Efficacy of Submucosal Dexamethasone Injection on Postoperative Adverse Outcomes Following Third Molar Surgery.

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Author's Contribution:

A.B. and M.K. conceived and planned the research. A.B. carried out the experiments. S.N and A.B. planned and carried out the simulations. A.B. and M.A. contributed to sample preparation. F.H. contributed to the interpretation of the results. A.B. AND F.A. took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript.

ABSTRACT:

Introduction: The most common dento-alveolar procedure is surgical removal of an impacted third molar, which is associated with post-operative pain, swelling, and trismus.

Objective: To determine the post-operative outcomes of submucosal dexamethasone injection in third molar surgeries.

Materials and methods: It was a Descriptive Study conducted in Department of Oral & Maxillofacial Surgery, Liaquat College of Medicine & Dentistry, Karachi between November 7, 2019 to May 6, 2020. All patients who fulfilled the inclusion criteria and visited to LCMD, Karachi were included in the study. Informed consent was taken after explaining the procedure, risks and benefits of the study. In our study, all the patients (n=65) received a 4mg submucosal dexamethasone injection 10 mins before the surgery following local anesthesia. The duration of surgery was recorded with postoperative outcomes in terms of pain, trismus and swelling were measured on 3rd and 7th day. All the collected data were entered into the proforma attached at the end and used electronically for research purpose.

Results: The mean SD of age was 25.9 ± 7.2 years. Right side surgery was documented in 39 (60%) patients, while left side surgery was documented in 26 (40%) patients. On the third and seventh day, the mean SD of VAS pain score was (5.9 ± 3.2), (3.8 ± 4.4), swelling was (2.5 ± 1.1), (0.9 ± 0.6) mm, and trismus was (16.9 ± 9.7), (11.8 ± 9.1) mm, respectively.

Conclusion: It is to be concluded that a significant difference in outcomes was observed between the third and seventh post-operative days in patients who had submucosal dexamethasone injections in third molar surgeries.

Keywords: Submucosal dexamethasone, third molar surgery, impaction, pain, trismus and swelling

INTRODUCTION:

The extraction of the third molar is one of the most common procedures used by oral and maxillofacial surgeons in the clinical setting (1, 2). Due to the presence of loose connective tissue and high vascularity, such surgical approaches are frequently associated with post-operative complications such as pain, edema, and trismus, all of which have a significant impact on the patient's morbidity (3). Despite improvements in surgical technique and perioperative care, these complications are triggered by an inflammatory reaction in the region of intervention, which causes vasodilation and the emergence of potent pro-inflammatory mediators (4).

A broad range of drugs have been used to prevent post-operative inflammation. Corticosteroids are amongst the most commonly used classes of drugs, owing to their potent anti-inflammatory properties and comparative safety in healthy individuals (5). It is used as a preventive measure to limit perioperative swelling in maxillofacial surgeries (6).

Corticosteroids reduce circulating lymphocytes, inhibit capillary dilatation and fibroblast proliferation, and alter prostaglandin and leukotriene synthesis at every stage of the inflammatory process (7). The inflammation caused by tissue damage is a major contributor to the development of postoperative pain. Therefore, the locally applied glucocorticoids inhibit signal transmission in nociceptive C-fibers and ectopic neuroma discharge in injured nerves (8).

Dexamethasone is useful in reducing pain due to its potential anti-inflammatory effects, and it is currently the most powerful anti-inflammatory drug with a long half-life. Even at physiological

doses, dexamethasone is considered safe for periods of less than two weeks (9). Previous researches has shown that using corticosteroids during surgery reduces postoperative discomfort after removing impacted mandibular third molars (10, 11).

