Effect of Single Dose Intramuscular Methylprednisolone Injection into the Masseter Muscle on the Surgical Extraction of Impacted Lower Third Molars: a Randomized Controlled Trial

Vyas N,[1] Agarwal S,[1] Shah N,[1] Patel D,[1] Aapaliya P[2]

[1]Department of Oral and Maxillofacial Surgery

Ahmedabad Dental College and Hospital

Gujarat, India

[2]Department of Public Health Dentistry, Pacific Dental College and Hospital

Rajasthan, India

Corresponding Author

Pankaj Aapaliya

Department of Public Health Dentistry

Pacific Dental College and Hospital

Rajasthan, India

E-mail: Pankaj_aapaliya@yahoo.com

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ABSTRACT

Background

Lower impacted third molar surgical extraction usually causes post-surgical sequelae like pain, trismus and swelling as a result of postoperative inflammatory response.

Objective

The aim of this study was to evaluate and compare the efficacy of single dose 40-mg (1cc) of methylprednisolone acetate, injected into the masseter muscle, preoperatively one hour before the surgery or post-operatively, immediately following the surgical removal of impacted lower third molars, in controlling most common postoperative sequelae, i.e. trismus, pain and swelling of facial soft tissue.

Methods

A randomized control study was done of 60 patients. Each patient was categorized in two groups, group I and group II, according to the time of receiving methylprednisolone acetate. Group I was injected 40mg of methylprednisolone acetate into the masseter muscle via the intrabuccal approach, one hour before the surgery. Group II was injected 40mg of methylprednisolone acetate into the masseter muscle via the intrabuccal approach, immediately after suturing of the surgical wound. The washout period was one month after the first operation. Evaluation were made of postoperative pain, trismus and swelling. The numeric pain scale (NPS) was used for pain assessment.

Results

When the patients were administered methylprednisolone acetate preoperatively, showed superior results in terms of oral aperture, pain and all the facial swelling parameters, with statistically significant differences versus the postoperatively administered methylprednisolone acetate ($p < 0.05$).

Conclusions

A single dose of 40 mg (1cc) methylprednisolone acetate injected into the masseter muscle preoperatively is more effective in reducing pain, trismus and swelling, when compared to that administered postoperatively.

KEY WORDS

Impacted lower third molars, intramuscular injection, masseter muscle, methylprednisolone

INTRODUCTION

The surgical removal of lower third molars is the most frequent intervention in oral surgery. This procedure is often associated with significant post-surgical sequelae like pain, trismus and swelling as a result of postoperative inflammatory response that may have both a biological and social impact.[1] Careful surgical technique is effective in limiting tissue damage and swelling.[2] Since cortisol is the body's own anti-inflammatory agent, glucocorticoids may be the most appropriate anti-inflammatory drug to use.[3]

These agents act by inhibiting the body's inflammatory response to injury through various mechanisms, with a reduction of fluid transudation and therefore oedema. Prolonged corticosteroid use can delay healing and increase the susceptibility to infection. But single dose of glucocorticoid had not been documented with any postoperative complication in the literature.[3] The biological half life of methylprednisolone is 18-36 hours, and it is considered to be an intermediate-acting steroid.[2] Its plasma half life is 180 minutes.

Many studies with the submucosal, intraalveolar, intravenous, intramuscular and oral use of glucocorticoids had been reported.[1,3-5] But the study with the intra masseter injection of glucoccorticoids had been rarely conducted. Orally and intravenously administered glucocorticoidsd requires frequent dosing to maintain blood level.[3] Intramuscular administration allows the use of repository (acetate) drug forms, which provide a slow absorption and a prolonged duration of effect.[6] The locally administered steroids acts directly on eicosanoids and hence prevent inflammatory processes. Moreover, a locally applied glucocorticoid has direct inhibitory effect on signal transmission in nociceptive C-fibers and ectopic neuroma discharge in injured nerve.[7]

Since the onset of the biologic action of most of the glucocorticoids through altered protein synthesis takes 1 to 2 hours, the administration of glucocorticoids 1 to 2 hours before surgery might be beneficial, as the inflammatory response to surgery are activated immediately after the incision.[7] Rarely any study comparing the merit and demerit of timing of intra masseter muscle administration of the glucocorticoids during surgical removal of lower third molars is been reported in literature. But still, being paucity of literature, the present study was to evaluate and compare the efficacy of single dose 40 mg (1cc) methylprednisolone acetate when injected into the masseter muscle via the intrabuccal approach, preoperatively, one hour before surgery or post-operatively, immediately following the surgical removal of lower third molars under local anesthesia, in controlling most common postoperative squeal, i.e. trismus, locoregional pain and swelling of facial soft tissues.

