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RESEARCH ARTICLE

EVALUATION OF POST-OPERATIVE SEQUEL ON ADMINISTRATION OF DEXAMETHASONE, VIA DIFFERENT ROUTES, IN THIRD MOLAR SURGERY

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ABSTRACT

A study was undertaken to compare the effects of different routes of administration of dexamethasone, namely intra-space injection of Twin mix, intraoral-submucosal, intramuscular, intravenous and per-oral administration, on post-operative sequel after mandibular impacted third molar surgery. The study was carried out on 60 patients presenting with class II position B impaction of mandibular third molars. Ten patients were randomly allocated to each of the six study groups. A ten-point visual analogue scale was utilized to assess the pain intensity, and specific facial measurements were measure to assess the postoperative facial edema. Maximal mouth opening was measured inter-incisally, pre and post-operatively, to evaluate trismus. All dexamethasone groups demonstrated better outcomes than the control group. The intraoral submucosal group showed least edema, & least reduction in mouth opening, and also, most favorable result, for pain control on 1st & 3rd post operative day. Pre operative use of submucosal dexamethasone proved most potent in reducing the post operative swelling and trismus demonstrating statistically significant results. From our study, we can conclude that single pre operative dose of submucosal dexamethasone effectively improves the post operative outcomes in the surgical management of impacted mandibular third molars.

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INTRODUCTION

Surgical removal of impacted lower third molar is still one of the most recurrent procedure carried out by Oral and Maxillofacial surgeons. John Hunter (Hunter, 1771) was precise to have noted as early in 1771 that *'this cutting of the dens sapientiae is often attended with an inconvenience'*. He also discussed the problems of what is now recognised as pericoronitis, and that *'nothing but the removal of the tooth or teeth will remove the evil in many cases'*. The lower third molars present characteristic anatomic challenge, i.e. the presence of a thick buccal plate, further fotified by the external oblique ridge, make for the unyielding nature of the bone at the site. The tooth is encased in an area of mandible where a relatively thin ramus joins the thick body. The grain of forces run longitudinally across this site, predisposing the lower jaw to fracture should any uncontrolled forces be applied. The presence of lingual nerve and inferior alveolar canal in close vicinity further warrant more care during incision, bone guttering, and instrumentation. All these factors amount to increase in intra operative time, muscle fatigue, post operative pain and trismus.

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The post operative sequel often becomes more discomforting than the symptoms for which the patient needed treatment. Apart from severe complications such as dysaesthesia, severe infection, fracture and dry socket, post-operative sequel of pain, facial swelling and trismus adversely impact the patient's quality of life & lead to distress. The.use of antiseptic mouthwash, corticosteroid, muscle relaxant, drain, cryotherapy, antibiotics, and physiotherapy has proven to reduce postoperative discomfort. Many dentists routinely employ corticosteroids after impaction surgery, but based on generalized, nonspecific recommendations. Corticosteroids may not be indicated in all wisdom teeth extractions, but only in cases of moderate to severe surgical difficulty. Messer and Keller (1975) observed and noted a "significant" reduction in clinical edema, pain, and trismus in 5000 patients by using 4 mg of intramuscular dexamethasone immediately post surgery. (Messer and Keller, 1975) The administration route for corticosteroid is contentious during impaction surgery. Many clinicians prefer the intra venous route, some stick to the peroral-route, while numerous other routes are also available like the intramuscular, and intraoral-submucosal. Some surgeons have also suggested other sites for the intramuscular injection like masseter and medial pterygoid muscles, apart from the conventional deltoid and gluteus muscles.

Every injection is another prick for the patient apart from the injection already being administered for local anaesthesia, and will also demand some skill on the part of the administrator. This study encompasses a comparative evaluation, on post-operative sequel, the effects of different routes of administration of dexamethasone in mandibular impacted third molar surgery.

