

Is the Efficacy of Dexamethasone Dependent upon the Route of Administration for Postoperative Sequelae after Third Molar Surgery?

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Abstract:-

Background: Administration of corticosteroids at the time of surgical removal of mandibular third molar is a practice that oral surgeons often follow. However, the need for the steroid and the most apt route of administration is still a subject of study.

Purpose: The present study aimed to evaluate the effect of four different routes of administration of dexamethasone (8mg) on postoperative pain, swelling, and trismus after third molar surgery.

Study design, setting, sample: It was a single-centered randomized controlled clinical trial conducted on 75 patients. All the selected patients were chosen based on specific inclusion criteria and each of them underwent a single-sided mandibular third molar extraction. There were five groups with fifteen patients in each. Group 1 was control where no steroid was administered. The rest of the four groups were provided with local injection of dexamethasone or peroral tablet or regional injection of dexamethasone on deltoid muscle or intravenous dexamethasone injection. The study variables were facial swelling, trismus, and pain. All these variables were assessed preoperatively, on postoperative day 1,5, and 7.

Results: Trismus (interincisal mouth opening) had set in the most in the control group which sustained until postoperative day 7. The least trismus was seen in the group with local submucosal dexamethasone injection. Similarly, swelling was highest in the control group. The least effected group was the one with intravenous dexamethasone injection. In terms of pain, the most effective route was the local dexamethasone injection.

Conclusion: Trismus and pain were best controlled with local injection, while swelling was best controlled by the intravenous route.

Keywords:- Dexamethasone, Molar, Pain, Route, Swelling, Trismus.

I. INTRODUCTION

Impacted teeth retain their place within the jawbone unless they are surgically extracted or exposed to make them erupt into the oral cavity. The most commonly impacted tooth is the mandibular third molar, and it often becomes the source of discomfort for an individual. Even if an impacted third molar is in a dormant stage or has erupted in the oral cavity, it is considered for extraction in case of prosthetic rehabilitation or orthodontic management of dentition. The procedure of surgical removal of a third molar leads to considerable local tissue damage and disrupts the regional physiologic balance. The usual aftereffects of such a procedure are pain, swelling, trismus, and a resultant impact on the individual's quality of life.

The limited accessibility to the mandibular third molar region, along with the unique anatomical factors make the surgery all the more complicated. The risk of ramus fracture, damage to the lingual nerve, and the presence of inferior alveolar canal are some of the most important factors to keep in mind while performing a mandibular third molar extraction.

The surgical trauma brings about a cascade of inflammatory responses which are responsible for the postoperative pain and swelling. As the inflammatory mediators come into action, the symptoms reach their peak in about two days post-extraction.(1)

As a measure to inhibit or reduce the post-operative complications, a commonly used modality is to administer corticosteroids. Corticosteroids inhibit phospholipase A2, thus stopping the conversion of phospholipids into arachidonic acid in the local cells. This, in turn, decreases the prostaglandin and leukotriene synthesis, finally dipping the neutrophil accumulation and reducing inflammation(1). However, there is a lack of consensus about the route or dosage of corticosteroids, and probably all such extractions do not need corticosteroids or are of lesser value. The varied routes of injecting the drug are intravenous, peroral, intramuscular, and intramuscular (masseter, medial pterygoid, deltoid and gluteus muscles).(2)

Dexamethasone is 20-30 times more potent than cortisol, while having the least depressive effect on leukocyte chemotaxis and, thus, causes minimal immunosuppression. Its half-life is 36-54 hours, and has a longer duration of action than methylprednisolone. Hence, dexamethasone is the most preferred drug by oral surgeons because of its adequate potency and long half-life.(3)

It appears that dexamethasone has analgesic benefits too. A meta-analysis by Waldron et al., involving 45 studies with 5796 patients receiving dexamethasone 1.25–20 mg, reported that the patients experienced comparatively lesser postoperative pain, required less opioids in postoperative period, requested for their first analgesic dose at a later time, and even the total dosage for rescue analgesia was lesser.(4)

Regarding the route of administration, since oedema and inflammation are the aftermaths of local tissue damage, it is advisable to deliver the steroid to the traumatised tissue specifically.(5) With the decrease in inflammation, the secondary benefits of corticosteroids are a reduction in pain and trismus; because as such steroids do not have any direct impact on muscle contraction. In fact, the pain control brought about by a per oral (tablet) drug is reportedly similar to not providing any steroid.(2)

The primary aim of the present study was to evaluate the effect of four different routes of administration of dexamethasone on postoperative pain, swelling, and trismus after third molar surgery.

II. MATERIALS AND METHODS

This randomized, prospective, and controlled study was conducted at the Department of Oral and maxillofacial surgery, Rama Dental College, Hospital and Research centre. The study spanned from September 2022 to February 2023. This study was reviewed and approved by the local Institutional Ethics Committee. Informed consent was obtained from all eligible patients. The total sample size was 75. All patients were recruited into the study after obtaining their written consent.

