5%) females. The mean age was 30.8±9.6 years, range 18 to 52 years. Vertical, Position A and Class II were the most common pattern of third molars in the present study, Table 1.

There was no statistically significant difference in duration of operation between the two groups, Table 2.

Table 1. Pattern of third molars based on radiographic examination, n=51

Classification	Categories	n(%)
Winter's classification (Angulation of third molar)	Mesioangular	15(29.4)
	Vertical	18(35.3)
	Horizontal	10(19.6)
	Distoangular	8(15.7)
Pell and Gregory classification (Position of tooth in relation to the occlusal plane)	Position A	24(47.1)
	Position B	22(43.1)
	Position C	5(9.8)
Pell and Gregory category (space available between the anterior border of ascending ramus and the distal aspect of the 2nd molar)	Class I	19(37.3)
	Class II	29(56.9)
	Class III	3(5.9)

Table 2. Comparison of duration of operation between dexamethasone and placebo groups, n=51

Dexamethasone (Mean±SD)	Placebo (Mean±SD)	Mean difference	95% Confidence Interval		p-value
			Lower bound	Upper bound	
43.67±8.23	44.22±9.06	-0.549	-2.089	0.991	0.477

Paired t-test, p-value<0.05 statistically significant

Mean VAS score at post-operative day 1 was significantly higher in placebo group (3.24) than Dexamethasone group (2.51), p-value 0.039. However, there was no statistically significant difference in mean VAS scores at post-operative day 3 (p-value 0.087) and post-operative day 7 (p-value 0.851), Figure 1

Mean facial dimension at post-operative day 3 was found to be significantly higher in placebo group than dexamethasone group (p-value 0.001).

However, there was no statistically significant difference in mean facial dimension measurements between the two groups pre-operatively, at post-operative day 1 and post-operative day 7, Table 3.

There was no statistically significant difference in mean maximal mouth opening between two groups pre-operatively (p-value 0.308) and at any post-operative time points, Table 4.

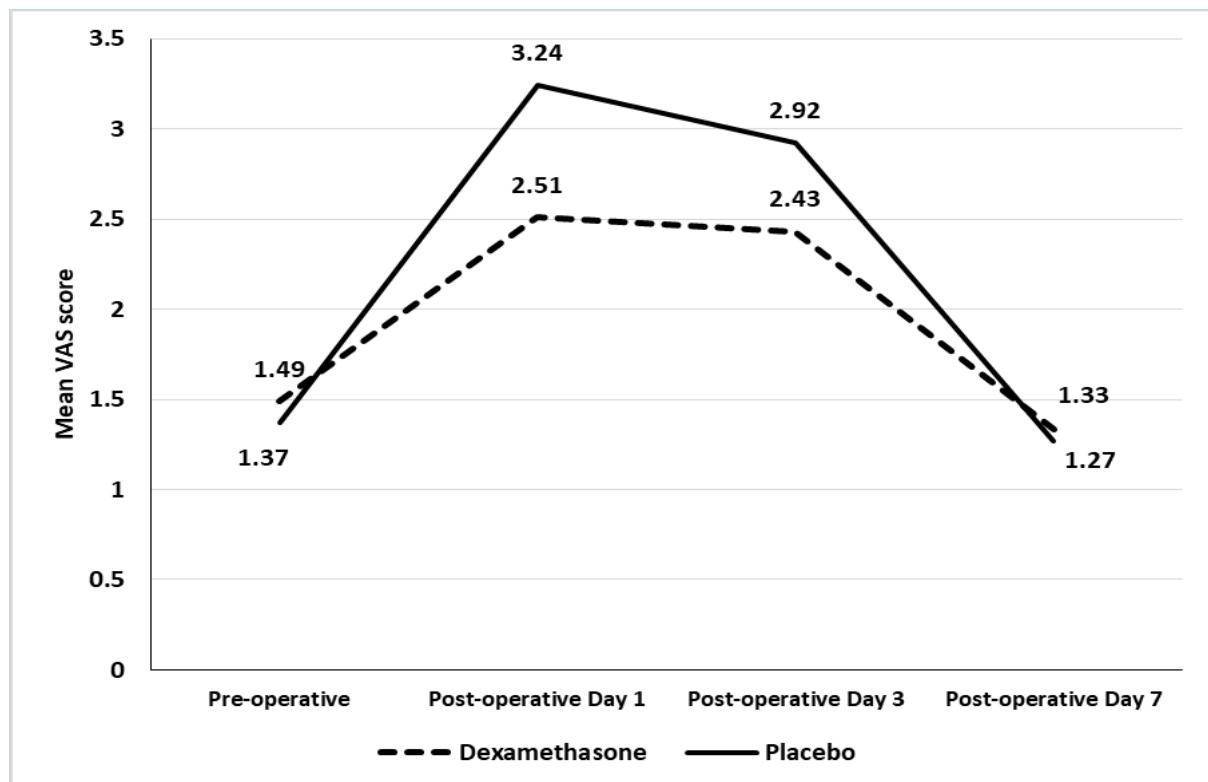


Figure 1: Line diagram showing comparison of VAS score using paired t test between dexamethasone and placebo groups, n=51

