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Mannitol Reduces Pain and Trismus after Impacted Mandibular Third Molar Surgery: A Comparative Study

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ABSTRACT

Objective: To compare the efficacy of local 20% W/V Mannitol infiltration with the standard care for minimizing postoperative pain, edema, and trismus after impacted mandibular third molar removal.
Study Design: Quasi-experimental study.
Place and Duration of the Study: Armed Forces Institute of Dentistry, Rawalpindi, Pakistan, from May 2024 to Jul 2025.
Methodology: Forty subjects who underwent extraction of impacted mandibular third molar were divided into two equal groups, i.e., Mannitol and control group. In group A, apart from standard treatment, 20% w/v Mannitol infiltrated, while in group B, only standard treatment was applied. Pain assessment was done after 6, 24, and 48 hours, while swelling and trismus were recorded before surgery and 48 and 72 hours after surgery.
Results: There was a significant decrease in pain after surgery for Mannitol at 6 hours [6.00 (1.00) versus 9.00 (1.00); $p<0.001$] and 24 hours [3.00 (1.00) versus 5.00 (0.50); $p<0.001$] when compared with controls. The amount of swelling was significantly decreased at 48 hours [7.00 (1.00) versus 11.00 (1.00); $p<0.001$] and 72 hours [5.00 (1.00) versus 6.00 (2.00); $p=0.001$]. Trismus was also significantly decreased in the Mannitol group at 48 and 72 hours ($p<0.001$). Within-group analysis showed significant improvements in pain, swelling, and trismus over time in both groups ($p<0.001$).
Conclusion: Local 20% W/V Mannitol infiltration effectively decreases early postoperative pain, swelling, and trismus after third molar surgery, providing a non-steroidal supplement to postoperative management.

Keywords: Mannitol, Postoperative Pain, Swelling, Trismus.

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INTRODUCTION

In oral and maxillofacial surgery, the surgical extraction of impacted mandibular third molars is one of the most common operations conducted.[1] This often results in postoperative pain, swelling, and trismus.[2] Local tissue damage, vascular leakage, and the release of inflammatory mediators are the causes of these aftereffects.[3] Early postoperative recovery and patient satisfaction may be negatively impacted by these sequelae, which can significantly impair speech, mastication, and oral hygiene.[4] Nonsteroidal anti-inflammatory medications (NSAIDs), corticosteroids, and local therapies are used in conventional management to lessen fluid production and inflammation.[5] After third molar surgery, corticosteroids—more especially, Dexamethasone—have been shown time and time again to be useful in reducing pain and swelling.[6] Yet worry regarding systemic influence and contraindication in some patients emphasizes the necessity for other procedures to manage postoperative inflammation effectively.[7]

Current research has investigated the application of osmotic agents like Mannitol as an adjuvant in pain and edema management. Mannitol, which is a sugar alcohol, acts by reducing inflammation with its osmotic effect, its ability to scavenge free radicals, and promoting an anti-inflammatory environment.[8] Randomized controlled trials using local Dexamethasone infiltration have found significantly reduced pain scores, analgesic consumption, and trismus at 48 and 72 hours compared to control groups ($p<0.05$).[9]

The evidence on mannitol for dental surgery sequelae is very scant. The great majority of high-quality trials on third molar postoperative morbidity target corticosteroids (several RCTs and meta-analyses provide evidence for benefit on edema and pain) and NSAIDs. Thus, there is an evident gap in the research to establish Mannitol's effect on pain and trismus. The objective of the current research is to assess the safety and effectiveness of local 20% w/v Mannitol infiltration in alleviating postoperative pain and

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trismus after impacted mandibular third molar removal.

METHODOLOGY

The quasi-experimental study was performed at the Department of Oral and Maxillofacial Surgery, Armed Forces Institute of Dentistry (AFID), Rawalpindi, Pakistan, from May 2024 to July 2025. Ethical clearance of the research was obtained from the Institutional Review Board (IRB) of AFID before starting (Dated May 2024, Approval No.1285). Written informed consent was obtained from all participants following a description of the study purpose, procedures, benefits, and hazards. Consecutive sampling technique was used for patient sampling.

