

Efficacy of Various Routes of Dexamethasone Administration in Reducing Postoperative Sequelae Following Impacted Third Molar Surgery

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Abstract

Aim: To compare the efficacy of intravenous (IV), intramassetric (IM) submucosal (SM) routes & oral routes of dexamethasone administration post impacted third molar removal surgery. **Type of Study:** Prospective randomized comparative clinical study. **Materials and Method:** This prospective comparative study included 60 patients with Class II and position B type of impaction (according to Pell and Gregory's classification). Patients were randomly divided into 4 groups. Group A, B, C & D patients received 8mg dexamethasone immediately post-surgical tooth removal via the IV, SM and IM route & oral respectively. Assessment of swelling, mouth opening and pain was done at intervals of 1st, 3rd and 7th post-op days. **Results:** The average age of the patients was 27 years. The mean time taken was 20 mins 40 seconds. The IV group showed minimal swelling and better pain control on the 3rd post op day (statistically significant). All 4 routes showed comparable mouth opening results. **Conclusion:** IV administration of dexamethasone post third molar surgery has been the traditional way because of its faster onset of action and increased efficacy; IM and SM routes are also comparably effective although oral route had the best patient acceptance.

Keywords: Dexamethasone, route of administration, third molar surgery

INTRODUCTION

The surgical extraction of impacted third molars is the most frequent minor surgical intervention in oral surgery.^[1,2] This invasive procedure elicits an inflammatory response which may manifest mainly as pain, swelling, and trismus. Sometimes, an exacerbated response may lead to moderate-to-severe short-term transient effects on the quality of life.^[3] These postextraction morbidities often become the reason for reluctance and hesitation in getting the tooth removed.

The reduction of these comorbidities using several strategies has been an area of interest in the field of minor oral surgery. Surgical strategies include different flaps, bone cutting techniques, and sectioning techniques among others. However, these may not be effective in all clinical situations. Consequently, a lot of research has gone into the field of pharmacological agents to reduce postextraction sequelae.^[4]

Corticosteroids are potent modulators of inflammation that act by inhibiting phospholipase A2, a chemical mediator that plays a vital role in the arachidonic acid pathway. Inhibition of this pathway leads to a reduction in the production of inflammatory mediators, such as interleukin-1, prostaglandins, and leukotrienes.^[5]

Various studies have examined the influence of corticosteroids before or after the extraction of third molars, with good results

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observed.^[6-8] Dexamethasone has been employed for years in oral surgery due to its powerful mechanism of action and prolonged half-life.^[9] Several protocols for the administration of dexamethasone in the third molar surgery have been proposed. The route of administration of dexamethasone has been a topic of contention, with researchers still unable to find a consensus on the most effective way to reduce postextraction sequelae.^[10-13]

This study aims to compare different routes, namely intravenous (IV), intramassetric (IM) submucosal (SM), and oral for the administration of dexamethasone immediately postoperatively, which very few researchers have done. The objective is to try and identify the simplest and the most effective route to minimize postoperative discomfort and to ensure early return to normalcy.

MATERIALS AND METHODS

Appropriate approvals and permissions were obtained from the Institutional Review Board and Ethical Committee for the study (No. SRGCDs/2017/601).

Sample size

With the power of the study of 80% and α error probability of 0.05, the total sample size for statistically significant and reliable results was 60 patients. In the present study, gender factor could be considered as the baseline covariate that can be a source of bias; hence, stratification was done based on gender, then simple randomization was done to divide the patients into four groups.

Type of study

This was a prospective randomized comparative clinical study with a duration of 3 years. The study was a single center study and all the procedures were performed by a single surgeon.

Statistical tool used

One-way analysis of variance (ANOVA) ($P < 0.001$ taken as significant) was used for statistical analysis.

Inclusion criteria

- Patients in the age group of 18–45
- Patients with Class II position B third molar according to the Pell and Gregory's classification.

Exclusion criteria

- Patients with existing active infections
- Patients with systemic disorders
- Patients on long-term steroids
- Pregnant and lactating women.

Informed written consent was obtained from all the patients. They were then randomly divided into four groups:

- Group A: IV route
- Group B: SM route
- Group C: IM route
- Group D: Oral route (tablets).

Surgical technique

The initial preoperative assessment was done for all patients. All the patients were operated on by a single surgeon. Following standard surgical and aseptic protocols, the patients were

prepared for the surgical procedure. Classical inferior alveolar nerve block along with lingual nerve block was administered. A standard Ward's incision was utilized to gain access and the tooth was delivered after adequate bone cutting and tooth splits as was deemed necessary. Care was taken to ensure minimal trauma to the tissues. Post extraction, the socket was copiously irrigated using 5% povidone-iodine solution diluted with equal parts of normal saline. The flap was sutured back with 3–0 silk sutures (BBS) Black Braided Silk using two interrupted sutures.