Inclusion Criteria: ASA class I subjects above 18 years, medically fit for a surgical procedure, requiring elective surgical extraction of mandibular third molars with Class II Position B mesioangular impaction, as per the Pell and Gregory's classification, were included, after taking in written an informed consent.

Exclusion Criteria: The presence of acute infection and/or edema and pain at the time of surgery, systemic disorders or history of complications linked with local anaesthetics. Patients with active or incompletely treated tuberculosis, active viral or fungal infections, active acne vulgaris, primary glaucoma, or patients with a history of acute psychoses or psychotic tendencies.

Patients & methods: 60 patients were included & randomly divided into 6 groups irrespective of any bias. The mode of administration of dexamethasone for each group was:
Group 1: Intra-space injection of twin mix
Group 2: Submucosal dexamethasone
Group 3: Intramuscular dexamethasone
Group 4: Intravenous dexamethasone
Group 5: Per-oral dexamethasone
Group 6: Control group, no dexamethasone

Formulation of 2.8 ml Twin mix for injection[3] (Table 1)

Local anaesthetic (1.8 ml)	Dexamethasone solution for injection (1 ml)
Lignocaine hydrochloride IP 21.3 mg/ml	Dexamethasone sodium phosphate IP 4 mg/ml
Adrenaline (as bitartrate) IP 0.005 mg/ml	Sodium methylparaben IP 0.15 %w/v
Sodium chloride IP 6.0 mg/ml	Sodium propylparaben IP 0.02 %w/v
Sodium metabisulphite IP 0.5 mg/ml	Water for injection IP q.s
Methyleparaben IP 1.0 mg/ml	
Water for injection IP to make 1 ml	

Surgical technique: All surgical procedure was performed by a single clinician. A conventional Ward's incision was used, which starts from a point approximately ¼ inch down in the buccal sulcus, near the junction of the posterior & middle thirds of the second molar & moves upwards to the distobuccal angle of the second molar at the gingival margin & then cervically behind the tooth to the middle of its posterior surface. From here the incision extends backwards & buccally, & at its final continuation penetrating the cheek tissues only at mucosal depth & extending laterally for about an inch. A full thickness mucoperiosteal flap was raised. Bone guttering & teeth sectioning was done wherever deemed necessary using a surgical carbide bur no. 701 on a straight surgical micro-motor/hand piece, with normal saline irrigation. Closure was done with interrupted 3-0 silk sutures.

Evaluation criteria: patients will be evaluated on the following criteria:

1. Pain: Visual analogue scale will be used to assess the overall pain intensity.
2. Swelling: Facial swelling will be recorded using measurements between the tragus and menton.
3. Maximal mouth opening: Inter-incisal distance pre and post-operatively to assess trismus.
4. Paresthesia: Any post operative paresthesia if it occurs.
   Patients were followed for a week after the surgery, with evaluation on the 1st, 3rd & the 7th post operative day.

Results: Table 1a, Table 1b, Table 2a, Table 2b, Table 3a, Table 3b

DISCUSSION

In 1965, Linenberg (Linenberg, 1965) worked with one of the new synthetic adrenocortical steroids, dexamethasone, to limit edema and reduce trismus and pain after oral surgical procedures, and due to his studies, the use of steroids gained popularity in oral surgical procedures. Dexamethasone is a effective synthetic glucocorticoid class of steroid drug that possess anti-inflammatory and immunosuppressant qualities.