The sample size calculation was made with the help of G*Power software version 3.1 based on the primary outcome measure (postoperative pain). The calculation was made on the basis of pain values given by Jagtap *et al*.[10] These authors found that mean postoperative pain values in the control group were 7.2±1.1 and 5.8±1.0 in the experimental group in one day after surgery. Mean difference between groups was equal to 1.4 VAS units, while the pooled SD equaled 1.05, which gave effect size of 1.33 (Cohen's d). Having chosen a two-tailed test, power of 80%, and significance level of $\alpha = 0.05$, the minimum sample size was calculated to be 10 participants for each group. However, considering the quasi-experimental nature of the study, possible selection bias due to lack of randomization, interindividual variability in postoperative inflammation, and possible participant drop-out, the sample size was increased to 20 participants for each group (total n=40). A total of 64 individuals were assessed for eligibility, of which 24 dropped out. A final sample of 40 participants were further allocated to their respective groups (Figure).

Inclusion Criteria: Patients in the range of 18–35 years, both genders, medically fit (ASA I or II), with one impacted mandibular third molar of similar difficulty (Pell and Gregory Class II–B) to be removed surgically were included.

Exclusion Criteria: Pregnant females or lactating women, patients with diseases that make surgery or anesthesia contraindicated, having acute pericoronitis, infection, or abscess at the site of surgery, with allergy to study medications (mannitol, lidocaine, or NSAIDs), and who received corticosteroids, analgesics, or anti-inflammatory medications in the past week before operation.

The inclusion criteria-based patients were divided into Group-A (mannitol group) and Group-B (control group) through a non-random assignment method. Selection bias was avoided by recruiting all subjects on the basis of pre-set inclusion criteria, subjecting them to surgery through the same surgeon according to standard operative procedure, and evaluation by an independent examiner. The demographic/clinical profile of both the groups was also compared to make sure that both were comparable. The local anesthesia was standardized among all subjects through the use of the Gow-Gates method utilizing 1.8 mL Articaine with Epinephrine 1:100,000. All surgical operations were carried out by an experienced surgeon following the same standardized surgical approach to reduce the influence of procedural bias. Subjects under Group-A were given local infiltration of 20% w/v Mannitol, besides the standard post-operative treatment, while Group-B was given only standard post-operative treatment. The standard post-operative treatment involved giving Tab Brufen 400 mg, Tab Augmentin 625 mg and giving post-operative instructions verbally and in writing.

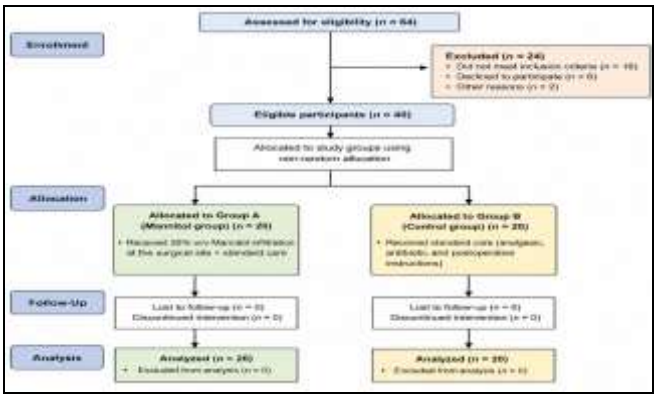


Figure: Patient Flow Diagram

Three milliliters of 20% w/v Mannitol was injected submucously with the use of a 5 ml syringe and 20 gauge needle on the buccal and distobuccal surface of the impacted mandibular third molar of Group-A, after having achieved adequate local anesthesia (10 mins after local anesthesia administration) and prior to carrying out the surgical operation. The selected quantity was thought to be adequate to give localized distribution at the surgical site without causing tissue distention. The 20% w/v concentration was chosen as it is the standard commercially available formulation of Mannitol and

has been reported to have osmotic and anti-inflammatory effects which may reduce post-operative edema and inflammatory sequelae. In all cases the extractions were carried out by the same surgeon to eliminate operator related variability.