- Group A patients: 8 mg dexamethasone IV was injected into the median cubital or the radial vein
- Group B patients: 8 mg dexamethasone was injected around the operated site SM
- Group C patients: 8 mg dexamethasone was injected into the massetric muscle (IM)
- Group D patients: 8 mgs dexamethasone (Decmax® 8 mg) tablet given orally.

The patients were given standard postoperative instructions and were told to apply an ice pack on the region intermittently for the next 6 h. All patients were put on 500 mg of amoxicillin thrice daily for 5 days and paracetamol (500 mg) combination thrice a day for 3 days.

All patients were followed up at the intervals of 1st postoperative day, 3rd postoperative day, and 7th postoperative day. The statistical tools used were mean values with standard deviation and one-way ANOVA test to compare the mean values.

Suture removal was done on the 7th postoperative day if the healing was deemed to be satisfactory.

The followings were assessed:

- Swelling: Evaluated by a modification of the tape measuring method described by Schultze-Mosgau *et al.*^[14] Two measurements were made between three reference points: tragus, pogonion, and the corner of the mouth [Figure 1]. The preoperative sum of the two measurements was considered as the baseline for that side
- Trismus: Measured as the difference in maximal mouth opening (taken as the distance between upper and lower central incisors, assessed by a measuring tape to the nearest mm) before and after the operation
- Pain: Postoperative pain was evaluated using a visual analog scale (VAS) 100 mm long that ranged from 0= "no pain" to 100 = "the worse possible pain"

RESULTS

Data obtained were analyzed using SPSS™ 1.8 (IBM, USA) statistical software package. Of the 60 patients who met the inclusion criteria, 38 were male and 22 were female. The age of the patients ranged from 18 to 45 years, with the average age being 27 years. The average time taken from the placement of incision to the completion of surgery (placement of the last suture) was 20 min 50 s. The duration of the surgery and the number of rescue analgesics consumed by the patients were evaluated for the control of possible confounding factors that could influence responses regarding the three variables studied (swelling, pain, and trismus).

The mean swelling on day 1 was comparable in all the four groups. However, on the 3rd day, the reduction of swelling was marked in the IV and the IM (SM) group as compared to the IM group and oral group, which was statistically significant. The same trend was observed on the 7th postoperative day with the swelling decreasing to day 1 measurements in the IV and SM groups [Figure 2].

On the 1st postoperative day, the reduction in the mouth opening was least in the oral group. However, on the 3rd postoperative day, a further decrease in the mouth opening was observed in the oral group, but the IV and SM group patients showed marked improvement in mouth opening with mean values higher than those observed in the IM group. On the 7th day, mouth opening had returned to normal baseline preoperative values [Figure 3]. The mean pain score was lesser in the IV group on the 1st postoperative day. It was comparable in the IM, SM, and oral groups. The same trend was seen on the 3rd postoperative day. The difference was statistically significant on both the days. All patients had no pain on the 7th postoperative day [Figure 4]. Table 1 depicts ANOVA analysis of observed readings and the associated *P* values.

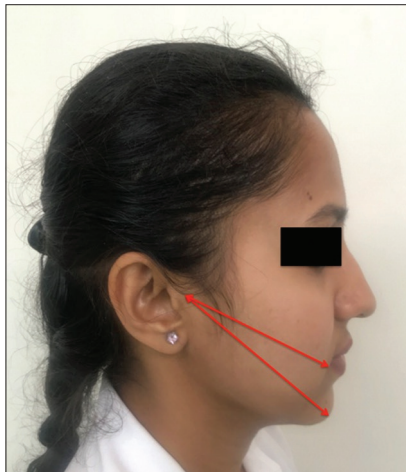


Figure 1: Schultze-Mosgau^[14] method of assessing swelling

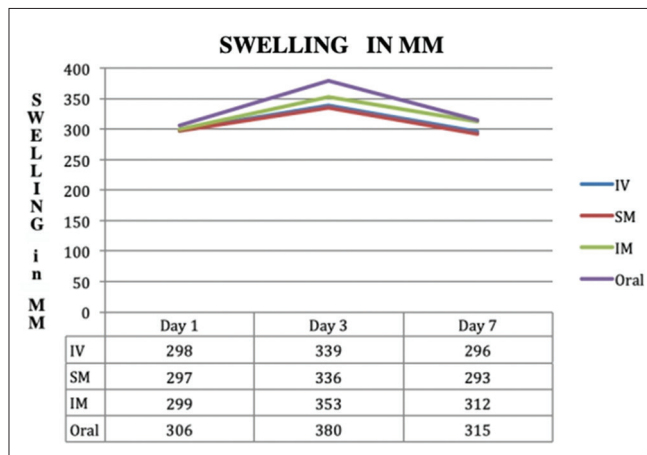


Figure 3: Graph comparing mean swelling values

DISCUSSION

Surgical extraction of the third molar is one of the most common procedures performed by maxillofacial surgeons. Like any surgical procedure, these are also associated with postoperative sequelae such as pain, swelling, and trismus. The degree and severity of these depend on many factors such as individual physiologic response to the procedure, duration of surgery, amount of tissue trauma, and manipulation among many others.^[15]