- **Inclusion criteria:** age between 18 and 45 years, totally impacted mandibular third molars of class C, 1, 2, and 3 according to the Pell–Gregory classification. The teeth were extracted for indications, such as pre-orthodontic preparation, prevention of post-orthodontic relapse, pain and discomfort as reported by the patient.
- **Exclusion criteria:** the use of medications that could interfere with the healing process, habit of smoking, presence of any systemic disease and pregnant and/or lactating females.
- **Sampling:** Patients were randomized to five study groups by the primary researcher. There were sealed envelopes with patient names in each. The envelopes were prepared by an assistant who was not involved in the surgical procedure or data analysis. The first 15 patients were put in the control group while the rest were assigned to four groups, with 15 patients in each. Thus, the groups were:

- Group 1 - control
- Group 2 - local injection of dexamethasone
- Group 3 - oral dexamethasone tablet
- Group 4 - regional injection of dexamethasone on deltoid muscle
- Group 5 - intravenous dexamethasone injection

A. Administration of dexamethasone:

As mentioned above, group 1 patients received no preoperative or postoperative steroids. Group 2 patients received a single dose of injection dexamethasone(8mg) into the masseter intra-buccally in the immediate postoperative period after the surgical wound was sutured; group 3 patients received an oral tablet one hour prior to the procedure; group 4 patients received a single dose of the injection in deltoid muscle in the immediate postoperative period; and group 5 patients received the same dosage via intravenous route.

B. Removal of the impacted third molar:

All patients were premedicated with amoxicillin and clavulanic acid 1 g oral tablets (one tablet every 12 hour) three days prior to the scheduled surgery, and a non-inflammatory state was confirmed clinically. All the surgeries were performed by the same oral surgeon. 2% lidocaine hydrochloride and 1:200,000 adrenaline was used to anaesthetise the inferior alveolar nerve and lingual nerve, and local infiltration of the buccal fold. Surgical access was kept the same for all the patients and involved a linear incision on the alveolar ridge aligned with the buccal region of the second molar, followed by a vertical incision. A triangular flap was raised and bone around the third molar was removed under irrigation with 0.9% saline solution. Post extraction, the alveolus was irrigated with 10 ml 0.9% saline solution and the site was sutured with 3–0 silk. All patients were advised to continue the same antibiotic for the next two days and 0.2% chlorhexidine gluconate solution were prescribed for 5 days. On postoperative days 5 and 7, all patients were recalled for assessment of the study variables, while on day 7 the sutures were removed.

C. Study variables:

The primary outcome variables were postoperative oedema, measured at 1st, 5th and 7th day postop. The secondary outcomes of interest were trismus and postoperative pain.

Trismus/Inter-incisal mouth opening - the distance between the upper and lower incisal borders of the central incisors was measured using a digital calliper. (6)

Oedema – The following three facial lines were considered : the distance from the external canthus of the eye to the gonion angle, the distance from the lower border of the tragus to the mouth commissure on the operated side, and the distance from the lower border of the tragus to the soft pogonion.(6)

Pain – a 10-point VAS scale was used which was provided to the patients on the days of evaluation.

III. DATA ANALYSIS

The significance of differences between the groups was calculated with the help of the Statistical Package for the Social Sciences (SPSS version 12, SPSS Inc., USA). Descriptive statistics included mean (SD), and the analysis of variance (ANOVA) or the chi square test, as appropriate, was used to assess the significance of differences. Different variables within groups were compared by repeated-measures ANOVA. Probabilities of less than 0.05 were accepted as significant.

IV. RESULTS

The patients ranged from 18 to 45 years of age, the mean being 29.6 years.

In all the groups, inter-incisal opening reduced on postoperative day 1, with the least opening being 2.51mm in group 1. However, the mouth opening improved by postoperative day 7, with the best being 4.26mm in group 2, followed by 3 and 4. The most effected group was 1, with an opening of 3.74mm.(Table 1)

Postoperative swelling was maximum in group 3 at 15.78mm on postoperative day 1. But by day 7 the group with maximum swelling was group 2 (13.7mm), followed by 3 (13.69mm). While the least swelling on postoperative day 7 was seen in group 5(12.32mm).(Table 2)

Table 1: Inter-group comparison of Inter-incisal distance (mm)

