

Comparison of Serratiopeptidase and Dexamethasone in Controlling Oedema Following Surgical Extraction of Impacted Mandibular Third Molar

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ABSTRACT

Introduction: The extraction of the lower impacted third molar teeth is always associated with varying degrees of inflammation that may have a social impact for the patients.

Objective: To compare the effectiveness of dexamethasone and serratiopeptidase in the control of swelling following surgical extraction of impacted mandibular third molar.

Methodology: This non-randomised controlled trial was conducted among 180 individuals undergoing extraction of mandibular third molar in the Oral Surgery department of Kathmandu Medical College and Teaching Hospitals (KMCTH) at Duwakot, Bhaktapur and at Sinamangal, Kathmandu, Nepal from 2021 October to 2022 February. Among them, 90 patients received dexamethasone and 90 received serratiopeptidase. Effectiveness of these drugs in post-operative swelling were evaluated. Data were analysed in SPSS version 20. Mean standard deviation, median, frequency and percentage were calculated. Wilcoxon Sign Rank test was done for pairwise comparison of each medication. Mann-Whitney U test was done for comparing pre- and post-operative swelling among two medications.

Result: Significant differences were observed in both the groups when preoperative gonion to corner of mouth ($p < 0.001$), tragus to corner of mouth ($p < 0.001$), outer canthus to gonion ($p < 0.001$), and cheek girth measurements ($p < 0.001$) were compared with three consecutive post-operative period measurements. However, when two groups were compared, there was no significant differences observed in these measurements in either preoperative or three post-operative observation periods.

Conclusion: The findings of this study showed that both dexamethasone and serratiopeptidase were equally effective in controlling the post-operative swelling.

Keywords: Dexamethasone; impaction; oedema; serratiopeptidase.

INTRODUCTION

Surgical extraction of impacted mandibular third molar is routine procedures with inevitable post-operative complications like facial swelling, trismus, pain which adversely affects quality of life.¹⁻³ Post-operative facial swelling depends upon nature of surgery and patient factors.⁴ Tissue injury prompts inflammation, releasing mediators like bradykinin, serotonin, and histamine, which cause vasodilation, increased vessel permeability, and fluid accumulation in interstitial spaces, resulting in oedema.^{5,6}

Citation

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The swelling is maximum at second and third post-operative day and begins to reduce by fourth day.^{3,7,8} Post-operative oedema can be managed with cold therapy, drains, and pharmacological agents like antihistamines, steroids, and enzyme or combinations of these based on severity. No single modality fully controls post-operative swelling.³ Steroids are considered to be best in controlling swelling.^{3,9} Dexamethasone is a long acting potent glucocorticoid, with minimal mineralocorticoid action, acts as an anti-inflammatory agent interfering the pathways that release inflammatory mediators and vasodilation.^{5,10} Short term use of steroids, does not cause adrenal suppression with clinically insignificant side effects.^{4,11,12} Serratiopeptidase, a proteolytic enzyme, breaks down bradykinin, powerful vasodilator, thus minimise post-operative oedema.^{6,13} Limited studies have examined the effectiveness of these two pharmacotherapies in managing post-operative swelling, however, there have been no publications focussing on the Nepali population as of yet. This study aims to compare the effectiveness of dexamethasone and serratiopeptidase to control oedema following surgical extraction of impacted mandibular third molar.

METHODOLOGY

This quantitative non-randomised controlled trial was conducted among 180 individuals who visited the Oral and Maxillofacial Surgery Department of Kathmandu Medical College and Teaching Hospital (KMCTH) at Duwakot, Bhaktapur and at Sinamangal, Kathmandu, Nepal from 2021 October to 2022 February. Ethical approval was obtained from the Institutional Review Committee of the same institute (Ref. 0410202105). Informed consent was taken from all the study participants prior to the study. A convenience sampling method was used for selection of study participants. Individuals with bony impaction, partially erupted third molars and individuals willing to participate were included in the study. Those with contraindications of extractions such as haemangioma, haemophilia, recent history of myocardial infarction, recent swelling, or infection in the area of surgery, patients under proteolytic drugs or steroids, pregnant patients and patients with contraindication for use of steroids such as peptic ulceration, hypertension, immunocompromised patients were excluded.