METHODS

A randomized, control study was done of 60 patients with average age of 30 years (range 18 – 42 years) who have visited outpatient Department of Oral and Maxillofacial Surgery from January 2013 to July 2013. The inclusion criteria were: healthy subjects, aged over 18 years who had bilateral symmetrically impacted mandibular third molars and required extraction of both the lower third molars.

Exclusion criteria included a history of immunocompromised disease, a history of allergy to amide type of local anaesthesia, bisulphide; contraindication of corticosteroids; recent use of anti-inflammatory drugs or antibiotics within past 1 month; pregnant and lactating women; long term use of any drug; or those who used other drugs during the observation period. The study protocol was reviewed and approved by the institutional ethical committee. Informed consent was obtained in all cases before surgical extraction.

The same surgeon operated on all the patients using a standard technique. Both extractions on the same patient were carried out at the interval of one month. Anesthesia was by standard inferior alveolar nerve block and long buccal nerve block using 1.8 ml of 2% lignocaine hydrochloride with adrenaline 1: 80,000. Triangular mucoperiosteal flap was reflected and the underlying bone was exposed. Then ostectomy and tooth sectioning was done as required, under continuous irrigation with normal saline. After complete extraction of tooth, socket was debrided, irrigated, hemostasis achieved and flap was sutured back by interrupted sutures using 3-0 black silk. The following postoperative medication were prescribed: Amoxicillin 500 mg p.o. every 8 hours during 7 days or erythromycin 500 mg p.o. every 8 hours during 7 days for patients allergic to penicillin; diclofenac sodium 50 mg p.o. every 8 hours during 3 days, and 0.12% chlorhexidine mouth rinses twice a day for 15 days.

The patients were randomized to receive 40 mg (1cc) of methylprednisolone acetate injection into the masseter muscle via intrabuccal approach, either preoperatively 1 hour before the surgery or postoperatively, immediately after the surgery. Measurements of facial parameters and mouth opening were made preoperatively and 2nd and 7th day after surgery. Unforced mouth opening was measured with callipers. Facial swelling was recorded as a distance between the following reference points on face by silk thread: tragus–lip commissure, gonion–lip commissure and gonion–external canthus of the eye. Postoperatively, pain was assessed by numeric pain scale (NPS) every hour for 6 hours from the end of surgery, and then during the next 3 days once in the morning and again at bedtime.

The data was coded and entered into Microsoft Excel spreadsheet. The data were statistically analysed, using IBM SPSS Statistics (version 19.0) by means of the paired Student's t test. Probabilities of less than 0.05 were accepted as significant.

RESULTS

There was no complication attributed to the use of methylprednisolone acetate or the surgical procedure.

Table 1 and 2 presents pre and post-operative measurements of mouth opening and facial swelling between the Group I and Group II. There was no significant difference between both the groups preoperatively. But on 2nd and 7th postoperative day a significant statistical difference was observed between the groups in both mouth opening and facial swelling. (p<0.000)

Table 1. Measurements of mouth opening (Mean ± SD) among groups.

	Group I (cms)	Group II (cms)	p value
Preoperatively	4.10 ± 0.71	4.24 ± 0.87	0.45
Postoperative - 2nd day	3.30 ± 0.41	2.87 ± 0.38	<0.00*
Postoperative - 7th day	4.10 ± 0.44	3.79 ±0.47	<0.00*

*Statistically significant p < 0.0.5

Table 2. Measurements of facial swelling (Mean ± SD) among groups.

	Tragus–Lip Commissure			Gonion–Lip Commissure			Gonion–External Canthus of the Eye		
	Group I (cms)	Group II (cms)	p value	Group I (cms)	Group II (cms)	p value	Group I (cms)	Group II (cms)	p value
Preoperatively	10.51 ± 0.74	10.51 ± 0.74	0.24	9.57 ± 0.60	9.59 ± 0.62	0.34	11.49 ± 0.88	11.51 ± 0.83	0.45
Postoperative - 2nd day	11.20 ± 0.83	11.78 ± 0.94	<0.00*	10.47 ± 1.17	11.06 ± 1.20	<0.00*	12.40 ± 1.04	12.93 ± 0.97	<0.00*
Postoperative - 7th day	10.61 ± 0.77	10.94 ± 0.77	<0.00*	9.62 ± 1.06	10.04 ± 1.02	<0.00*	11.60 ± 0.94	11.88 ± 0.90	<0.00*

*Statistically significant p < 0.0.5

The Group I patients who were administered methylprednisolone acetate preoperatively showed less compromised mouth opening (Table 1) and swelling (Table 2) on 2nd and 7th day postoperatively than the patients given methylprednisolone acetate postoperatively. Hence, the difference was statistically significant.