Timeline	Groups	Mean	SD	P value
Pre-Op	Group 1	4.19	0.35	0.049*
	Group 2	4.29	0.46	
	Group 3	4.28	0.38	
	Group 4	4.38	0.38	
	Group 5	3.94	0.47	
POD 1	Group 1	2.51	0.72	0.065
	Group 2	3.03	0.38	
	Group 3	2.76	0.30	
	Group 4	2.85	0.46	
	Group 5	2.67	0.50	
POD 5	Group 1	3.19	0.52	0.001*
	Group 2	3.72	0.40	
	Group 3	3.55	0.29	
	Group 4	3.65	0.35	
	Group 5	3.24	0.44	
POD 7	Group 1	3.74	0.44	0.006*
	Group 2	4.26	0.41	
	Group 3	4.11	0.32	
	Group 4	4.15	0.36	
	Group 5	3.86	0.53	

Statistical Analysis: ANOVA one way test. *: Statistically significant at P<0.05. POD: postoperative day

Table 2: Inter-group comparison of swelling (mm) at different durations.

Timeline	Groups	Mean	SD	P value
Pre-Op	Group 1	12.00	0.74	0.000*
	Group 2	13.54	1.88	
	Group 3	13.19	1.18	
	Group 4	12.31	1.01	
	Group 5	11.63	0.79	
POD 1	Group 1	13.40	0.65	0.000*
	Group 2	15.32	1.62	
	Group 3	15.78	1.01	
	Group 4	14.59	1.11	
	Group 5	14.10	0.90	
POD 5	Group 1	12.91	0.63	0.000*
	Group 2	14.37	1.59	
	Group 3	14.43	1.38	
	Group 4	13.42	0.83	
	Group 5	13.21	0.81	
POD 7	Group 1	12.40	0.65	0.001*

	Group 2	13.70	1.84
	Group 3	13.69	1.04
	Group 4	12.69	0.96
	Group 5	12.32	0.70

Statistical Analysis: ANOVA one way test. *: Statistically significant at P<0.05. POD: postoperative day

The pain was perceived to be highest in group 4, at a mean of 3.20, on postoperative day 1. It gradually reduced by day 7, and was highest in group 3(1.2) and lowest in group 2(0.20), followed by group 4(0.27). (Table 3).

Table 3: Inter-group comparison of pain.

Timeline	Groups	Mean	SD	P value
Pre-Op	Group 1	0.33	0.82	0.113
	Group 2	0.27	0.46	
	Group 3	0.00	0.00	
	Group 4	0.07	0.26	
	Group 5	0.00	0.00	
POD 1	Group 1	2.60	0.74	0.009*
	Group 2	2.60	1.12	
	Group 3	2.93	0.59	
	Group 4	3.20	0.68	
	Group 5	2.20	0.56	
POD 5	Group 1	1.33	0.49	0.000*
	Group 2	0.87	0.74	
	Group 3	2.20	0.86	
	Group 4	1.53	0.64	
	Group 5	1.13	0.52	
POD 7	Group 1	0.33	0.62	0.000*
	Group 2	0.20	0.41	
	Group 3	1.20	0.68	
	Group 4	0.27	0.46	
	Group 5	0.93	0.59	

Statistical Analysis: ANOVA one way test. *: Statistically significant at P<0.05. POD: postoperative day

On POD 1, the pain, swelling and trismus were similar or clinically insignificant, except for swelling in the control group, when pair-wise comparison was done for all the five groups (table 3)

Table 4: Inter group comparisons between the groups at Post-op Day 1.

Groups	Inter-incisal distance (mm)		Swelling(mm)		Pain score	
	Mean difference	P value	Mean difference	P value	Mean difference	P value
1 Vs 2	0.52	0.041*	1.92	0.000*	0.00	1.000
1 Vs 3	0.25	0.628	2.38	0.000*	0.33	0.755
1 Vs 4	0.34	0.336	1.18	0.035*	0.60	0.212
1 Vs 5	0.16	0.901	0.70	0.418	0.40	0.609
2 Vs 3	0.27	0.581	0.46	0.784	0.33	0.755
2 Vs 4	0.18	0.856	0.73	0.373	0.60	0.212
2 Vs 5	0.36	0.280	1.22	0.029*	0.40	0.609
3 Vs 4	0.09	0.989	1.19	0.033*	0.27	0.874
3 Vs 5	0.09	0.985	1.68	0.001*	0.73	0.076
4 Vs 5	0.18	0.856	0.48	0.753	1.00	0.005*

Statistical Analysis: Tukey’s post hoc test. *: Statistically significant at P<0.05.

Intergroup analyses also revealed that on POD 7, trismus had considerably reduced and was similar for all the groups. Remarkably, pain showed significant differences at many intergroup comparisons. Still, the cumulative observation suggests the most effective pain control to be offered by the local submucosal injection.(Table 4)

Table 5: Inter group comparisons between the groups at Post-op Day 7.