Table 1a: Intergroup comparison of increase in facial dimension (mm)

Group	Day 1		Day 3		Day 7	
	Mean	Range	Mean	Range	Mean	Range
Group I	1.75±1.65	0.00-4.50	0.80±1.03	0.00-3.00	0.25±0.49	0.00-1.50
Group II	1.60±0.99	0.50-4.00	0.75±1.09	0.00-3.00	0.35±0.63	0.00-1.50
Group III	2.55±1.12	1.00-4.00	1.45±0.96	0.00-3.00	0.50±0.41	0.00-1.00
Group IV	2.05±0.93	0.00-3.50	1.25±0.95	0.00-3.00	0.30±0.67	0.00-2.00
Group V	3.60±1.81	2.50-8.50	2.35±1.27	1.00-5.50	0.90±0.61	0.00-2.00
Group VI	5.05±3.35	3.50-14.50	3.40±2.88	2.00-11.50	1.55±2.51	0.00-8.50
Total	2.77±2.15	0.00-14.50	1.67±1.74	0.00-11.50	0.64±1.19	0.00-8.50

Table 1b: Inter-group comparisons for mean increase in facial swelling [Analysis of Variance (ANOVA)]

	p Day 1	p Day 3	p Day 7
Between Groups	0.001	0.002	0.107

Table 2a: Intergroup comparison of decrease in mouth opening (mm)

Group	Day 1		Day 3		Day 7	
	Mean	Range	Mean	Range	Mean	Range
Group I	21.40±12.42	6.00-42.00	15.40±11.08	2.00-37.00	8.85±10.09	0.00-28.50
Group II	18.15±6.87	7.00-30.00	10.35±7.21	4.00-24.50	4.85±6.13	0.00-19.00
Group III	27.10±7.28	15.00-36.00	18.80±6.52	10.00-30.50	8.40±4.03	3.00-15.00
Group IV	23.75±5.43	13.00-30.00	14.30±4.30	6.00-20.00	6.05±5.10	1.00-16.00
Group V	23.40±4.90	15.00-30.00	14.30±5.31	8.00-22.00	6.60±4.45	2.00-17.00
Group VI	25.00±6.93	13.00-34.00	15.50±8.26	2.00-30.00	10.15±8.30	1.00-25.00
Total	23.13±7.90	6.00-42.00	14.78±7.55	2.00-37.00	7.48±6.68	0.00-28.50

Table 2b: Inter-group comparisons for mean reduction in maximal mouth opening (MMO) [Analysis of Variance (ANOVA)]

	p Day 1	p Day 3	p Day 7
Between Groups	0.175	0.261	0.508

Table 3a: Intergroup Comparison of Pain (By VAS Scores)

Group	Day 1		Day 3		Day 7	
	Mean	Range	Mean	Range	Mean	Range
Group I	2.70±1.95	0.00-7.00	1.20±1.55	0.00-4.00	0.40±0.97	0.00-3.00
Group II	3.00±1.15	1.00-5.00	1.00±0.67	0.00-2.00	0.10±0.32	0.00-1.00
Group III	3.50±1.58	1.00-6.00	1.70±1.34	0.00-4.00	0.40±0.70	0.00-2.00
Group IV	3.40±1.43	2.00-7.00	1.90±1.37	0.00-5.00	0.50±0.85	0.00-2.00
Group V	4.30±1.49	2.00-6.00	2.10±1.10	0.00-4.00	0.30±0.48	0.00-1.00
Group VI	5.10±2.08	2.00-8.00	2.80±1.03	1.00-4.00	1.00±0.82	0.00-2.00
Total	3.67±1.77	0.00-8.00	1.78±1.30	0.00-5.00	0.45±0.75	0.00-3.00

Table 3b: Inter-group comparisons between various study groups (VAS) scores (Kruskall-Walis H test)

Group	Mean Rank	Mean Rank	Mean Rank
Group I	21	21.2	27.55
Group II	24.5	20.1	23.65
Group III	29.7	29.55	29.85
Group IV	27.5	31.85	30.75
Group V	38	36.05	28.95
Group VI	42.3	44.25	42.25
Total	H=11.286 (df=5); p=0.046(Significant)	H=14.465 (df=5); p=0.013(Significant)	H=9.589 (df=5); p=0.088(Significant)