Table 3. Measurements of postoperative pain (Mean ± SD) among groups according to numeric rating scale.

		Group I	Group II	p value
Day 0	6th hour	3.80 ± 0.56	4.55 ± 0.93	<0.000*
	Morning	3.23 ± 0.73	4.08 ± 0.83	<0.000*
Day 1	Night	3.10 ± 0.81	3.85 ± 0.80	<0.000*
	Morning	2.28 ± 0.75	3.28 ± 0.72	<0.000*
Day 2	Night	1.78 ± 0.95	3.05 ± 0.88	0.01*
	Morning	0.60 ± 0.87	1.98 ± 0.95	0.02*
Day 3	Night	0.30 ± 0.65	1.43 ± 1.01	0.01*

*Statistically significant p < 0.0.5

A statistically significant decrease was noted in postoperative pain, 6 hours immediately after surgery and during 3 days after the extraction in the Group I patients receiving methylprednisolone acetate preoperatively (Table 3).

DISCUSSION

In day to day practice, surgical removal of the lower third molar is the most common procedure carried out by oral surgeon, which may eventually led to postoperative sequel like pain, trismus and swelling.[5]

Numerous non-steroidal anti-inflammatory drugs such as ibuprofen, flubiprofen and fenbrufen have been used to reduce edema, pain and trismus by inhibiting prostaglandin synthesis. These drugs suppress the post-operative pain without prominent anti-inflammatory properties and hence cannot reduce the postoperative morbidity significantly.[8]

Steroids are among the most potent anti-inflammatory drugs, the most powerful of which are glucocorticoids.[9,10] This property of corticosteroids have led to their wide spread use during third molar removal.[1] When single dose of glucocorticoid is given parenterally and preoperatively in combination with orally admininstered non-steroidal anti-inflammatory drugs, during the surgical removal of third molar, results in greater pain relief than did the administration of non-steroidal anti-inflammatory drugs alone.[11]

Glucocorticoids exert their action at virtually every step in the inflammatory process, which leads to decreased capillary dilatation, decreasing circulating lymphocytes, inhibiting fibroblast proliferation, and inhibiting prostaglandins and leukotrienes. The suppression of these factors exerts a profound effect on tissue inflammation and thus offers a potent therapeutic tool in managing patients postoperatively.[12] It is important to keep in mind that glucocorticoids must be present at the site of inflammation to elicit their anti-inflammatory effect.[13] The body's natural glucocorticosteroid is hydrocortisone, also called cortisol. The normal daily output by the adrenal glands is reported to be between 15 mg and 30 mg, but up to 300 mg can be supplied in times of crisis.[14] Gersema and Baker stated that the dose of glucocorticoids administered should exceed the maximum daily output of endogenous steroid, for maximum anti-inflammatory effect.[15]

Steroids are contraindicated in the conditions such as patients with active or latent peptic ulcers, Cushing's syndrome, hypertension, osteoporosis, diabetes mellitus, psychotic tendencies, acute or chronic infections and hepatic problems.[1]

In choosing an agent best suited for short-term high-dose therapy, a steroid with the minimal mineralocorticoid activity that maintains a therapeutic plasma level throughout the immediate postoperative period (when the acute inflammatory reaction is more intense) and produce minimal sodium retention, should be preferred.[14] Methylprednisolone meets these requirements, since it has no mineralocorticoid activity, the half-life is approximately 18– 36 h, and the drug is 5-fold more potent than hydrocortisone.[16] The acetate forms of this drug have low solubility that acts as a sustained-release depot, giving these forms some clinical advantage when a longer effect is needed.[17]

In the present study, a single dose of 40 mg (1cc) methyprednisolone was selected. Single dose of methylprednisolone when injected i.v. showed a non-significant decrease in plasma cortical level, hence indicated normal hypothalamic-pituitary-adrenal axis fuction.[15,18] Rebound swelling can occur if the duration of use of steroid is inadequate; therefore, it is important to maintain levels of short-duration steroids formulations for more than one day.[14,16] So to prevent the rebound oedema, a sustained release form of steroid, such as methylprednisolone acetate in a higher single dose of 40 mg should be used,as in the present study.[17]

Long-term use of steroids can delay healing and increase susceptibility to infection, but these effects are not clinically significant with the typical short-term usage protocols in oral surgery.[19] In the present study no adverse effects of single dose of 40 mg (1cc) methylprednisolone acetate, when used intramuscularly were observed or reported.