Assessment of pain was done by using Visual Analogue Scale (VAS) at 6, 24 and 48 hours after the surgery. Swelling was determined using facial linear measurements taken from three points: (a) tragus to pogonion, (b) gonion to lateral canthus, and (c) gonion to labial commissure. Each was measured in millimeters with a flexible measuring tape. The three measurements were taken at each assessment time point, and the average of the three measurements was calculated to obtain the final swelling score used for statistical analysis. Assessment of swelling was done before the surgery and at 48 and 72 hours after the surgery. Trismus was evaluated through assessment of the maximal interincisal distance at baseline, 48-, and 72-hours after the surgery. All the measurements were taken by a trained, calibrated examiner who was not involved in the surgical procedures and was unaware of the treatment allocation, thereby minimizing assessment bias.

Data was collected and analyzed using statistical package for social sciences (SPSS) version 23. Normality of the data was assessed using Shapiro-Wilk test. Age and baseline interincisal distance were normally distributed whereas all other variables followed a non-normal distribution. Continuous variables such as age, post-operative pain, swelling and trismus were presented as Mean±SD or median (interquartile range) depending upon data normality. Discrete variables on the other hand were presented as frequencies and percentages. Intergroup comparisons of normally distributed variables including age were performed using independent samples t-test. Measurements of postoperative pain, swelling and trismus were compared using Mann–Whitney U test. The Friedman test was used to compare postoperative pain, swelling,= and trismus within each group at different time points. Qualitative variables including gender and tooth angulation were compared using Fisher exact test. A *p*-value less than or equal to 0.05 was considered significant.

RESULTS

A total of 40 patients completed the final analysis and the mean age of the participants was 26.50±.12 years in Group-A and 24.95±4.55 years in Group-B (p=0.520). No significant difference in gender distribution among both groups was seen (p=0.527). The predominant tooth angulation was mesioangular in both groups (45% vs. 50%), followed by vertical impactions (30% vs. 35%). No statistically significant group differences were noted on these baseline characteristics (p>0.05) (Table-I).

Table-I: Baseline Demographic and Clinical Characteristics of Study Participants (n=40)

Variables	Groups		*p*–value
	Group-A (n = 20)	Group-B (n = 20)	
Age Mean±SD	26.50±5.12	24.95±4.55	0.520*
Gender, n (%)			
Male	9(45%)	11(55%)	0.527**
Female	11(55%)	9(45%)	
Tooth Angulation, n (%)			
Vertical impactions	6(30%)	7(35%)	1.000***
Mesioangular impactions	9(45%)	10(50%)	
Distoangular impactions	1(5%)	0(0%)	
Horizontal impactions	4(20%)	3(15%)	

** Independent sample's t-test, ** Chi-square test, *** Fisher's exact test*

Postoperative pain VAS in the mannitol group at 6 hours was 6 in group (median 6.00 vs. 9.00, p<0.001) and 24 hours (median 3.00 vs. 5.00, p<0.001) was significantly lower and remained so with no statistically significant difference at 48 hours. Swelling in Group-A was also decreased at 48 hours (7.00 vs. 11.00, p<0.001) and 72 hours (5.00 vs. 6.00, p=0.001). Trismus at 48- and 72-hours was significantly lower in Group A than Group B (p<0.001), indicating reduced postoperative trismus in the mannitol group (Table-II). Significant changes in pain, swelling, and trismus across the different assessment periods in both Group-A and Group-B (p<0.001) was observed, indicating progressive postoperative recovery in both groups (Table-III). Clinically, these results show that mannitol markedly reduces postoperative pain, swelling, and recovery of mouth opening after third molar removal.