Groups	Inter-incisal distance(mm)		Swelling(mm)		Pain score	
	Mean difference	P value	Mean difference	P value	Mean difference	P value
1 Vs 2	0.52	0.010*	1.30	0.019*	0.13	0.966
1 Vs 3	0.37	0.118	1.29	0.020*	0.87	0.001*
1 Vs 4	0.41	0.072	0.29	0.952	0.07	0.998
1 Vs 5	0.12	0.935	0.08	1.000	0.60	0.036*
2 Vs 3	0.15	0.873	0.01	1.000	1.00	0.000*
2 Vs 4	0.11	0.946	1.01	0.113	0.07	0.998
2 Vs 5	0.40	0.079	1.38	0.010*	0.73	0.005*
3 Vs 4	0.03	0.999	1.00	0.120	0.93	0.000*
3 Vs 5	0.25	0.469	1.37	0.011*	0.27	0.690
4 Vs 5	0.29	0.342	0.38	0.890	0.67	0.015*

Statistical Analysis: Tukey's post hoc test. *: Statistically significant at P<0.05.

V. DISCUSSION

The present clinical trial compared the varied routes of administration of dexamethasone, and also evaluated the effect when no steroid was used at all in surgical removal of mandibular third molar. The comparisons were done between the local submucosal, peroral tablet, intramuscular on deltoid muscle, and intravenous routes; while the control group had patients who were not administered the steroid. The local submucosal route was found to be most effective in reducing pain and trismus. As expected, pain, swelling, and trismus were remarkable on the postoperative day 1 for all the five groups, which gradually fell down until day 7. Compared to the control group, all the other four groups showed better response to pain, swelling and trismus.

Conventionally, dexamethasone is injected either intravenously or intramuscularly. Nevertheless, an individual who is already distressed due to an impacted tooth and an upcoming surgery, might not wish to be pierced at a second site barring the local region for local anesthesia. So, it is imperative to provide the least discomfort to such a patient. A patient might be more compliant when injected on an already anesthetised intraoral region. This is what has been found in the present study, that an intraoral submucosal injection is more effective than any other route. Hence, such an injection can be opted for after the local anesthesia has set in.

Priyadarshini et al compared five routes of administration of 4mg dexamethasone (intraspace Twin mix, intraoral submucosal, intramuscular, intravenous, and peroral). The oedema, trismus, and pain were best controlled in the intraoral submucosal group. This is in line with the present study.(2) Klongnoi et al. propose that edema makes the tissue tense which leads to tension pain. Since dexamethasone reduces the edema, pain also diminishes subsequently.(7)

Contrary to the present study, Noboa et al. reported no significant differences between the submucosal injection and peroral tablet. While there seems no distinct reason for the contradiction, one may consider the findings to be based on the varied demographic population and the differences in pain perception.(8)

A systemic review and meta-analysis, published in 2017, studied the clinical efficacy of submucosal intraoral or the intramuscular extraoral administration of dexamethasone in reducing the postoperative sequelae after third molar extraction. Out of the 340 titles and abstracts that were screened only 4 randomized clinical trials cleared the inclusion criteria and included in the meta-analysis. This analysis reported no statistical differences in postoperative pain, swelling and trismus while comparing the two routes.(9)

Bhargava et al. conducted a trial on 60 patients with class II position B impaction of mandibular third molars. There were five study groups (intra-space injection of Twin mix, submucosal dexamethasone, intramuscular dexamethasone, intravenous dexamethasone and per-oral dexamethasone) and a control group. The overall findings reiterate the efficacy of steroids, while the authors report that local infiltration of steroid as Twin mix brought about similar clinical effects as the other routes.(10)

A study by Antunes et al. compared oral administration and local injection of dexamethasone into the masseteric muscle reported similar efficacy in both the groups. It is same as the present study, which also reported no statistical difference between the two routes, except for pain, which was better controlled in the local injection group.(11)

Thus, it can be finally stated that corticosteroids indeed have a beneficial effect in reducing pain, improving trismus and diminishing swelling after the surgical removal of a mandibular third molar. This has also been stated in other studies too that compared steroid administration against a control group.(12) Based on the present study findings, it can be further said that the local injection of 8mg dexamethasone is a better alternative to the other routes. Probably, this is more beneficial in the clinical scenario where a local injection will render a patient more compliant as opposed to an injection at a distant site.

VI. CONCLUSION

Overall, the control group patients had the maximum trismus on postoperative day 1, while the least was seen with local dexamethasone injection. In terms of swelling, the highest impact was seen in the control group again, but the best response was found with intravenous dexamethasone injection. Similarly, for pain, the most effective route was the

local dexamethasone injection. Thus, trismus and pain were best controlled with local injection, while swelling was best controlled by the intravenous route. The authors failed to find a definitive reason for the finding related to swelling and trismus, because based on literature, a reduction in swelling should go hand-in-hand with reduction in trismus, which was not the case in the present study.

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