Table 3. Comparison of facial dimension measurements pre- and postoperative between dexamethasone and placebo groups, n=51

Time intervals	Dexamethasone (Mean±SD)	Placebo (Mean±SD)	Mean difference	95% CI		Dexamethasone (Mean±SD)	
				Lower bound	Upper bound		
Pre-operative	119.49±5.85	118.53±6.01	0.967	-0.220	2.154	0.108	
Post-operative day	D1	120.01±6.08	120.65±5.73	-0.641	-1.828	0.545	0.283
	D3	120.92±6.47	123.08±5.82	-2.169	-3.353	-0.984	0.001
	D7	118.73±6.61	120.01±6.38	-1.282	-2.568	0.004	0.051

Paired t-test, p-value<0.05 statistically significant

Table 4. Comparison of maximal mouth opening in mm at pre- and postoperative between dexamethasone and placebo groups, n=51

Time intervals		Dexamethasone (Mean±SD)	Placebo (Mean±SD)	Mean difference	95% CI		Dexamethasone (Mean±SD)
					Lower bound	Upper bound	
Post-operative		48.05±7.09	48.94±5.84	-0.892	-2.631	0.847	0.308
Post-operative day	D1	41.81±9.46	40.94±9.59	0.869	-1.797	3.534	0.516
	D3	44.87±7.21	43.87±7.54	1.008	-0.897	2.913	0.293
	D7	46.52±7.14	47.19±7.12	-0.671	-2.377	1.036	0.434

Paired t-test, p-value<0.05 statistically significant

Discussion

This study found that pain at post-operative day 1 was significantly higher in placebo group (3.24) than Dexamethasone group (2.51), and facial oedema was more on day 3 in placebo group than dexamethasone group.

Many authors have advocated the use of corticosteroids to limit postoperative oedema due to their suppressive action on trasudation,^{15,16,17} and some have made definitive recommendations based on randomized clinical trials.^{15,18} A systematic review on the use of corticosteroids and nonsteroidal anti-inflammatory medication for the management of pain and inflammation after third molar surgery found that a single large dose or a short duration of corticosteroid therapy causes few adverse effects and can be valuable in minimizing complications post third molar surgery.⁴ In the present comparative study, patients with bilaterally symmetrical lower third molars were enrolled in whom one of the extraction sides was used as study in random while the contralateral side acted as control. The main advantage of a split-mouth study is its high efficiency, as each patient serves as their own control, eliminating inter-subject variability (like age, genetics, oral hygiene) and requiring fewer participants for to detect treatment effects. It also offers superior precision by comparing treatments within the same person, making results more reliable.¹⁹

In split-mouth studies involving surgical tooth extractions, common clinical protocols use a washout period of at least two weeks between procedures. This duration is considered sufficient for the effects of a single dose of dexamethasone to resolve and prevent carry-over effects between the two surgical sites. A single dose can suppress the body's natural cortisol production (hypothalamic-pituitary-adrenal axis) for up to one week, with most values returning to normal by that time.²⁰ Thus, in present study we kept the washout period of 2 weeks.

We did not observe significant difference in surgical times between the groups because the surgeon and the pattern of third molars was bilaterally symmetrical. There were no adverse effects like nausea, dizziness, injection site reaction observed. The only disadvantage was that patients had to wait half hour before the operation.

Preoperatively, both groups demonstrated comparable baseline facial measurements. Dexamethasone decreased post-operative facial swelling by reducing the release of inflammatory mediators.²¹ On postoperative day 3, when maximum swelling is expected,^{17,18} the dexamethasone group showed significantly lesser facial dimensions compared to the placebo group. However, on postoperative day 7, there was a comparable decreased swelling in both groups. Studies have reported a significant decrease in facial swelling on day 2

after operation using dexamethasone given pre-operatively.^{6,22} However, both reported non-significant effects on swelling at seventh post-operative day, similar to our study. The results suggest that while oedema gradually subsides and recovers within seven days, dexamethasone significantly prevents excessive swelling in the initial days which can be due to its half-life of 36-72 hours.