Different administration routes have been used for these drugs in oral surgery.[20] The use of oral forms might cause gastrointestinal upset, and steroids are best taken with food.[14] Effectiveness of the oral route of administration is dependent on patient compliance, and repeated dosing is required to maintain adequate blood levels during the postoperative period. Success of oral glucocorticosteroids in reducing the postoperative sequelae after third molar surgery is questionable.[21] Studies using intravenous dosing suggest that a single preoperative intravenous dose results in immediate but unsustained improvement in pain, swelling, and trismus. Hence, intravenous dosing may require postoperative supplemental drug administration (oral or intramuscular) to be optimally effective.[22]

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.[17,21,23] Thus intramuscular administration of glucocorticoids alleviate the need for repeated dosing and patients compliance.

Few reports of the administration of the glucocorticoids in the region adjacent to the surgical trauma (the masseter muscle in present study) have been published.[21,24,25] 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.[26] The steroids act directly on such eicosanoids and hence prevent inflammatory processes. Moreover, locally applied glucocorticoids have direct inhibitory effect on signal transmission in nociceptive C-fibers and ectopic neuroma discharge in injured nerve.[7]

Glucocorticoids when administered into the masseter muscle, reduces the postoperative sequel like swelling, pain and trismus following the surgical removal of lower third molar, which is also observed in the present study.[21,24,25]

Most of the effects of glucocorticoids are mediated through an altered protein synthesis, so onset of biologic action is generally 1 to 2 hours, depending on the route of administration. Because activation of the early mediators of the metabolic response to surgery occurs immediately after the surgical incision, the administration of glucocorticoids later than 1 to 2 hours before surgery might be too late to benefit fully from the anti-inflammatory effects of glucocorticoids.[7]

Various studies have shown that when glucocorticoid are administered parentally and preoperatively, the marked reduction in inflammation and trismus can be achieved in the postoperative period.[15,16,25,27-29] The same was observed in present study.

Pain measurement is difficult to establish, because its perception and intensity are multifactorial, encompassing sensorial and affective factors. Although the NRS may show deficiencies regarding understanding (especially related to old age) and precision, it provides a validated and meaningful measure of pain.[9] The method used in this study to measure facial swelling and trismus (divider and silk thread) is valid, easy to use and inexpensive. Other methodological approaches have also been described, such as clinical observation, subjective palpation and the use of malleable metal rods, a compass, photographic techniques, stereophotography and computed tomography.[20]

CONCLUSION

Hence on the basis of the present study, it can be stated that single dose of 40 mg (1cc) methylprednisolone in acetate form when used intramuscularly and administered adjacent to the surgical site, masseter muscle in present study, provide potent anti-inflammatory effect. This effect is significantly enhanced when the glucocorticoid are administered one hour before the surgery, then when administered postoperatively, following third molar surgical removal.