It is 25 times more potent than cortisol in its glucocorticoid action, with minimal mineralocorticoid effect, and a half life of 36-54 hours, making it preferred drug for a single shot therapy in dealing with surgically induced inflammation. (Darpan Bhargava *et al*., 2013) This study compared post operative sequel of intra-space injection of dexamethasone in pterigomandibular space as Twin mix and other routes of administering steroids via intraoral submucosal, intramuscular, intravenous and per-oral tablets. The regime for corticosteroid administration (4 mg, preoperatively) used in this study was based on the inferences of studies by Tiwana *et al*. (2005) and Grossi *et al* (2007). Tiwana *et al*. found that preoperative

administration of corticosteroids provided a better clinical outcome, whereas Grossi *et al*. observed that dose regimes of 4 or 8 mg had no statistical significant differences on the clinical outcome. All the dexamethasone groups showed lesser swelling than the control group (Table 1a).

The intraoral submucosal group showed least edema, followed by twin mix, intravenous, and intra muscular groups. Among the dexamethasone groups, the Per Oral Group showed maximum increase in edema, and its difference with the Control Group was not found to be statistically significant (p=0.499). This is in agreement with preceding studies, which highlight that when dexamethasone is applied submucosally, its anti-edema effect increases (Messer and Keller, 1975Pedersen 1985). F. Graziani stresses that the genesis of facial edema is dependent on trauma to tissues during the surgery. Direct administration of the steroid in the traumatized tissues will help combat the inflammation-related events (Graziani *et al*., 2006). Differences in increase in facial dimension on day 3 continued to be statistically significant (p=0.002) (Table 1b) with the Intraoral Submucosal Group showing least edema followed by Twin Mix & Intravenous groups. Although the Intramuscular & PerOral Groups showed better mean values than the Control Group, the difference was not found to be statistically significant. On the 7th post operative day the differences in increase in facial dimension was not found to be statistically significant (p=0.107) (Table 1b). At Day 1, decrease in mouth opening in our study population ranged from 6 to 42 mm. Maximum mean decrease in mouth opening was observed in Intramuscular Group (27.10±7.28 mm) while minimum decrease in mouth opening was observed in Intraoral Submucosal Group (18.15±6.87 mm) followed by Twin Mix, Per Oral, Intravenous and lastly Control Group (Table 2a). On comparing between the Groups in decrease in mouth opening, differences were found to be statistically insignificant (p=0.175). On the 3rd (p=0.261) & the 7th (p=0.508) post operative day (Table 2b), the between the Groups comparison continued to remain statistically insignificant. These findings seem to confirm other previously reported data, since steroids do not exert any direct effects on muscle contraction. Statistically non significant benefits could be secondary due to decreased degree of local inflammation (Graziani *et al*., 2006; Ustun *et al*., 2003; Boworn Klongnoi *et al*., 2012; Huffman, 1977; Ross Beirne and Brian Hollander, 1986). The relationship between trismus and pain has been noted before (Van Gool *et al*., 1977; Szmyd *et al*., 1965; Anne Pedersen, 1985). Hence it might be anticipated that mouth opening after surgery of impacted mandibular third molars is painful and therefore limited from its full extent. This hypothesis has been established by an electromyographic study by B. E. Greenfield, & J.R. Moore where they inferred that restricted mandibular movements post surgery reflects a voluntary act to avoid pain (Greenfield and Moore, 1969). Pain was noted on VAS scale. In the present study pain score ranged from 0 to 8 with a mean score of 3.67±1.77. Maximum mean pain score was observed in Control Group (5.10±2.08) while minimum mean pain score was in Twin Mix Group (2.70±1.95). When comparing group differences in Pain score (Table 3a) at day 1, significant result (p=0.046) was obtained, with Twin Mix & Intra oral Submucosal routes clearly showing most favorable outcomes, in stark contrast to Per Oral Tablet route & Control Group, which showed worst outcomes. Although the Intravenous & Intramuscular groups showed lesser mean pain scores than Per Oral Tablet & Control Group the difference was statistically insignificant. Acute postoperative pain following impaction surgry is mainly a consequence of inflammation due to tissue injury (Ong and Seymour, 2003). The action of corticosteroids in preventing postsurgical pain is divisive. According to Beirne & Hollander, dexamethasone in particular seems to reduce pain after surgery (Ross Beirne and Brian Hollander, 1986). Numerous studies demonstrate that pain reduces with dexamethasone, but an apparent pathway for this effect has not been established. Boworn Klongnoi *et al* suggest that edema makes the tissue tense and leads to tension pain that is reduced when dexamethasone decreases the edema (Boworn Klongnoi *et al*., 2012). Differences in VAS scores continued to remain statistically significant (p=0.013) even on the 3rd post operative day, showing better pain reduction in the Intraoral Submucosal Group & Twin Mix Group when compared to Control & Per Oral Tablet Group. When we correlate this finding with the results Beirne and Hollander (1986) obtained with methlyprednisolone we can clearly see the benefit of the long half life of dexamethasone in controlling pain even on the 3rd post operative day. On the 7th post operative day only Intraoral Submucosal Group showed highly significant difference with the Control group (p=0.007) (Table 3b).

