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Determination of Anti-Inflammatory and Analgesic Efficacy of Ascorbic Acid after Impacted Third Molar Surgery

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ABSTRACT

Objective: To evaluate the clinical efficacy of Ascorbic acid in relieving pain and inflammation following surgical removal of the third molar.

Study Design: Quasi-experimental study.

Place and Duration of Study: Armed Forces Institute of Dentistry, Rawalpindi Pakistan, from Jan to Mar 2023.

Methodology: Sixty participants who required surgical extraction of the impacted third molar were included and segregated equally into two groups. Group-A received Amoxicillin with Clavulanic acid (625 mg) thrice a day and Metronidazole (400 mg) twice daily, while Group-B received Amoxicillin with Clavulanic acid (625 mg) thrice daily, Ascorbic acid (500 mg) twice daily and Metronidazole (400 mg) twice daily. Both the groups received Naproxen Sodium as per requirement (550 mg). Pain, trismus, facial swelling, and requirement of analgesic consumption were evaluated on the seventh post-operative day.

Results: There was a statistically significant difference in reducing the intensity of pain (p<0.01), severity of facial swelling and trismus (p<0.01) and requirement of analgesic consumption between Group A and B (p<0.001).

Conclusion: Our study concluded that Ascorbic acid after surgery effectively reduces pain intensity, the severity of facial swelling and trismus, and the requirement for analgesic consumption so that ascorbic acid may be used as an adjuvant therapy with other conventional drugs.

Keywords: Ascorbic acid; Molar, Analgesics, Inflammation, Anti-inflammatory agents.

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INTRODUCTION

Third, molar surgery is one of the most frequently used surgical procedures by oral and maxillofacial surgeons. Assessment of the third molar is determined by clinical and radiological examination.[1] Many inflammatory reactions occur after oral surgical procedures that are not restricted to the oral cavity and can be imitated in the soft tissues of the face.[2]

Postsurgical pain, facial swelling, and reduction in mouth opening that ascend following surgical removal of impacted third molar are usually irritating for the patients and may affect life's comfort.[3] After surgical extraction of the third molar, pain is persistent due to the consequence of surgical trauma and emission of chemical mediators, particularly bradykinin, prostaglandins, serotonin, and histamine.[4] After the third molar extraction, one of the most postoperative complications associated with it is trismus, as a manifestation of swelling, pain or both.[5]

Sometimes, it is quite difficult for the surgeon to control pain due to many reasons involved in pain development, but most of these are linked to inflammatory processes due to the consequences of surgical trauma. Many therapeutic strategies have been developed to control these with various antibiotics, steroids, nonsteroidal anti-inflammatory drugs and topical antibiotic dressing.[6] However, these therapies are associated with poor compliance, repeated infection and a huge economic burden on the patient and society.[7] Ascorbic acid has anti-inflammatory, anti-nociceptive and antioxidant properties. It is one of the substantial constituents of collagen synthesis. It has a substantial role in the immune function.[8] The literature shows that vitamin C deficiency leads to pain, which was entirely lessened within a week or two by taking vitamin C supplementation supplements. It is thought that ascorbic acid's anti-nociceptive properties depend on its antioxidant properties by scavenging a wide range of reactive oxygen species (ROS).[9,10] Worldwide, few clinical studies assess the role of ascorbic acid in relieving trismus, facial swelling, and pain. The aim of the study is to explore the effect of ascorbic acid on trismus, facial swelling and pain after surgical removal of wisdom teeth in the Pakistani population.

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METHODOLOGY

The quasi-experimental study was conducted at the Department of Oral Surgery, Armed Forces Institute of Dentistry (AFID), in collaboration with the Department of Pharmacology, Army Medical College (AMC), Rawalpindi Pakistan, from January to March 2023 after approval from the Ethics Review Committee of AMC, the National University of Medical Sciences (ERC/ID/255), and AFID. The sample size was calculated using the World Health Organization sample size calculator based on postoperative complications, which was 2.6%.[8]

Inclusion Criteria: Individuals of either gender aged more than 18 years requiring third molar surgery with one-third impacted tooth were included.

Exclusion Criteria: Pregnant or lactating women, periapical and periodontal disease and any comorbid conditions such as diabetes and hypertension were not included.

Patients fulfilling the inclusion criteria were included through randomization by lottery method (Figure) and divided equally into two groups: Group-A (n=30) received Amoxicillin with Clavulanic acid (625 mg) thrice daily and (400 mg) Metronidazole twice daily for five days. This was considered as Control Group. Group-B (n=30) received Amoxicillin with Clavulanic acid (625 mg) thrice daily, Metronidazole (400 mg) twice daily for five days and Ascorbic acid 500 mg twice daily for seven days. This was considered as the Test Group. Both groups received Naproxen Sodium (550 mg) as per requirements.