The sample size was calculated using the following formula:

With reference to the study done by Kumar et al.,⁷ the sample size of 180 was calculated using formula: $n = 2SD^2(Z_{1-\alpha/2} + Z_{\beta})^2 / (m_1 - m_2)^2$; where,

$Z_{1-\alpha/2} = 1.96$ at 95% confidence interval; $Z_{\beta} = 0.84$ at 80% power; $m_1 =$ mean swelling size of dexamethasone group at day-3 after surgical extraction = 113.62; $m_2 =$ mean swelling size of serratiopeptidase group at day-3 after surgical extraction = 116.30; SD = standard deviation where, $SD = (SD_1 + SD_2) / 2 = (6.53 + 5.94) / 2 = 9.5$.

Applying these values in the formula provided above, the sample size (n) = 84.90. Now, adding 5% of attrition rate, final sample size in each group was around 90 (180 in total). Oral examination was done by the investigator himself and data were recorded on every follow up visits. Patients were divided into two groups, Group A and Group B and prescribed with Serratiopeptidase and Dexamethasone alternatively as they undergo surgical extraction with time until the sample size in each group was reached. Group A received 1 mg dexamethasone, half hour preoperatively and then at every eighth hour post-operatively for three days. Group B received 10 mg serratiopeptidase eighth hourly for three days. The facial volume was measured from corner of mouth to tragus, corner of mouth to gonion and outer canthus to gonion both preoperatively and post-operatively immediately, first, second, third day post-operatively using vernier caliper. The obtained data was entered into the Microsoft Excel sheet and analysed using SPSS software, version 20 (IBM Corp., Armonk, N.Y., USA). Mean standard deviation, median, frequency and percent were calculated. Wilcoxon Sign Rank test was done for pairwise comparison of each medication. Mann-Whitney U test was done for comparing pre-and post-operative swelling among two medications.

RESULT

Among the 180 participants divided in two groups, mean age of Dexamethasone group was 30.07 ± 7.97 years, among them males were 44 (48.89%) and females 46 (51.11%). In Serratiopeptidase group, mean age was 27.21 ± 7.98 years with 37 (41.11%) males and 53 (58.89%) females. The extraction site of study participants' showed similar distribution (Figure 1). On comparison of preoperative gonion to corner of mouth, tragus to corner of mouth, outer canthus to gonion and cheek girth measurements with three consecutive post-operative period measurements (Figure 2), significant differences were observed for both the dexamethasone and serratiopeptidase groups (Tables 1-4). However, there was no any significant difference observed in these measurements between two groups in either preoperative or three post-operative observation periods (Table 5).

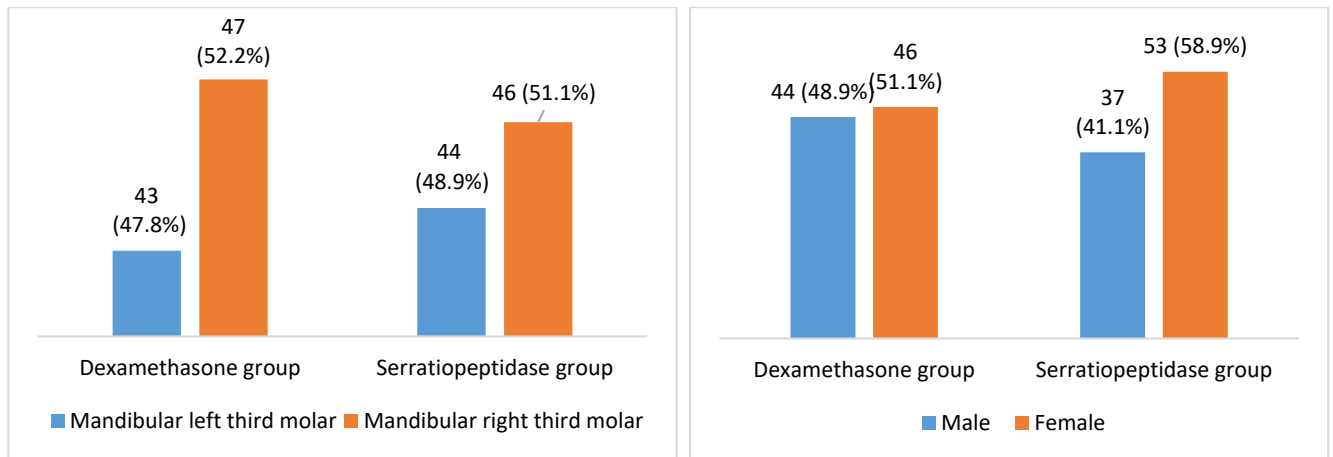


Figure 1: Distribution of extraction site and study participants.