Although there are numerous recognized methods to reduce postoperative pain, swelling, and trismus, such as antibiotics and surgical techniques, the use of corticosteroids has been shown to significantly reduce inflammation. The purpose of our clinical trial is to look into the effects of submucosal administration of 4mg dexamethasone on reported outcome after the surgical procedure. A submucosal route provides local effects while avoiding systemic administration. Furthermore, submucosal administration near the surgical site is a site that dentists or oral surgeons can access with minimal additional training or equipment. There has previously been no study in Pakistan that evaluates the post-operative outcomes in relation age, duration and site of surgery following sub mucosal dexamethasone injection in third molar surgeries. As a result, because our population is genetically and geographically distinct from other populations, therefore the post-operative outcomes of sub mucosal dexamethasone injection in patients undergoing 3rd molar extraction in the Pakistani population was evaluated.

2. METHODOLOGY:

2.1 STUDY DESIGN

In this study, an exploratory Descriptive Study Design was used.

2.2 STUDY SETTING

The study was conducted at the Department of Oral & Maxillofacial Surgery, Liaquat College of Medicine & Dentistry, Karachi.

2.3 DURATION OF STUDY

The study lasted six months, from November 7, 2019 to May 6, 2020, after the synopsis was approved.

2.4. SAMPLE SIZE:

The sample size was calculated using the open WHO sample size calculator, using the mean trismus on the seventh day, which was 40.4 (8.1) in the study group, with a confidence interval of 95 percent and an absolute precision of 0.02. The calculated total sample size was 65 (12).

2.5. SAMPLING TECHNIQUE:

Non-probability, Consecutive Sampling

2.6. SAMPLE SELECTION

2.6.1. INCLUSION CRITERIA

- Patients who came to LCMD in Karachi, Pakistan, for surgical extraction of an impacted mandibular third molar under local anaesthesia.
- All mesioangular and vertical impactions with Pell and Gregory classification categories A and B and ramus relationship class 1. 41
- Patients who provided informed consent to participate in the study and ranged in age from 18 to 35 years.
- Patients with no postoperative medication allergies.
- Patients who were nonsmokers, non-alcoholics, and did not have any systemic diseases, were not systemically compromised, and were not on long-term steroid therapy.

2.6.2. EXCLUSION CRITERIA ▪

- The patient had any severe or critical dental diseases and was unable to respond.
- Patients who are already on steroids.
- Medically compromised patients.
- Patients who had a steroid contraindication.
- Patients who have recently received antibiotics and anti-inflammatory medications (within the last two weeks).

2.7. DATA COLLECTION PROCEDURE: The ethical committee approved the conduct of clinical research in the Oral and Maxillo-facial Department of Liaquat College of Medicine and Dentistry. Patients with symptomatic impacted mandibular third molars who presented to LCMD and met the inclusion criteria were included in our study. The surgical procedures were referred to patients by the Oral Diagnosis department.

Before enrolling in the study, informed and written consent was obtained. Before surgery, all patients have their interincisal distance and facial measurements taken (point A-tragus to corner of lip and point B-lateral canthus of eye to angle of mandible). All procedures were carried out under local anaesthesia by a single operator. All patients underwent a similar nerve block technique (inferior alveolar, lingual, and long buccal nerve blocks), as well as a similar incision (Ward's incision) and flap design (full thickness mucoperiosteal flap), with closure done with a simple interrupted suture (silk suture 3/0).

Following surgery, all patients were given a five-day course of antibiotics and analgesics. Just after local anaesthesia, all patients (n=65) received a 4mg submucosal dexamethasone injection 10 minutes before surgery. The duration of the surgery was recorded. On the third and seventh

days, postoperative outcomes in terms of pain, trismus, and swelling were measured according to the operational definition.

STATISTICAL ANALYSIS: Data was entered and analyzed on SPSS version 23.0 Mean ± SD was calculated for quantitative variables like age, pain, swelling, trismus, duration of surgery. The frequencies and percentages were calculated for quantitative variables e.g. gender, duration and site of surgery. Effect modifiers like age, site and duration of surgery were controlled through stratification. Post stratification ANOVA / Independent t test was applied by taking $p \leq 0.05$ as significant value

RESULTS:

In this study, 65 patients were included to assess the post-operative outcomes of sub mucosal dexamethasone injection in third molar surgeries.