A further unwanted consequence of the surgical removal of mandibular third molars is the occurrence of paresthesia of the inferior alveolar or lingual nerves. Since dexamethasone has been shown to reduce post-operative oedema, it was decided to investigate the specific effect of dexamethasone on neurapraxia following removal of mandibular third molars as it was felt that this effect may reduce nerve damage caused by pressure or oedema. However, unfortunately (for the study purpose of course!) none of the patients reported any sensory deficit, & so the role dexamethasone can have on post surgical paresthesia following removal of impacted mandibular third molars could not be assessed. Steroid administration along with surgical removal of wisdom teeth has apparently never led to specific general complaints (Linenberg, 1965; Ware *et al*., 1963). In the present study, there was no increased frequency of local complications. Specifically, short-time steroid administration to healthy individuals does not increase the risk of delayed healing and local infection. Unfortunately, patients' preference was not recorded in the present investigation. In evaluation of the overall effect of the treatment, this must be of major importance. The ultimate goal in the treatment of patients should be total comfort with lack of complications, and this is an end for which we all should strive. Our surgical techniques should be based on this desire, and as we treat greater numbers of patients, our clinical judgment of what is required for patients should become increasingly acute. With knowledge of our past experiences in the treatment of many patients, we should reasonably predict that "with this procedure, in my hands, on this patient, under these circumstances, this result can be expected." In the current study, use of Intraoral Submucosal Dexamethasone clearly showed most desirable outcomes. Grossi G.B. *et al*. too reciprocate similar advantages of the Submucosal route, and reason that, injection of even low-dose dexamethasone in the surgical site achieves a higher effective drug concentration at the site of injury without loss due to distribution to other compartments or the onset of elimination[6]. Al-Khateeb *et al*. (1996) state that the submucosal infiltration technique does not require clinician's expertise or additional armamentarium as it is a local infiltration of the steroid submucosally around the site of surgery.

Patients who seek third molar surgery not only expect the surgeon to explain the risks and benefits of the planned

procedure, but also the details of recovery from the surgery. Lopes *et al*. (1995) reported the results of a study that included a questionnaire sent out 12 months after removal of wisdom teeth. Twenty-two percent of respondents considered that they still had a persistent problem! Meticulous surgical techniques will minimize the sequelae of inflammation but cannot prevent them altogether. The pre operative use of submucosal dexamethasone most effectively reduced the post operative, swelling and trismus showing statistically significant results. Pain control was found to be very slightly better in the Twin Mix Group than the Submucosal Group. Also, the sub mucosal dexamethasone posses many advantages over the other routes of administration. From our study, we can conclude that the single pre operative dose of submucosal dexamethasone effectively improves the post operative quality of life in the surgical management of impacted mandibular molars. A larger series is indicated to validate these findings & also obtain more statistically significant results. Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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