Acute postoperative pain following third molar extraction is predominantly a consequence of inflammation caused by tissue injury.²³ It has been reported that steroids can be related to a reduction in the number of analgesic tablets used after surgical extractions.^{16,24} Dexamethasone in particular appears to decrease pain after surgery.^{6,22,25} In addition to reducing release of inflammatory mediators, its ability to reduce swelling may amplify their analgesic effect by lessening pain that arises from tissue tension. In the present study, patients who received intravenous dexamethasone reported significantly lower pain levels compared to placebo group on post-operative day 1. By post-operative day 7, pain levels had substantially decreased in both groups and were nearly identical, indicating similar recovery in both groups by one-week post-surgery. A comparative study on 64 patients undergoing third molar extraction who were administered 4 mg of dexamethasone either submucosal or intravenous found that intravenous group expressed statistically significant ($p < 0.01$) reduction in pain compared to the submucosal group during immediate and second postoperative days.² But, by post-operative day 7, pain levels had substantially decreased in both groups and were nearly identical, which is similar to our study. A comparative study found that intravenous administration of 8 mg dexamethasone significantly decreased post-extraction pain compared to intralesional 8 mg dexamethasone.²⁶ This effect of dexamethasone on limiting pain intensity was also observed in another study.⁷ However, a study was unable to show that administration of a steroid significantly reduced pain.²⁷ This contradiction might be due to difference in pain evaluation method where postoperative pain

was evaluated by having the patients report the number of analgesic tablets required whereas we used VAS scale which was subjective to patient's perception of pain.

It is worth mentioning that corticosteroids have been reported to have synergistic effects with both local anaesthesia given for surgery²⁸ and analgesics particularly NSAIDs prescribed post-surgery as well.^{29,30} Thus, it is unclear at this point whether the reduced pain experienced by patients has arisen from their synergistic effect with local anaesthetic agents given or from their synergistic effect with the analgesics prescribed. Detailed studies with pain as the primary outcome are needed to confirm the present observation.

Trismus can be a manifestation of pain, swelling or both.³¹ In a randomized prospective double-blind study,²⁶ both preoperative local infiltration and intravenous administration of 8 mg dexamethasone significantly reduced postoperative trismus after surgical removal of mandibular third molars. Similar study found that pre-operative intravenous dexamethasone effectively reduced trismus.^{32,33} However, in the present study, no statistically significant differences in trismus were observed between the two groups at any postoperative time point, indicating that intravenous dexamethasone administration failed to provide beneficial effects against trismus following third molar surgery. A meta-analysis of randomized controlled trials on the effect of submucosal injection of dexamethasone after third molar surgery showed no statistically significant effect regarding trismus.³⁴ Another study also found no significant differences between the intramuscular 8 mg dexamethasone and control groups on the maximum interincisal distance preoperatively, immediately after surgery, and on postoperative days 2 and 7.²³ It is known that inflammation may only be one of the many factors leading to trismus after a third molar surgery. Other factors that may exacerbate trismus include prolonged surgical time, traumatic extraction, accidental injection of a local anaesthetic agent into the medial pterygoid muscle and surgical difficulty due to tooth pattern which vary between studies.

Additionally, differences in dosage and routes of administration among the studies may have produced such varied results.

In the present study, swelling was assessed as the differences in distance between number of external facial points which is a commonly used method. It is important to highlight that the measurement of facial swelling is difficult to accurately quantify, since the facial surface is irregular and convex. In addition, the same quantity of swelling may occur internally or externally, depending on the facial area involved, and can be more or less visible, which hinders comparisons. Furthermore, this method is less sensitive for three-dimensional swelling compared to facial volumetry (photogrammetry, 3d imaging).³⁵ There are different ways for pain assessment. The present study used subjective VAS score which unlike objective measures like number of rescue analgesic tablets consumed can be less reliable.³⁶ The systemic effects of iv dexamethasone (transient metallic taste, mild euphoria) even after a short term administration³⁷ could potentially un-blind patient/assessor introducing bias. The present study considered short 7day observation which covers inflammatory phase but does not capture delayed complications/resolution of sequelae. Comparisons regarding timing of administration, different dose regimens and routes of administration would have further heightened the clinical impact of this study.

Some of the limitations of this study are assessments of pain relied on a subjective VAS which may be influenced by individual patient perception and is less objective than quantifiable measures such as analgesic consumption. Evaluating facial swelling through linear measurements between external landmarks is a conventional technique unlike advanced methods like 3D volumetry for oedema. Systemic effects of intravenous dexamethasone (e.g., transient metallic taste) could reveal group allocation to participants or the assessor, introducing measurement bias. The limited seven days observation may not capture delayed complications. Finally, a single centre study with a sample predominantly

comprising female patients may affect the generalizability of the findings. Future research with wider population, objective outcome measures, longer follow-up, and comparisons across different doses would help to further clarify the role of dexamethasone.

Conclusion

The pre-operative intravenous administration of a single dose of 8 mg dexamethasone appears promising in reducing post-operative pain and swelling following third molar surgery with virtually no adverse effects. It is about time clinicians rethink their reluctance to use this safe and simple method in third molar surgery, especially with just one dose given pre-operatively.

Author contribution

Conception, design: USG, AB, RJ; Data acquisition: All; Data analysis, interpretation: RSJ; Drafting: USG, AB; Revision: All; Final approval of the version to be published: All; Agreement to be accountable for all aspects of the work: All.

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Conflict of interest

None

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Supplementary material

Data and supplementary material that support the findings of this study are available from the corresponding author upon reasonable request.

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