Table-II: Comparison of Postoperative Pain, Swelling, and Trismus between Mannitol and Control Groups at Different Time Points (n=40)

Variables	Timepoints	Groups		*p*-value
		Group-A (n = 20)	Group-B (n =20)	
Postoperative Pain [Median (IQR)]	6 hours	6.00 (1.00)	9.00(1.00)	<0.001
	24 hours	3.00 (1.00)	5.00 (0.50)	<0.001
	48 hours	1.00 (1.00)	1.00 (1.00)	0.445
Swelling [Median (IQR)]	Baseline	6.50 (1.00)	7.00 (2.00)	0.192
	48 hours	7.00 (1.00)	11.00 (1.00)	<0.001
	72 hours	5.00 (1.00)	6.00 (2.00)	0.001
Trismus [Median (IQR)]	Baseline	44.00 (3.00)	42.00 (5.00)	0.253
	48 hours	41.50 (4.50)	33.00 (4.00)	<0.001
	72 hours	33.5 (3.00)	25.5 (2.00)	0.001

£ Mann-Whitney U test

Table-III: Within-group comparison of Postoperative Pain, Swelling, and Trismus at different time points in the Study Groups

Variables	Timepoints	Groups	
		Group-A (n = 20)	Group-B (n = 20)
Postoperative Pain [Median (IQR)]	6 hours	6.00 (1.00)	9.00 (1.00)
	24 hours	3.00 (1.00)	5.00 (0.50)
	48 hours	1.00 (1.00)	1.00 (1.00)
p-value§		<0.001	<0.001
Swelling [Median (IQR)]	Baseline	6.50 (1.00)	7.00 (2.00)
	48 hours	7.00 (1.00)	11.00 (1.00)
	72 hours	5.00 (1.00)	6.00 (2.00)
p-value§		<0.001	<0.001
Trismus [Median (IQR)]	Baseline	44.00 (3.00)	42.00 (5.00)
	48 hours	41.50 (4.50)	33.00 (4.00)
	72 hours	33.5 (3.00)	25.5 (2.00)
p-value§		<0.001	<0.001

§ Friedman test

DISCUSSION

The 20% w/v Mannitol solution had significantly less postoperative pain score in the early postoperative period (p<0.001). There was also significant reduction in swelling in the Mannitol group in comparison to the control group in 48 hours and 72 hours after surgery (p<0.001). In addition, there was significant increased mouth opening in the 48 hours and 72 hours in the Mannitol group, showing reduced trismus after operation (p<0.001). These findings suggested that mannitol is associated with clinically significant early relief of discomfort and mouth opening following impacted mandibular third molar surgery.

De Santana-Santos et al. indicated swelling and trismus are most intense at around 48 hours post-operatively, decreasing gradually by Day 7.[11] Pérez-González *et al*. also recorded maximum swelling at 24–48 hours with significant reduction thereafter (p<0.05), also noting patient-related aspects like BMI and anatomy can affect severity.[12] These observations are consistent with our findings that postoperative swelling peaked at 48 hours and reduced by 72 hours and Mannitol group showed significantly reduced trismus when compared with control group.

Mannitol has been used in combination with Lignocaine for achieving better pulpal anesthetic outcomes in a study by Pathak *et al*.[13] In our study, however, we used Mannitol as an additional intervention postoperatively for reduction of pain and swelling. The study primarily compared pain between two groups who received Mannitol or a placebo and reported Mannitol reduced post-operative pain and trismus.[10]

When comparing our findings with corticosteroid studies, the effect size of Mannitol was clinically significant. A randomized clinical study evaluating submucosal Dexamethasone found that patients receiving the corticosteroid exhibited significantly lower pain scores at 24 hours and improved mouth opening, alongside reduced facial swelling compared with placebo by He *et al*.[14] Another meta-analysis concluded that Dexamethasone provided a moderate-to-large effect in decreasing postoperative inflammatory complications, particularly during the early postoperative period when edema and trismus typically peak by Suleman *et al*.[15] While Mannitol works by a distinct mechanism—establishing an osmotic gradient to move interstitial fluid into the vascular space—our findings reveal similar reductions in swelling and trismus in the early postop period. This would indicate that Mannitol represents a non-steroidal option for controlling postoperative symptoms. Mannitol and steroid combination has been tried as local injections postoperatively in hand and limb surgeries for reduction of inflammation and has shown promising results by Choi *et al*.[16]