All participants were counselled preoperatively, and informed consent was obtained from each participant. Demographic details were recorded. Assessment of pain, a dose of Naproxen Sodium, facial swelling, and trismus were assessed on the seventh postoperative day.

Pain was assessed using a Visual Analogue Scale (VAS) with "0 mm" showing" no pain" and "10 mm" showing "worst possible pain" at different time intervals: T0 (immediately after surgery as a baseline), T1 (24 hours postsurgical), T2 (48 hours postsurgical) and T3 (72 hours postsurgical). Trismus was measured by using a finger basic diagnostic in which the maximum incisal edge of the upper and lower incisor was measured at different time intervals: T0 (24-48

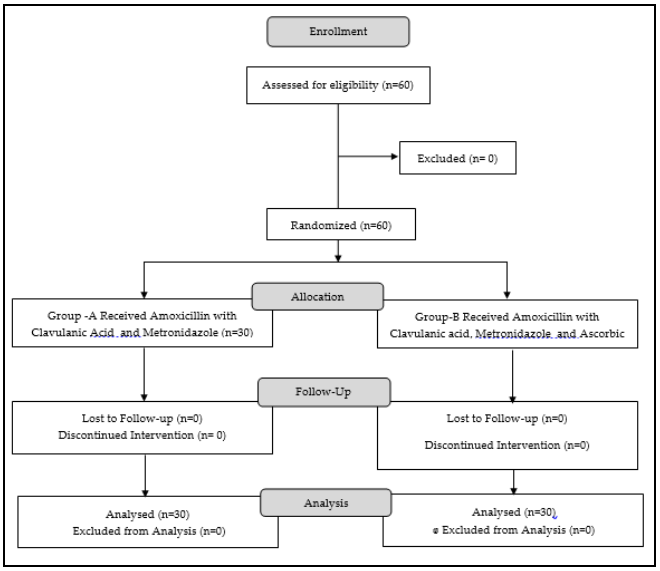

Figure: Patient Flow Diagram (n=60)

postsurgical as a baseline), T1 (72 hours postsurgical) and T2 (7th day postsurgical). The measured of facial swelling was estimated using a six-point VAS, where 0 shows "no swelling", and 5 shows "extreme severe swelling" at different time intervals: T0 (24-48 postsurgical as a baseline), T1 (72 hours postsurgical) and T2 (7th day postsurgical).[11,12]

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. For non-parametric data, the Whitney U test was applied, and was expressed as the median and interquartile range (IQR). The level of significance was set at $p \leq 0.05$.

RESULTS

Of 60 participants, the mean age was 31.43±6.65 in Group-A, while in Group-B, the mean age was 30.13±7.45. There was a statistically significant difference in the frequency of pain between the control and study groups ($p<0.001$) (Table-I). The difference in postoperative trismus was statistically significant between the groups (Table-II). The severity of facial swelling was reduced in both groups; however, ascorbic acid had a better response than the Control Group (Table-III). Every participant in the Control Group adhered to a daily regimen of taking 550 mg of Naproxen Sodium twice daily without skipping doses. The median value of Group-A was 5500mg (5500 - 5500), while in Group-B was 2200mg (1100-2750), and there was a statistically significant difference between

the two groups for analgesic consumption (p<0.01) (Table-IV).

Table-I: Comparison of Pain between Study Groups (n=60)

Pain	Group-A (n=30)	Group-B (n=30)	*p*-value
Baseline			
Mild	4(13.33%)	4(13.33%)	0.307#
Moderate	2(6.66%)	6(20%)	
Severe	24(80%)	20(66.6%)	
At 24 hours			
None	0(0%)	0(0%)	0.001*
Mild	2(6.66%)	14(46.6%)	
Moderate	8(26.6%)	8(26.6%)	
Severe	20(66.6%)	8(26.6%)	
At 48 hours			
None	0(0%)	1(3.33%)	<0.001*
Mild	4(13.3%)	18(60%)	
Moderate	13(43.3%)	10(33.3%)	
Severe	13(43.3%)	1(3.33%)	
At 72 hours			
None	0(0%)	3(10%)	<0.001*
Mild	10(33.3%)	23(76.6%)	
Moderate	15(50%)	4(13.3%)	
Severe	5(16.6%)	0(0%)	

Table-II: Comparison of the Trismus between Study Groups (n=60)

Trismus	Group-A (n=30)	Group-B (n=30)	*p*-value
Baseline			
Mild	1(3.33%)	5(16.6%)	0.065#
Moderate	10(33.3%)	14(46.6%)	
Severe	19(63.3%)	11(36.6%)	
At 72 hours			
Mild	1(3.33%)	4(13.3%)	0.01*
Moderate	16(53.3%)	23(76.6%)	
Severe	13(43.3%)	3(10%)	
At 7th day			
Mild	16(53.3%)	28(93.3%)	
Moderate	14(46.6%)	1(3.33%)	<0.001*
Severe	0 (0%)	1(3.33%)	

DISCUSSION

After the removal of an impacted tooth, the occurrence of trismus, pain and facial swelling frequently creates a situation in which patients retreat from social life.[12] Our aim in this study was to determine ascorbic acid's analgesic and anti-inflammatory effect following surgical removal of the third molar.