Table 1: Gonion to corner of mouth measurement (mm) of dexamethasone group (N = 92).

Time of measurement	Mean \pm SD (median)	Difference from preoperative measurement (median)	p-value
Dexamethasone group (n = 90)			
Preoperative (Baseline)	96.32 \pm 1.89 (96)	-	-
Post-operative (Day 1)	110.93 \pm 4.74 (111)	14.61 \pm 4.39 (15)	<0.001
Post-operative (Day 2)	104.30 \pm 3.23 (104)	7.98 \pm 3.0 (9)	<0.001
Post-operative (Day 3)	102.0 \pm 3.32 (102)	5.68 \pm 3.06 (5.50)	<0.001
Serratiopeptidase group (n = 90)			
Preoperative (Baseline)	96.71 \pm 1.87 (97)	-	-
Post-operative (Day 1)	111.52 \pm 3.84 (112)	14.81 \pm 3.42 (15)	<0.001
Post-operative (Day 2)	105.7 \pm 3.14 (105.50)	8.46 \pm 2.59 (8.5)	<0.001
Post-operative (Day 3)	102.61 \pm 3.15 (103)	5.90 \pm 2.65 (6)	<0.001

*Wilcoxon Sign Rank Test; Statistically significant at p <0.05

Table 2: Comparison of Preoperative with post-operative tragus to corner of mouth measurement (mm).

Time of measurement	Mean \pm SD (median)	Difference from preoperative measurement (median)	p-value
Dexamethasone group (n = 90)			
Preoperative (Baseline)	105.19 \pm 3.40 (105)	-	-
Post-operative (Day 1)	111.20 \pm 5.62 (110)	6.01 \pm 4.11 (6)	<0.001
Post-operative (Day 2)	105.73 \pm 4.81 (106)	0.54 \pm 3.67 (1)	<0.001
Post-operative (Day 3)	102.46 \pm 3.92 (103)	-2.73 \pm 3.63 (-3)	<0.001
Serratiopeptidase group (n = 90)			
Preoperative (Baseline)	104.82 \pm 3.00 (105)	-	-
Post-operative (Day 1)	112.14 \pm 5.73 (112)	7.32 \pm 3.99 (8)	<0.001
Post-operative (Day 2)	107.10 \pm 4.23 (107)	2.28 \pm 2.20 (2)	<0.001
Post-operative (Day 3)	103.43 \pm 3.48 (103)	-1.39 \pm 2.90 (-2)	<0.001

*Wilcoxon Sign Rank Test; Statistically significant at p <0.05

Table 3: Comparison of Preoperative with post-operative gonion to outer canthus measurement (mm).

Time of measurement	Mean \pm SD (median)	Difference from preoperative measurement (median)	p-value
Dexamethasone group (n = 90)			
Preoperative (Baseline)	106.41 \pm 2.77 (106)	-	-
Post-operative (Day 1)	111.72 \pm 4.10 (112)	5.31 \pm 3.62 (7)	<0.001
Post-operative (Day 2)	106.66 \pm 5.40 (108)	0.244 \pm 5.53 (2)	<0.001
Post-operative (Day 3)	103.30 \pm 5.30 (104)	-3.11 \pm 5.26 (-2)	<0.001
Serratiopeptidase group (n = 90)			
Preoperative (Baseline)	106.23 \pm 2.69 (106)	-	-
Post-operative (Day 1)	112.53 \pm 3.88 (112.50)	6.30 \pm 2.75 (7)	<0.001
Post-operative (Day 2)	108.39 \pm 3.29 (108)	2.16 \pm 1.82 (2)	<0.001
Post-operative (Day 3)	104.79 \pm 3.97 (105)	-1.44 \pm 2.64 (-1.0)	<0.001

*Wilcoxon Sign Rank Test; Statistically significant at p <0.05

Table 4: Comparison of Preoperative with post-operative cheek girth measurement (mm).

