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Original Article

The Effectiveness of Submucosal Administration of Methylprednisolone and Dexamethasone in Comparison to Placebo after Third Molar Surgery: A Double Blinded, Parallel Arm Randomized Clinical Trial

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Abstract

Background: Third molar or wisdom tooth removal is the most recorded surgery in all maxillofacial clinics globally. Post-operative complications can range from crucial complications such as damage to inferior alveolar nerve, infection, fracture of mandible, dry socket to frequent complains like pain, edema and swelling which can disturb the daily routine of patients.
Objective: To compare effect of submucosal administration of dexamethasone 8mg and methylprednisolone 40 mg with placebo (saline) one hour prior to third molar surgery in reducing the post operation sequelae after the third molar removal surgery.
Study type, settings & duration: This double blinded, parallel arm randomized clinical trial was carried out in Oral and Maxillofacial Ward of Islamic International Dental College, Islamabad from January to June 2019.
Methodology: The trial was registered in Australian and New Zealand international trial registry. The sample size was calculated by WHO calculator. A VAS variance was stated as 3 for drugs and 14 for intergroup. Errors were set as alpha =0.05 and beta=0.2. A total sample size was calculated to be 90 patients. A total of ninety patients were included and were divided into three groups. Each group had thirty patients. Group A was given submucosal dexamethasone 8 mg (2ml) before the start of the procedure and after injection of local anesthesia. Group B was given 40 mg (2ml) subcutaneous methyl prednisolone and group C was just given local anesthesia and saline injection (2ml) and served as placebo group. Trismus and mouth opening were evaluated using the Vernier calipers and distance between upper central and lower central incisor tooth was measured. Swelling was evaluated using a tape measure method. Three readings were taken in each patient for three reference points: A. Tragus to external angle of the eye, B. Tragus to lateral angle of the mouth, C. External angle of the eye to gonion. Pain was evaluated by using visual analogue scale from 1 to 10 and number of analgesics consumed by the patient on post op days. Data was analyzed using SPSS and is represented in form of tables.
Results: Submucosal injection of dexamethasone was significantly better in control of swelling at 24 and 48 hours post operatively than methylprednisolone and placebo. Dexamethasone was significantly better at control of trismus than methylprednisolone and placebo at 24 and 72 hours postoperatively.
Conclusion: Submucosal injection of dexamethasone can be given pre operatively in third molar impactions patients to control post op sequel like swelling, trismus and pain.
Key words: Dexamethasone, methylprednisolone, placebo, trismus.

Introduction

Third molar or wisdom tooth removal is the most recorded surgery in all maxillofacial clinics globally.[1] Several indications for removal of the impacted third molar are pericoronitis, orthodontic treatment, pathologies associated with impacted teeth and damage to adjacent teeth.[2] Surgical removal is followed by significant post-operative concerns that can have significant impact on both social and routine life of patients. Post op complications can range from crucial complications such as damage to inferior alveolar nerve, infection, fracture of mandible, dry socket to frequent complains like pain, edema and swelling.[3,4] These complains are common sequelae after the extraction but they can be problematic for the patient as they can have significant influence on the daily life and activities of patients. Multiple studies have been conducted to control these symptoms with help of multiple drugs and therapies.[5]

Several methods including use of different types and routes of corticosteroids have been used to reduce the discomfort and improve the quality of life postoperatively. Corticosteroids are one of the regularly used pharmacological drugs in reducing the post op sequel because it blocks the body inflammatory response.[6,7] Glucocorticoids are a type of corticosteroids naturally produced by body. It helps in reduction of inflammation by inhibition of phospholipase A2, which is the first enzyme that converts phospholipids into arachidonic acid, consequently blocking the synthesis of inflammatory products like prostaglandins, leukotrienes which are involved in production of the symptoms of inflammation.[8] Commonly used glucocorticoids in reducing the effects of inflammation are methylprednisolone and dexamethasone.[9]

Several studies have demonstrated that methyl prednisolone can lessen post op swelling and pain after third molar surgery.[10,11] Eminand Yakup concluded that intravenous methylprednisolone before surgery can significantly lessen post op edema, trismus and pain as compared to control group in third molar surgery.[12,13] Chaudhary et al. compared two different routes of administration of dexamethasone. They concluded that there is no significant difference in the oral and intravenous route of administration in control of post op complications.[14] Another study compared administration of two different oral doses 4mg and 8 mg prior to surgery and concluded that 8 mg of dexamethasone was better in decreasing symptoms than 4mg of dexamethasone.[15] Warraich et al. compared oral route of administration to intramuscular route and concluded same effects on post op swelling trismus and pain.[16]

Systemic use of corticosteroids can lead to immunosuppression which is why the medical use of this kind of drugs should be adequate, rational and for restricted time and dose because, according to endocrinology analyses, this therapy begins to produce immunosuppression on the 5th day of use of drug that can take up to nine months to return to normal levels in some patients.[17]

Few studies have compared dexamethasone and methylprednisolone administration prior to third removal surgery.[18-20] This is no consensus regarding the ideal route, dosage, timing or duration of administration of corticosteroid therapy. There are several variances in the methods used for assessing clinical parameters.[21,22]

The purpose of this study was to compare the effect of submucosal administration of dexamethasone 8mg and methylprednisolone 40 mg with placebo (i.e. saline) one hour prior to surgery in reducing the post op sequelae after third molar removal surgery.