Although the phenomenon of inflammatory reaction plays a vital role in postoperative healing, an exaggerated response often leads to severe patient discomfort. Since the maxillofacial region is richly vascularized and has areas of loose connective tissue, the inflammatory responses tend to be significant.^[16]

Corticosteroids are well-known adjuvant to surgery for suppressing tissue mediators of inflammation, thereby reducing transudation of fluids and lessening edema. Dexamethasone is a highly selective, long-acting, synthetic corticosteroid, which has potent anti-inflammatory action. It exerts basic glucocorticoid action and is approximately 25 times more potent than hydrocortisone, 6 times than of prednisolone, 4 times that of methyl prednisolone and triamcinolone, and equipotent to betamethasone.^[17]

The effects of corticosteroids on pain control are still debated and not very clear. Studies have not been able to attribute

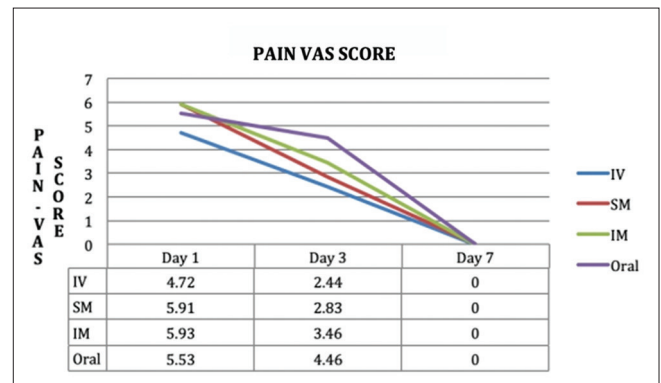


Figure 2: Graph comparing mean pain visual analog scale scores

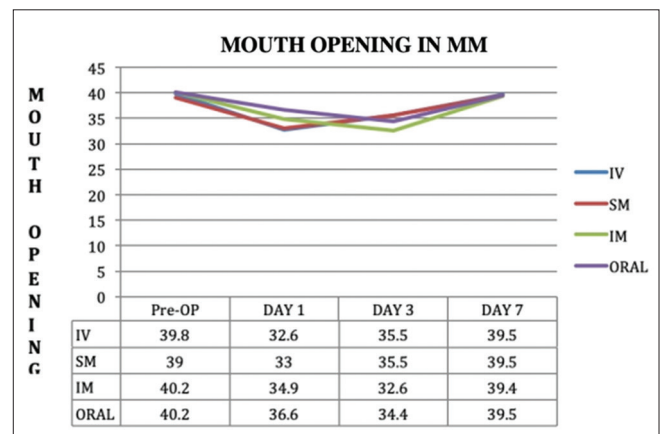


Figure 4: Graph comparing mean mouth opening values

Table 1: Statistical analysis of gathered data

| | Mean±SD | | | | F score | P |
|----------------------|---------------|---------------|----------------|----------------|---------|--------|
| | Oral | IM | IV | SM | | |
| Pain | | | | | | |
| 1 st day | 5.532±0.775 | 5.933±0.798 | 4.722±0.669 | 5.916±0.792 | 14.008 | <0.001 |
| 3 rd day | 4.466±0.511 | 3.466±0.516 | 2.4444±0.511 | 2.8333±0.557 | 15.248 | <0.001 |
| 7 th day | 0 | 0 | 0 | 0 | NA | NA |
| Swelling | | | | | | |
| 1 st day | 306.000±7.282 | 299.000±8.569 | 298.3889±7.492 | 297.5000±8.918 | 0.110 | 0.896 |
| 3 rd day | 380.000±6.450 | 353.000±6.740 | 339.444±6.491 | 336.666±6.154 | 26.194 | <0.001 |
| 7 th day | 315.622±4.675 | 312.400±6.577 | 296.722±4.675 | 293.416±6.111 | 44.911 | <0.001 |
| Mouth opening | | | | | | |
| Preoperative | 40.199±1.220 | 40.200±1.320 | 39.833±1.504 | 39.083±1.676 | 1.910 | 0.162 |
| 1 st day | 36.663±2.014 | 34.933±2.016 | 32.666±2.142 | 33.083±1.676 | 5.472 | 0.006 |
| 3 rd day | 34.044±1.239 | 32.666±2.142 | 35.055±1.349 | 35.583±1.240 | 7.793 | 0.001 |
| 7 th day | 39.455±1.455 | 39.466±1.552 | 39.500±1.339 | 39.583±1.443 | 0.023 | 0.978 |