Time of measurement	Mean \pm SD (median)	Difference from preoperative measurement (Median)	p-value
Dexamethasone group (n = 90)			
Preoperative (Baseline)	68.01 \pm 2.56 (68)	-	-
Post-operative (Day 1)	72.64 \pm 4.03 (72)	4.63 \pm 4.79 (5)	<0.001
Post-operative (Day 2)	66.52 \pm 4.16 (67)	-1.49 \pm 4.98 (-1)	<0.001
Post-operative (Day 3)	64.71 \pm 4.14 (65.50)	-3.30 \pm 4.69 (-3)	<0.001
Serratiopeptidase group (n = 90)			
Preoperative (Baseline)	67.98 \pm 2.24 (68)	-	-
Post-operative (Day 1)	72.16 \pm 3.79 (71)	4.18 \pm 4.15 (3)	<0.001
Post-operative (Day 2)	66.17 \pm 4.14 (66)	-1.81 \pm 4.66 (-1.0)	<0.001
Post-operative (Day 3)	64.10 \pm 4.17 (64)	-3.88 \pm 4.31 (-4)	<0.001

*Wilcoxon Sign Rank Test; Statistically significant at p <0.05

Table 5: Comparison between dexamethasone and serratiopeptidase group measurements.

Time of measurement	Medication	Mean \pm SD (median)	p-value
Preoperative			
Gonion to corner of mouth	Dexamethasone	96.32 \pm 1.89 (96)	0.166
	Serratiopeptidase	96.71 \pm 1.87 (97)	
Tragus to corner of mouth	Dexamethasone	105.19 \pm 3.40 (105)	0.477
	Serratiopeptidase	104.82 \pm 3.00 (105)	
Outer canthus to gonion	Dexamethasone	106.41 \pm 2.77 (106)	0.728
	Serratiopeptidase	106.23 \pm 2.69 (106)	
Cheek girth	Dexamethasone	68.01 \pm 2.56 (68)	0.769
	Serratiopeptidase	67.98 \pm 2.24 (68)	
Post-operative day 1			
Gonion to corner of mouth	Dexamethasone	110.93 \pm 4.74 (111)	0.365
	Serratiopeptidase	111.52 \pm 3.84 (112)	
Tragus to corner of mouth	Dexamethasone	111.20 \pm 5.62 (110)	0.314
	Serratiopeptidase	112.14 \pm 5.73 (112)	
Outer canthus to gonion	Dexamethasone	111.72 \pm 4.10 (112)	0.310
	Serratiopeptidase	112.53 \pm 3.88 (112.50)	
Cheek girth	Dexamethasone	72.64 \pm 4.03 (72)	0.175
	Serratiopeptidase	72.16 \pm 3.79 (71)	

Post-operative day-2			
Gonion to corner of mouth	Dexamethasone	104.30 ± 3.23 (104)	0.089
	Serratiopeptidase	105.7 ± 3.14 (105.50)	
Tragus to corner of mouth	Dexamethasone	105.73 ± 4.81 (106)	0.074
	Serratiopeptidase	107.10 ± 4.23 (107)	
Outer canthus to gonion	Dexamethasone	106.66 ± 5.40 (108)	0.118
	Serratiopeptidase	108.39 ± 3.29 (108)	
Cheek girth	Dexamethasone	66.52 ± 4.16 (67)	0.246
	Serratiopeptidase	66.17 ± 4.14 (66)	
Post-operative day-3			
Gonion to corner of mouth	Dexamethasone	102.0 ± 3.32 (102)	0.201
	Serratiopeptidase	102.61 ± 3.15 (103)	
Tragus to corner of mouth	Dexamethasone	102.46 ± 3.92 (103)	0.113
	Serratiopeptidase	103.43 ± 3.48 (103)	
Outer canthus to gonion	Dexamethasone	103.30 ± 5.30 (104)	0.095
	Serratiopeptidase	104.79 ± 3.97 (105)	
Cheek girth	Dexamethasone	64.71 ± 4.14 (65.50)	0.117
	Serratiopeptidase	64.10 ± 4.17 (64)	

Mann-Whitney U test; Statistically significant at $p < 0.05$.

DISCUSSION

Post-operative facial oedema is a common side effect of most surgical procedures. The swelling often reaches its peak 48-72 hours after the surgery. It starts to lessen in the late post-operative phase. The surgeon can manage the degree of oedema allowing surgery by executing the procedure in a way that minimises the tissue damage.⁶ In this study, a comparison of the effect of dexamethasone and serratiopeptidase in reducing the post-operative facial oedema among the 180 individuals was done. One mg of dexamethasone was given half an hour before the surgery and continued thrice daily for three post-operative days in one group. The administration of the preoperative dose of dexamethasone maintains an adequate amount of drug in the blood before, during, and after the surgery, as dexamethasone is a long-acting corticosteroid. Since the appearance of swelling has been around four to five hours after surgery, preoperative administration of the drug would be very effective in preventing swelling.⁴ In another group 10 mg of serratiopeptidase was prescribed thrice daily for three post-operative days resulted in the reduction of swelling after the third post-operative day.