Nevertheless, all the aforementioned studies have not shown uniform results when it comes to the effect of anti-inflammatory drugs on postoperative complications. According to Al-Shamiri *et al*., preoperative and postoperative treatment with dexamethasone has been associated with similar results concerning pain and trismus complications; however, there were significant differences in the degree of edema reduction.[17] In a recently conducted systematic review by Singh *et al*., the comparison of dexamethasone and methylprednisolone in terms of postoperative pain and swelling has also shown no significant differences; however, dexamethasone had better results regarding early trismus.[18]

The clinical relevance of these results is their potential to alter patient care and postoperative counseling. Swelling and trismus, though self-limiting, represent two of the most unpleasant postoperative sequelae and may impact patient comfort, nutrition, and oral hygiene, as given by Aljohani *et al*.[19] Another study conducted by Mobilio *et al*. highlighted that swelling severity is directly related to surgical complexity and flap design, and regulation of these two factors can decrease postoperative morbidity.[20] Our results highlight the typical recovery course, which can help clinicians set realistic expectations for patients and plan interventions such as anti-inflammatory medications or physiotherapy if required.

The findings can be attributed to an inflammatory cascade caused by surgical trauma. The tissue manipulation elicits vascular permeability changes and fluid extravasation, which result in maximal edema 24–48 hours post-surgery, as stipulated by Marco *et al*.[21] Trismus early on would be attributed to inflammatory involvement of masticatory muscles, particularly the medial pterygoid as described by Santiago-Rosado *et al*.[22] As the inflammatory process resolves, a gradual remission of these symptoms ensues, accounting for the statistically significant improvement in our findings.

Our research utilized standardized clinical measurement at predetermined postoperative times, optimizing the validity of seen trends. Mannitol may become an affordable adjunct (or substitute) to steroids, especially among steroid-contraindicated patients. The trial lends itself to larger trials head-to-head comparing Mannitol with steroids, investigating optimal volume and concentration, and rigorously assessing safety (serum osmolality/electrolytes).

Limitations of the Study

Only short-term effects were measured, and interindividual variability in inflammatory response potentially affected outcomes. No direct comparison with other anti-inflammatory agents, including corticosteroids or a placebo in a parallel arm, was conducted, which would have yielded stronger comparative evidence. Additionally, measures of subjective symptoms, such as the Visual Analog Scale of pain, can introduce reporting bias even with standardized administration. The non-random allocation used in the current quasi-experiment may have contributed to selection bias. While the study participants were not allocated into groups randomly, a number of actions were taken to reduce such a bias. These included the application of predetermined eligibility criteria for participants, performing standardized operations by one surgeon, and assessment of results by an independent calibrated investigator. In addition, the baseline characteristics were similar between the two groups.

Conclusion

Mannitol infiltration locally reduces early postoperative pain, swelling, and trismus after impacted mandibular third molar surgery. It is most beneficial when used in the initial 48 hours after surgery—when inflammatory reactions usually reach their peak—resulting in enhanced patient comfort and functional recovery. Because of its non-steroidal mechanism of action and good safety profile, Mannitol could be a useful adjunct to routine postoperative management. Large-scale, multicenter randomized controlled trials comparing Mannitol directly with conventional anti-inflammatory drugs are required in the future to validate these findings and establish optimal dosing regimens. Future randomized controlled trials incorporating placebo-controlled interventions and double-blinding are recommended.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under:

MA & SUK: Conception, study design, drafting the manuscript, approval of the final version to be published.

AW & AI: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

FA & AQ: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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