Methodology

This double blinded, parallel arm randomized clinical trial of 06 months duration was conducted in oral and maxillofacial ward of Islamic International Dental College, Islamabad from January to June 2019.

The sample size was calculated by WHO calculator. A VAS variance was stated as 3 for drugs and 14 for intergroup. Errors were set as alpha =0.05 and beta=0.2. A total sample size was calculated to be 90 patients. The level for statistical significance is 0.05.

Patients in age group 20 to 40 years with level II mesioangular impactions according to the Pell and Gregory's classification and no medical conditions were included in the study.

Patients taking or requiring prophylactic antibiotics and anti-inflammatory drugs before surgical procedure, suffering from any chronic pain problems or mental disorders, pregnant or lactating women, reporting hypersensitivity to steroids or have acute pain like in case of pulpitis, abscesses, or other acute infections were excluded from the study.

There were three groups. There were 30 patients in every group. Group A was given submucosal dexamethasone 8 mg (2ml) before the start of the procedure and after injection of local anesthesia. Group B was given 40 mg (2ml) subcutaneous methyl prednisolone and group C was just given local anesthesia and saline injection (2ml) and served as placebo group.

An independent researcher "X" made cards for allocation with help of computer. He kept the original random allocation sequences in a distant place and operated with a copy. He opened the envelope for every patient at start of treatment and told Dr. A that which patient gets what form of intervention. Dr. A gave the patient one of three drugs. After this, Dr. B performed the surgical

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Authors Contribution

KA conceptualized the project did the data collection and literature search. Statistical analysis, drafting, revision & writing of manuscript were done by MF.

procedure (i.e impacted third molar removal). Before start of the surgical procedure patient was asked by another investigator Dr. C about the level of pain on the vas score from 1 to 10(1 being very mild pain and 10 being most severe pain). Trismus and mouth opening were evaluated using the Vernier calipers and distance between upper central and lower central incisor tooth was measured. Trismus was evaluated through measuring the interincisal opening at 2nd, 3rd and 7th day. Swelling was evaluated using a tape measure method. Three readings were taken from each patient for three reference points: A. Tragus to external angle of the eye, B. Tragus to lateral angle of the mouth, C. External angle of the eye to gonion. Swelling was evaluated by measuring the distance three reference points. The mean of three measurements was recorded pain was evaluated through the Vas score (0 being no pain mild and 10 being most severe) recorded by the patient and number of analgesics consumed by every patient on 1st,2nd,3rd and 7th post op day. Pain score was divided in mild (0-3), moderate (4-7) and severe (8-10) respectively. Post op pain, swelling and trismus were evaluated on 2st, 3rd and 7th post op day. Data analysis was done through SPSS. A p value of less than or equal to 0.05 was considered to be arbitrarily significant.

The informed, written consent for the application of sub mucosal infiltration was taken. Information was delivered in a layout and offered at a level that can be straight forwardly understood by patients. All the data acquired for research purpose was kept confidential to prevent disclosures of patient identity.

The Ethical approval was obtained from Institutional Review Board of Islamic International Dental College, Islamabad and trial was registered in international trial registry.

Results

The study included total 90 patients (55 females and 35 males) aged 20–40 years. There were 33 male patients and 51 female patients in age group 20 to 30. However, two male patients and 04 female patients were in age group 30 to 40. The duration of surgery of all was 25±05 minutes. No significant difference was found between the groups regarding the duration of surgery.

Post op swelling was evaluated by applying ANOVA on the means of reference points of all days. ANOVA showed significant difference (i.e. *p* value <0.005) on all days between groups. Post hoc test was applied to see the differences between the groups. On day one and two, dexamethasone is significantly better than methylprednisolone and placebo. On day three and four, there is no significant difference between dexamethasone and methylprednisolone but both of them are significantly better than placebo in control of swelling and edema as shown in Table-1.

On the 1st post op day, dexamethasone showed significant statistical difference in controlling trismus as compared to methylprednisolone and placebo. On 2nd post op day dexamethasone and methylprednisolone both showed significant statistical difference in control of trismus than control. On 3rd post op day, dexamethasone and placebo both showed significant difference with methylprednisolone. On 7th post day, dexamethasone showed significant difference in control of trismus with methylprednisolone and placebo as shown in Table-1.

One way anova and post hoc test was applied to evaluate the difference between groups.

Table 1: Post op swelling, trimsus and pain and differences in means and *p* value on postop day 1,2,3 and 7.