One way ANOVA ($P<0.001$ taken as significant). ANOVA=Analysis of variance; SD=Standard deviation; IV=Intravenous; IM=Intramuscular; SM=Submucosal; NA=Not available

definite analgesic properties to corticosteroids. Although thromboxane A₂ (TXA₂) levels decrease post steroid administration, prostaglandin PGE₂ levels which are the main pain mediators remain unaltered.^[18] However, reduction in swelling and trismus is perceived by many as alleviation of pain. Several authors^[5,12,13,18,19] have reported a reduction in pain but have not found the analgesic effect to be statistically significant.

IM route is a relatively simple technique of administering corticosteroids to reduce exacerbated inflammatory responses. The site of injection is close to the already anesthetized region which makes it a painless procedure. IM^[3] as well as SM route also ensures immediate local availability; however, their absorption depends on the local blood flow in the area of administration and could also be influenced by the presence of infection and severe inflammation. A similar treatment strategy had already been proposed by Messer and Keller,^[20] who administered 4 mg dexamethasone in three different parts of the masseter muscle and reported a significant reduction of pain, swelling, and trismus.

Local administration of steroids seems to be more advantageous due to the fact that eicosanoids act locally on the tissues from which they are released. Several of these eicosanoids are responsible for vasodilation, capillary permeability, and chemotaxis. The steroids act directly on such eicosanoids and hence prevent inflammatory processes. Moreover, locally applied glucocorticoids have a direct inhibitory effect on signal transmission in nociceptive C-fibers and ectopic neuroma discharge in the injured nerve.^[21] Intramuscular administration allows the use of repository (acetate) drug forms, which provide a slow absorption and a prolonged duration of effect. Intramuscular dosing studies suggest that this route of administration can be effective in a single dose given either preoperatively or postoperatively.^[22]

IV route offers faster onset of action and better bioavailability; however, its ability to ensure sustained pain control or improvement in swelling and trismus is still debated. Some patients consider IV

injections to be another invasive procedure and exhibit reluctance. Administering IV injections itself can be challenging in certain cases and is also associated with complications of its own.

In our study, we found trismus to be least in the IM group. We hypothesize that this could be because of direct injection into the masseter muscle, spasm of which is one of the major causes for trismus in the third molar infections and surgeries. We surprisingly observed an increase in trismus on the 3rd day in the IM group, which could be attributed to the trauma caused by the injection to the muscle. We recommend a one puncture technique with the rate of drug administration <1 ml/min.

Pain is a subjective matter and very difficult to evaluate because of its multifactorial variance, but the VAS has a proven track record in providing a valid measure of pain. In our study, a statistically significant reduction in pain was seen in the IV group on the 1st day and on the 3rd day. This could be attributed to quicker onset of action and instantaneous plasma steroid levels when given through the IV route.^[3]

Schmelzeisen and Frolich reported decreased swelling on the 1st postoperative day with the use of a 6 mg dexamethasone tablet, given both pre- and post-operatively. Markovic and Todorovic studied dexamethasone consumption 6 h postoperatively.^[6,14] In our study, we used 8 mg dexamethasone tablets immediately postoperatively.

In healthy individuals, the bioavailability of oral dexamethasone is around 70%–78% with negligible first-pass metabolism.^[23] Oral route generally has better acceptance among patients. Although it may be argued that oral dexamethasone has a longer onset of action, some studies have shown comparable results with parenteral routes which can be attributed to relatively longer duration of action.^[23,24] Eight milligrams of dexamethasone has shown equivalent action to the amount of endogenous cortisol released in response to tissue injury.^[25]

In this study, pain and swelling were least in IV group and mouth opening was reduced in oral and IM groups; the reason could be better bioavailability, faster onset of action, and increased plasma steroid levels by the IV route compared to other routes.^[3]

Various authors^[5,12,13,19,20] have reported a reduction in swelling with all the injectable routes. Our study indicates that even in oral routes, the overall results are comparable and it has better patient acceptance as it avoids injection in patients having a fear of needles.

CONCLUSION

Dexamethasone administration has proven to be effective in limiting the inevitable consequences of third molar extraction. IV route which has been the traditional route of administration shows maximum effectiveness and better pain control along with the fastest onset of action. Localized routes such as IM and SM have their advantages with comparable results. Oral administration of dexamethasone is also an effective method with maximum patient acceptance and compliance. We recommend both SM and oral routes as effective means for dexamethasone administration post third molar removal procedure. More studies with larger sample sizes may further validate our findings.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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