Results of our present study showed a statistically significant difference in reducing the severity of pain, facial swelling and trismus between the Control and Study Groups. Results of our present study showed a

Table-III: Comparison of the Facial Swelling between Study Group (n=60)

Facial Swelling	Group-A (n=30)	Group-B (n=30)	*p*-value
Baseline			
	n(%)	n (%)	0.135#
None	1(3.33%)	1 (3.33%)	
Slight	0(0%)	0(0%)	
Mild	0(0%)	1(3.33%)	
Severe	0(0 %)	5(16.6%)	
Very Severe	4(13.33%)	2(6.66%)	
Extremely Severe	25(83.3%)	21(70%)	
At 72 hours			
None	1(3.33%)	1(3.33%)	
Slight	0(6.66%)	2(6.66%)	
Mild	1(3.33%)	6(20%)	
Severe	9 (30%)	13(43.33%)	0.027*
Very severe	6(20%)	5(16.66%)	
Extremely Severe	13(43.33%)	3(10%)	
At 7th day			
None	5(16.66%)	16(53.33%)	
Slight	4(13.33%)	7(23.33%)	
Mild	9(30%)	5(16.66%)	
Severe	8(26.66%)	2(6.66%)	0.009*
Very Severe	2(6.66%)	0(0%)	
Extremely Severe	2(6.66%)	0(0%)	

Table-IV: Comparison of Analgesic Consumption (n=60)

Dose of Naproxen Sodium	Group-A (n=30) Median (IQR)	Group-B (n=30) Median (IQR)	*p*-value
	5500 (5500–5500)mg	2200 (1100-2750)mg	<0.001*

statistically significant difference observed in the requirement of naproxen sodium dose between the two groups. Similar to our finding, there was a study performed by Pisalsitsakul *et al*. where it was revealed that the addition of vitamin C (600 mg) three times a day after premolar extraction reduced the intensity of postoperative pain.[13] Another study conducted by Chaudhary *et al.* demonstrated that injectable vitamin C decreased the intensity of pain.[14] A study conducted by Gadge et al. showed that taking vitamin C supplements decreased postoperative pain after dental implant surgery.[15] Another study conducted by Mukherjee and Gowda showed that taking ascorbic acid (500 mg) reduced postoperative pain, pocket depth and clinical attachment loss in periodontal flap surgery.[16] Similar to our findings, another study conducted showed that injectable vitamin C reduced gingival inflammation.[17] A study conducted by Li *et al*. showed that taking (320 mg) of vitamin C supplement

for three months reduced gingival bleeding by increasing collagen formation.[18] Study conducted by Mahajani *et al*. showed that taking (1500 mg) of vitamin C reduced the gingival bleeding index.[19] Another study conducted by González-Serrano and his colleagues showed that the application of propolis extract, nanovitamin C and nanovitamin E reduced the postoperative pain, trismus, analgesic consumption and facial swelling, but there was statistically insignificant difference in facial swelling, trismus and analgesic consumption. [20]

The improvement observed in the mentioned parameters, such as reducing postoperative trismus intensity, minimizing facial swelling, alleviating pain, and decreasing the need for Naproxen sodium dosage, was achievable due to the anti-inflammatory and pain-relieving properties of ascorbic acid. Ascorbic acid plays an important role in inflammation by reducing the inflammatory cytokines such as interleukin 1 and 6, tissue necrosis factor α and proinflammatory cytokines such as C- C-reactive protein—the anti-nociceptive properties are based on antioxidants that scavenge the ROS. Hence, different studies support our findings as ascorbic acid has an ameliorating effect on pain, facial swelling and trismus as it is an antioxidant and anti-inflammatory agent, and its use is associated with fewer adverse effects. Hence, it is safe and can be prescribed to patients for oral surgery.[7,13]

CONCLUSION

Our study concluded that ascorbic acid given after surgery effectively reduces pain intensity, the severity of facial swelling and trismus and the requirement of analgesic consumption so that ascorbic acid may be used as an adjuvant therapy with other conventional drugs.

Conflict of Interest: None.

Authors' Contribution

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

MF: Data acquisition, data analysis, drafting the manuscript, critical review, approval of the final version to be published.

CMU & MN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SA & MS: 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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