The results revealed that 40 patients were between the ages of 18 and 25 years, and 25 patients were over the age of 25 years. 35 of the 65 patients had right-side third molar impaction, while the remaining 26 had left-side molar impaction.

The surgical procedure for 36 patients was completed in 25-40 minutes, while the procedure for 29 patients took more than 40 minutes **Table 1**.

TABLE 1: NUMBER OF PATIENTS ACCORDING TO THE FINDINGDS	
FINDINGS OF PATIENTS	**NO. OF PATIENTS**
Age (years)	
18-25	**40**
> 25 year	**25**
Site of surgery	
Right	**39**
Left	**26**
Duration of Surgery (mins)	
25-40	**36**
> 40	**29**

The results were analyzed as Mean ± S.D which is as follows:

- Age was 25.9±7.2 with C.I (24.1127.68)
- Duration of surgery was 37.2±8.7 with C.I (35.04…….39.35)
- VAS pain score on 3rd day was 5.9±3.2 with C.I (5.10…….6.69)
- Swelling on 3rd day was 2.5±1.1 with C.I (2.22…….2.77)
- Trismus on 3rd day was 16.9±9.7 with C.I (14.49…….19.30)
- VAS pain score on 7th day was 3.8±4.4 with C.I (2.70…….4.89)
- Swelling on 7th day was 0.9±0.6 with C.I (0.75…….1.04)
- Trismus on 7 th day was 11.8±9.1 with C.I (9.54…….14.05) as shown in **Table 2**.

TABLE 2: STATISTICS OF PATIENTS CHARACTERISTICS				
Characteristics	Mean ± S.D	Minimum	Maximum	95% Confidence Interval
Age in years	**25.9 ± 7.2**	**18**	**35**	**24.11 - 27.68**
Duration Of Surgery	**37.2 ± 8.7**	**25**	**60**	**35.04 - 39.35**
VAS of Pain (3rd Day)	**5.9 ± 3.2**	**1**	**8**	**5.10 - 6.69**
VAS of Pain (7th Day)	**3.8 ± 4.4**	**1**	**8**	**2.70 - 4.89**
Swelling in mm (3rd Day)	**2.5 ± 1.1**	**0**	**5**	**2.22 - 2.77**
Swelling in mm (7th Day)	**0.9 ± 0.6**	**0**	**5**	**0.75 - 1.04**
Trismus in mm (3rd Day)	**16.9 ± 9.7**	**5**	**25**	**14.49 - 19.30**
Trismus in mm (7th Day)	**11.8 ± 9.1**	**5**	**20**	**9.54 - 14.05**

Stratification of age, site of surgery and duration of surgery with respect to post-operative outcome of Pain, Swelling and Trismus showed significant difference in all the compared results as shown in **Table 3.**

Both the age group, the location of the surgeries, and the duration of the surgeries resulted in a significant reduction in the VAS Score of pain, swelling, and trismus. However, as shown in **Table 3**, the age group of 18-25 years, the right site of surgery, and the longer duration of surgery showed a slightly more significant change, with the exception of the shorter duration of surgery showing more valuable results in Trismus**.**