In the present study, it was observed that post-operatively in dexamethasone group the facial swelling measured from corner of mouth to gonion was statistically significant ($p < 0.001$) on first, second, and third post-operative days as compared to preoperative findings. Similar

findings were seen with serratiopeptidase group post-operatively at first, second, and third day. In dexamethasone group the facial swelling measured corner of mouth to tragus was statistically significant ($p < 0.001$) on post-operative day first, second, and third and similar findings with serratiopeptidase group was found post-operatively at day first, second, and third which was statistically significant ($p < 0.001$) as compared to preoperative findings this finding was consistent with the study done by Krishna BP et al.⁶ Statistically significant ($p < 0.001$) results were seen when preoperative value from outer canthus to gonion was measured as compared to post-operative findings at day first, second, and third on both groups. Cheek girth measurement was found to be statistically significant on both groups ($p < 0.001$) when preoperative and post-operative data were compared at day first, second, and third. This finding was consistent with the finding done by Krishna BP et al.⁶

In the present study, while comparing inter group preoperative data in both dexamethasone and serratiopeptidase, no statistically significant result was observed ($p > 0.05$). At post-operative day first, second, and third, comparing the values of facial oedema (corner of mouth to tragus, corner of mouth to gonion, outer canthus to gonion) between dexamethasone and serratiopeptidase group no statistically results was observed ($p > 0.05$). The findings were not consistent with other studies conducted by Kumar et al.⁷ As the majority of the participants had facial swelling preoperatively which might

affect the results comparing the effects of two drugs preoperatively and post-operatively.

Comparing cheek girth preoperatively and post-operatively at day first, second, and third between serratiopeptidase and dexamethasone group, no statistically significant results were observed ($p > 0.05$). In this study, it was noticed that both dexamethasone and serratiopeptidase were effective in minimising the post-operative inflammation. It was seen that both dexamethasone and serratiopeptidase were equally effective in reducing the facial oedema at post-operative days, first, second, and third. It was observed that there was no significant reduction in swelling when both the dexamethasone and serratiopeptidase groups were compared and this finding were not similar to the study conducted by Kumar et al.⁷ who observed significant reduction of swelling on the first and third post-operative days in patients taking dexamethasone than serratiopeptidase group.⁷ In the present study, there was a significant reduction in the extent of cheek swelling in the serratiopeptidase group at the second, and third post-operative days which was similar to the findings of Al-Khateeb et al.¹⁴

Similar studies were conducted comparing the administration of preoperative and post-operative dexamethasone and its effect on post-operative complications like facial oedema, trismus and pain. The results had proven that preoperative administration was superior when compared to post-operative administration regarding oedema.⁴ Other studies showed co-administration of dexamethasone and diclofenac sodium led to a significant reduction in both post-operative pain and swelling on days one and two when compared with diclofenac sodium alone.¹⁰ Nandini et al.¹¹ showed that dexamethasone injected to masseter was associated with a significant reduction in swelling on days one and two post-operatively compared with controls,

which agrees with the previous studies. Syed et al.¹² concluded that there is a significant reduction of pain, swelling, and improvement in mouth opening following submucosal injection of dexamethasone at the end of the first post-operative day with statistically significant results. Moraissi et al.¹³ concluded that preemptive submucosal injection of chymotrypsin yields a comparable effectiveness in decreasing post-operative sequelae following impacted mandibular third molars surgery when compared to oral serratiopeptidase and corticosteroids.

The limitation of the study is the small sample size of the study participants. Study was conducted among those patients undergoing surgical extraction of impacted third molars and single center for performing the study would not allow generalisation of the research findings.

CONCLUSION

The research findings showed dexamethasone and serratiopeptidase are equally effective in controlling post-operative facial oedema. This study will be helpful to provide knowledge on administration of dexamethasone and serratiopeptidase preoperatively and post-operatively in patient undergoing surgical extraction of impacted third molars and to prescribe the drugs more effectively with minimal adverse effects.

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