Post op Swelling	*Sum of Squares*	*df*	*Mean Square*	*p Value*
Day one	2207.400	2	1103.00	<0.005
Day two	869.089	2	434.544	<0.005
Day three	1449.622	2	724.811	<0.005
Day seven	1097.222	2	548.611	<0.005
Post op trismus				
Day one	206.422	2	103.211	<0.005
Day two	344.600	2	172.300	<0.005
Day three	930.156	2	465.078	<0.005
Day seven	314.756	2	157.378	<0.005
Post op pain				
Day one	252.067	2	126.033	<0.005
Day two	7.467	2	3.733	.486
Day three	52.622	2	26.311	<0.005
Day seven	150.467	2	75.233	<0.005

Table 2: Severity of pain on pre op, 1st, 2nd, 3rd and 7th post op day with all three drugs.

	Severity of Pain	*Drug Methylprednisolone*	*Dexamethasone*	*Control*
Day 0	mild	01	12	05
	moderate	21	13	21
	severe	08	05	04
Day 01	mild	0	0	0
	moderate	28	09	28
	severe	02	21	02
Day 02	mild	0	0	02
	moderate	24	25	22
	severe	06	05	06
Day 03	mild	04	0	0
	moderate	24	27	26
	severe	02	03	04
Day 07	mild	26	27	0
	moderate	03	03	27
	severe	01	0	03

On the 1st post op day, dexamethasone showed significant statistical difference in controlling pain as compared to methylprednisolone and placebo. On 2nd post op day there is no difference among the three approaches. On 3rd post op day, dexamethasone and placebo both showed significant difference in controlling pain with methylprednisolone. On 7th post day, dexamethasone showed significant difference in control of pain with both methylprednisolone and placebo as shown in Table-1.

To evaluate difference between post op pain, visual analogue score was noted at 1st, 2nd, 3rd and 7th post op day. Table-2 shows the severity of pain on pre op, 1st, 2nd, 3rd and 7th post op day with all three drugs.

Discussion

Corticosteroids are commonly used after surgery for overpowering inflammatory mediators, which in turn reduce transudation of fluids and edema.[22] Dexamethasone is a synthetic corticosteroid with a selective, long-acting and effective anti-inflammatory action.[23] It is reported to be four times more effective than that of triamcinolone and methylprednisolone, and equally effective as betamethasone.[24] The current study compared the efficacy of dexamethasone with methylprednisolone and placeboto launch an ordinal among their efficacies.

In the current study, same position of impacted teeth were selected with the assistance of a radiographs according to Pell and Gregory's classification and duration of surgery was also evaluated to avoid confounding with respect to difficulty of impaction.

A study has compared different routes of administering dexamethasone and found that there was no significant difference in different routes hence it can be said that there is no dire need to administer drug through intravenous route as it is difficult to access in many conditions and it has its associated complications. [25,26] Along with procedure related complications, it can be traumatic for the patients who are trypanophobic. Kocker et al. compared five different routes of administration of methylprednisolone and reported less trismus in all patients given methylprednisolone regardless of its route of administration.[27] Therefore the current study used the submucosal routes for all drugs because it is safe and equally effective.

Limited mouth opening after surgery is a complication that impedes patient's daily routine activities such as intake of food, drinks and oral hygiene measures. Trismus is significant on 2nd post op day and Ranjbar et al. concluded that dexamethasone is better at controlling trismus at 48 hours as compared to methylprednisolone.[28] Conversely the current study shows dexamethasone and methylprednisolone both are equally effective in control of trismus at 48 hours but at 72 hours dexamethasone is significantly better at controlling trismus than methylprednisolone and placebo, this is because dexamethasone has long lasting action in comparison to methyl prednisolone which has intermediate action and shorter half-life than dexamethasone.

Alcantara and Falsi et al. conducted a study between dexamethasone and methylprednisolone in control of swelling, pain and trismus after third molar

surgery and established that dexamethasone controls swelling better than methylprednisolone at all postoperative times and patients showed better mouth opening at 48 hours after surgery. However no statistically significant difference between drugs with regard to pain was found[29] where as in present study dexamethasone was better at controlling swelling on day one and day two but on day three and day seven there was no difference in dexamethasone and methylprednisolone but they were significantly better than control on all days. Patients also showed better mouth opening with dexamethasone at 24 and 72 hours post operatively but at 48 hours post operatively there was no difference between dexamethasone and methylprednisolone. However dexamethasone was better than placebo at all time intervals. There is statistical difference in control of pain by dexamethasone at day one and seven as compared to methylprednisolone and placebo.

The limitations of present study were that different factors of patients like their pain threshold, anatomy of roots and quantity of bone covering the tooth were not taken into consideration.

Patient physiognomies may be the main limitation of this study. Although the ages and time of surgery were similar, body mass indices of patients were not calculated. Advance studies are required to be commenced, which include split mouth study and above mentioned parameters on a larger scale.

The results of this research specify that although dexamethasone and methylprednisolone are both effective in reducing post-operative complications of impacted third molar teeth extraction but dexamethasone is better at control of swelling, trismus and pain than methylprednisolone and placebo.

Conflict of interest: None declared.

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