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REFERENCES

1. Graziani F, D'Aiuto F, Arduino PG, Tonelli M, Gabriele M. Perioperative dexamethasone reduces post-surgical sequelae of wisdom tooth removal. A split-mouth randomized double-masked clinical trial. *J Oral Maxillofac Surg*. 2006; 35: 241–46.
2. Kim K, Brar P, Jakubowski J, Kaltman S, Lopez E. The use of corticosteroids and nonsteroidal anti-inflammatory medication for the management of pain and inflammation after third molar surgery: A review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2009; 107: 630-40.
3. Schleimer RP. An overview of glucocorticoid anti-inflammatory actions. *Eur J Clin Pharmacol*. 1993; 45: 3-7.
4. Grossi GB, Maiorana C, Garramone RA, Borgonovo A, Beretta M, Farronato D et.al. Effect of submucosal injection of dexamethasone on postoperative discomfort after third molar surgery: a prospective study. *J Oral Maxillofac Surg*. 2007; 65: 2218–26.
5. Majid OW, Mahmood WK. Effect of submucosal and intramuscular dexamethasone on postoperative sequelae after third molar surgery: comparative study. *Br J Oral Maxillofac Surg*. 2011; 49: 647-52.
6. Buyukkurt MC, Gungormus M, Kaya O. The effect of a single dose prednisolone with and without diclofenac on pain, trismus, and swelling after removal of mandibular third molars. *J Oral Maxillofac Surg*. 2006; 64: 1761-66.
7. Holte K, Kehlet H. Perioperative Single Dose Glucocorticoid Administration: Pathophysiologic Effects and Clinical Implications. *J Am coll Surg*. 2002; 195: 694-712.
8. Leone M, Richard O, Antonini F, Rousseau S, Chabaane W, Guyot L et.al. Comparison of methylprednisolone and ketoprofen after multiple third molar extraction: a randomized controlled study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007; 103: 7-9.
9. Flower RJ. Advances in Prostaglandin and Thromboxane Research. New York: Raven; 1978. pg 211–36.
10. Skjelbred P, Lokken P. Reduction of pain and swelling by a corticosteroid injected 3 hours after surgery. *Eur J Clin Pharmacol*. 1982; 23: 141–46.
11. Hyrkas T, Ylipaavalniemi P, Okarinen VJ, Paakkari I. A comparison of diclofenac with and without single-dose intravenous steroid to prevent postoperative pain after third molar removal. *J Oral Maxillofac Surg.* 1993; 51: 634.
12. Markiewicz MR, Brady MF, Ding EL, Dodson TB. Corticosteroids reduce postoperative morbidity after third molar surgery: a systematic review and meta-analysis. *J Oral Maxillofac Surg*. 2008; 66:1881-94.
13. Melby JC. Adrenocorticostcroids in medical emergencies. *Medical Clinics of North America*. 1916; 45: 875.
14. Koerner KR. Steroids in third molar surgery: a review. *Gen Dent*. 1987; 35: 459-63.
15. Esen E, Tasar F, Akhan O. Determination of the anti-inflammatory effects of methylprednisolone on the sequelae of third molar surgery. *J Oral Maxillofac Surg*. 1999; 57: 1201–6.
16. Beirne O, Hollander B. The effect of methylprednisolone on pain, trismus, and swelling after removal of third molars. *Oral Surg Oral Med Oral Pathol*. 1986; 61:134–38.
17. Milles M, Desjardins PJ. Reduction of postoperative facial swelling by low-dose methylprednisolone: an experimental study. *J Oral Maxillofac Surg*. 1993; 51: 987-91.
18. Novak E, Stubbs SS, Seckman CE, Hearron MS. Effects of a single large intravenous dose of methylprednisolone sodium succlnate. *Clin Pharmacol Ther.* 1970; 11:711-717.
19. Bahn SL. Glucocorticosteroids in dentistry. *J Am Dent Assoc.* 1982; 105: 476-81.
20. Vegas-Bustamante E, Micó-Llorens J, Gargallo-Albiol J, Satorres-Nieto M, Berini-Aytés L, Gay-Escoda C. Efficacy of methylprednisolone injected into the masseter muscle following the surgical extraction of impacted lower third molars. *Int J Oral Maxillofac Surg*. 2008; 37: 260-63.
21. Montgomery MT, Hogg JP, Roberts DL, Redding SW. The use of glucocorticosteroids to lessen the inflammatory sequelae following third molar surgery. *J Oral Maxillofac Surg*. 1990; 48:179-87.
22. Sisk AL, Bonnington GJ. Evaluation of methylprednisolone and flurbiprofen for inhibition of the postoperative inflammatory response. *Oral Surg Oral Med Oral Pathol*. 1985; 60:137-45.
23. Klongnoi B, Kaewpradub P, Boonsiriseth K, Wongsirichat N. Effect of single dose preoperative intramuscular dexamethasone injection on lower impacted third molar surgery. *Int J Oral Maxillofac Surg*. 2012; 41: 376–37.
24. Messer EJ, Keller JJ. The use of intraoral dexamethasone after extraction of mandibular third molars. *Oral Surg Oral Med Oral Pathol* 1975; 40: 594-98.
25. Pederson A. Decadron phosphate in the relief of complains after third molar surgery. *Int J Oral Maxillofac Surg*. 1985; 14: 235-40.
26. Fleischli JW, Adams WR. Use of postoperative steroids to reduce pain and inflammation. *J Foot Ankle Surg*. 1999; 38: 232-37.
27. Holland CS. The development of a method of assessing swelling following third molar surgery. *Br J Oral Surg*. 1979; 17:104-14.
28. Neupert EA 3rd, Lee JW, Philput CB, Gordon JR. Evaluation of dexamethasone for reduction of postsurgical sequelae of third molar removal. *J Oral Maxillofac Surg*. 1992; 50:1177-82.
29. Dionne RA, Gordon SM, Rowan J, Kent A, Brahim JS. Dexamethasone suppresses peripheral prostanoid levels without analgesia in a clinical model of acute inflammation. *J Oral Maxillofac Surg*. 2003; 61: 997-1003.