TABLE 3: STRATIFICATION OF AGE, SITE OF SURGERY AND DURATION OF SURGERY WITH POST-OPERATIVE OUTCOME									
Characteristics	**Age (years)**			**Site of Surgery**			**Duration of Surgery (mins)**		
Value of Characteristics	**18 – 25 (n=40)**	**> 25 (n=25)**	**p-Value (Anova)**	**Right (n=39)**	**Left (n=26)**	**p-Value (Anova)**	**25 – 40 (n=36)**	**> 40 (n=29)**	**p-Value (Anova)**
VAS Pain Score 3rd Day	**5.6±3.0**	**5.3±3.3**	**0.0028**	**5.8±2.8**	**5.0±2.5 7**	**0.0001**	**5.7±2.8**	**5.6±2.5 7**	**0.0001**
VAS Pain Score 7th Day	**3.9±2.1**	**3.5±1.9**		**3.8±1.9**	**3.3±1.9**		**3.8±1.7**	**03.2±1.6**	
***p*-value**	**0.004**	**0.022**		**0.0004**	**0.008**		**0.0008**	**0.0001**	
Swelling (3rd day)	**5.7±3.0**	**5.8±3.2 7**	**0.0001**	**5.9±2.7**	**5.1±2.0 7**	**0.0004**	**5.9±3.0**	**5.3±2.6 7**	**0.0052**
Swelling (7th Day)	**3.6±2.2**	**3.2±2.0**		**4.1±2.6**	**3.4±2.4**		**4.3±2.9**	**3.6±2.4**	
***p*-value**	**0.0006**	**0.001**		**0.003**	**0.007**		**0.024**	**0.012**	
Trismus (3rd day)	**5.5±2.9**	**5.4±3.4 7**	**0.0042**	**5.8±2.7**	**5.2±2.3 7**	**0.0015**	**5.8±2.2**	**5.3±2.1**	**0.0001**
Trismus (7th Day)	**4.0±1.7**	**3.5±2.3**		**4.3±2.1**	**3.6±2.2**		**4.0±2.2**	**3.6±1.8**	
***p*-value**	**0.006**	**0.024**		**0.007**	**0.013**		**0.0008**	**0.001**	

DISCUSSION:

Oral invasive techniques, such as the most common surgical removal of impacted third molars, can result in significant post-operative adverse outcomes for the patient due to serious laceration and tissue trauma to soft and hard tissues enclosing it (13). As a result, patients may experience pain, swelling, and limited mouth opening. Swelling after third molar surgery is gradual and

begins about two days after the procedure (14, 15). However, while some inflammatory reactions can be beneficial to healing, excessive reactions can affect the patient's quality of life. As a result of that, many clinicians have aimed to minimize postoperative sequelae using anti-inflammatory drugs. The anti-inflammatory efficacy of corticosteroids has led to their widespread use when third molars are removed. To overcome these complications, doctors usually prescribe corticosteroids (15).

Corticosteroid therapy is one method for reducing postoperative pain, swelling, and trismus. These steroids are given at various doses and routes of administration and have been shown to be effective in controlling pain, inflammation and trismus. They work by blocking inflammatory mediators that cause blood vessel exudation and edema. They also have several analgesic properties due to their anti-inflammatory and prostaglandin inhibitory properties. Corticosteroids are most effective in the first 24 hours after surgery, but the effects can be observed for up to 3 days (5).

Dexamethasone is a synthetic corticosteroid that acts as an inflammation suppressor and decreases facial edema after oral surgical procedures. It has a long half-life and is the most potent anti-inflammatory drug that can be used for periods less than two week. Many studies have reported that DX given peri-operatively was effective in reducing postoperative discomfort (pain, trismus and edema) after impacted third molar surgical extraction (16-18). Although the mechanism of action is still unknown, however it is believed that anti-inflammatory effects have been linked to lower levels of prostaglandins and leukotrienes, which act as phospholipase pathway blockers, as well as inhibition of exudate formation, edema, trismus, and pain [85,86]. Dexamethasone can be administered intramuscularly, orally, endo-alveolarly, or submucosally.

However, due to the half-life and high efficacy of submucosal injection it is considered the easiest and most effective method (19-21)**.**

Considering the preceding scenario, we aimed to evaluate the effect of submucosal administration of dexamethasone in third molar surgery. In our study, the mean age of the patients was 25.9 ± 7.2 years. The study by Gümrükçü Z, et al. (22) found almost similar results, indicating that the mean age of the patients was 24.02 ± 5.7 years.

Another study conducted in Turkey by Dereci O, et al (23) stated the mean age of patients was 21.35 ± 4.18 years.

The current study discovered that the mean duration of surgery was 37.2 ± 8.7 minutes. Correspondingly, Majid OW et al. (24) found a concomitant result of mean surgical duration of 37 ± 8.8 minutes. In addition, Lim D et al. (25) reported a surgical time of 21.2 ± 4.0 minutes. This is primarily because the current surgical concept for removing an impacted mandibular third molar is less invasive and takes less time. Al-Shamiri HM et al. (26), on the other hand, reported a surgical procedure time of 44.6 minutes.

In recent study, the mean VAS pain score on 3rd and 7th days were noted as 5.9±3.2 and 3.8±4.4 VAS respectively. Likewise, Mojsa et al. in their study mentioned that patients who received dexamethasone after surgery had significantly less pain than those who received only placebo 24 hours later(27). Moraschini et al. performed a meta-analysis and discovered a statistically significant difference in pain relief favouring submucosal dexamethasone injection over the control group (28). According to Majid and Mahmood, a submucosal injection of 4 mg dexamethasone resulted in a statistically significant reduction in pain at all intervals(24). It has been suggested that Dexamethasone acts early in the inflammatory area, decreasing the

production of inflammatory mediators in the surgical area, resulting in a more significant decrease of swelling and edoema in that area, resulting in good control of early postoperative pain and more comfort for patients with low VAS scores (29).

In contrast to previous studies, Nair et al. found no significant difference in pain reduction between intraoperative submucosal injections of dexamethasone 4 and placebo (30).

In accord with Graziani et al., our statistics indicate that submucosal administration of dexamethasone 4 mg resulted in a highly substantial reduction in edema on the 3rd and 7th post-operative day however, Graziani et al, found similar results on 2nd post-operative day. This could be explained in part by the fact that the half-life of dexamethasone is 36 h to 54 h. On the seventh postoperative day also, a further reduction in the swelling measurements was observed. The findings of our study support previous research results (14, 31).

This study reported that prophylaxis administration of dexamethasone injection via the intra - oral submucosal route has a statistically significant impact on trismus reduction. These findings are consistent with that of Laureano and his colleagues (18). Furthermore, Markiewicz and his colleagues investigated that dexamethasone reduced edema and managed to improve the range of mouth opening (32). Deo et al. observed a significant decrease in swelling and trismus with submucosal dexamethasone use though (20). Majid's study demonstrated that dexamethasone 4 mg reduced swelling significantly (24).

In current study, in distribution of site of surgery, 39 (60%) were done with right side while 26 (40%) were on left side. Matzen et al. (33) reported that 52% surgeries were done on right site whereas 48% done were on right site.

Additionally, in our study, stratification of age, gender, type of impaction, class of impaction, occupation, site of surgery and duration of surgery were done with respect to post-operative outcome which made our study different from all previous studies.

For third molar surgeries, Dexamethasone is administered orally, intravenously, intramuscularly in the masseter, gluteal, or deltoid region, submucosally, or as an endo alveolar powder (34). The current study used the submucosal route because it is simple, painless, non-invasive, convenient for both the surgeon and the patient, and offers a cost-effective method (35). Submucosal injections do not require the same level of skill as intramuscular and intravenous injections (24). Furthermore, because third molar surgery is performed under local anaesthesia, it is possible to administer submucosal dexamethasone painlessly at the site of surgery, giving the submucosal route an advantage over the intravenous and intramuscular administration(36).

CONCLUSION:

Dexamethasone is an effective pharmacological agent to reduce post-surgical third molar removal sequelae such as pain, swelling, and trismus. Although steroid injection through submucosal route has been the traditional preferred technique owing to its faster onset of action and better pain control.

LIMITATIONS:

- It was an only centered study.
- One limitation of this study is that neither the patients nor the surgeon were blinded to the use of corticosteroids. However, this type of potential bias was minimized by objectively

measuring the discomfort and collecting data on the total elapsed time to remove each tooth.

FUTURE RECOMMENDATIONS:

- More far multi-center and long-term clinical studies are needed to validate the findings.
- Further different routes and different dosage of Dexamethasone must be evaluated for unrivalled results.

CONSENT:

The authors obtained written and informed consent from the patients and kept it.

COMPETING INTERESTS:

The researchers have stated that they have no competing interests.

Footnotes

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