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Original Article

Antibiotic Prophylaxis for Prevention of Dry Socket in Mandibular Third Molar Extraction Compared to Conventional Therapy

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ABSTRACT

Objective: To compare the effectiveness of a single preoperative oral dose of Amoxicillin and Metronidazole to conventional therapy for the prevention of dry socket.
Study Design: Quasi-experimental study.
Place and Duration of Study: Tertiary Care Dental Hospital, Rawalpindi Pakistan, from Mar to Aug 2024.
Methodology: A sample size of 225 patients, requiring surgical extraction for removal of mesioangularly impacted mandibular third molar was selected. Patients were distributed into three Groups: Group 1 received a single oral dose of Amoxicillin one hour prior to surgery, Group 2 received a single oral dose of Metronidazole one hour before surgery, and Group 3 patients received a 5-day antibiotic course post-surgery. Dry socket frequency was recorded on the 4th postoperative day.
Results: Four (5.8%) out of the 17(7.56%) patients who reported having dry socket were in the Amoxicillin Group, 3(6.3%) were in the Metronidazole Group, and 10(14.5%) were in the conventional therapy Group. Patients in all three Groups did not significantly differ in the frequency of presence of dry socket (p=0.162). Regarding differences in age, gender, and the reason for extraction, the difference was not statistically significant (p>0.05) between the Groups receiving Amoxicillin, Metronidazole, and conventional therapy.
Conclusion: The study indicated no protective effect of giving single oral dose of Amoxicillin or Metronidazole before the surgery compared to conventional therapy in preventing dry socket postoperatively. Nevertheless, dry socket presence was lesser in Groups receiving preoperative antibiotics compared to conventional therapy Group.

Keywords: Drug Therapy, Dry Socket, Oral Surgical Procedures, Postoperative Complications.

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INTRODUCTION

Dry socket also known as alveolar osteitis, is characterized as a painful, albeit not extremely rare, postoperative condition arising after dental extraction, most frequently after third molar surgery.[1] Its hallmark is premature loss or disruption of the initial blood clot that forms at the site of extraction resulting in an exposed bone surface and inflamed socket walls that usually appears within 1-3 days following extraction.[2,3] Patients usually complain of severe radiating pain, halitosis, and a foul taste in the mouth. The pathogenesis of alveolar osteitis is multifactorial and involves both patient-related factors—such as age, sex (with increased frequency in females), poor oral hygiene, smoking, hormonal effects, and systemic diseases—and procedural factors, like complexity and time taken for extraction, trauma during the procedure, and operator experience.[4,5]

According to Alsadat-Hashemipour *et al.*, the anatomical location of the extraction has a major impact on the risk, where third molars in the mandibular region have a significantly greater risk of developing dry socket in comparison to teeth in maxillary region, because of more dense bone and lesser vascularity.[6] Gangá *et al.*, recorded variation in the frequency of dry socket from 0.5% to 7% in the case of normal extractions, which reaches up to 1%–37.5% in third molar removals.[7] Arteagoitia *et al.*, and Falci *et al.*, highlighted that this increased risk is especially related to surgical removal of impacted mandibular third molars.[8,9] Due to these risks, prophylactic use of antibiotics has been assessed in various studies. Torof *et al.*, in a recent meta-analysis, indicated that occurrence of postoperative complications, including alveolar osteitis can be decreased by using Amoxicillin and Metronidazole. Yet, it also reported variation in outcomes in different clinical sites.[10]

Despite the literature having investigated different interventions developed for preventing and managing alveolar osteitis, no consensus on single-dose preoperative antibiotic regimens is evident. Most

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recent studies tend to differ in antibiotic usage, dosage, and timing, creating a lack of standardized preventive protocols. Hence, the current study seeks to determine the effect of a single oral dose of Amoxicillin and Metronidazole, administered before the surgery on the frequency of dry socket following surgical extraction of mandibular third molars relative to standard postoperative antibiotic therapy. By methodically assessing and directly comparing two different single-dose preoperative antibiotic regimens oral Amoxicillin and Metronidazole one hour prior to third molar extraction with a standard 5-day postoperative course of antibiotics, the study fills a major gap in clinical practice where overuse and variable prescribing are still prevalent. This strategy provides a streamlined, time-saving, and perhaps more sustainable option to lengthy antibiotic regimens, presenting novel comparative data that may guide future clinical recommendations for reducing antibiotic duration and enhancing patient adherence.

METHODOLOGY

This study was carried out at the Outpatient Oral and Maxillofacial Surgery Department at a Tertiary Care Dental Hospital, Rawalpindi, from March to August 2024. Ethical approval was received from the hospital's Institutional Review Board (Ref No.918/Trg dated 8 Jan 2023). A consecutive purposive sampling method was applied, and descriptive and clinical information was obtained from patients who needed surgery for removing mesioangularly impacted mandibular third molars with Pell and Gregory's Class 1 ramus relationship. A sample of 225 for this study was determined by OpenEpi, based on a standard two-proportion formula with a 95% confidence interval, a 5% margin of error and an infection/dry-socket rate of 2.5% in the antibiotic Group versus 15% in the control Group (absolute difference 14.1%).[11] After explaining the study's purpose, benefits, and potential risks, informed consent was obtained from all participants.

Inclusion Criteria: Patients having mesioangularly impacted mandibular 3rd molars with Pell and Gregory's Class I ramus relationship, both genders between the ages of 18 to 50 years, not having any systemic disease. Furthermore, the tooth to be extracted was not associated with any periapical pathology or cysts as confirmed by the panoramic radiograph.

Exclusion Criteria: Participants who were excluded from the study were those who smoked, pregnant or breastfeeding mothers, alcohol consumers, individuals taking anticoagulants or oral contraceptives, those already on antibiotics, patients suffering from renal or liver dysfunction, individuals having an allergy to antibiotics, and those unwilling to participate.

Under local anaesthesia, an oral and maxillofacial surgery postgraduate trainee with more than two years of clinical training and experience carried out each extraction surgically, supervised by a consultant oral and maxillofacial surgeon. This aimed to ensure uniformity in technique and reduce operator variability. Anaesthesia was administered to the inferior alveolar, lingual, and long buccal nerves, an incision was made using a scalpel with a No.15 blade and an envelope flap with a distal releasing incision was raised. Bone removal and tooth sectioning was done as needed with round and fissured burs using a micromotor straight handpiece, with cooling and irrigation done using normal saline solution. After tooth extraction, normal saline solution was used to irrigate and flush the socket. Sutures were placed using 3-0 Vicyrl, and the extraction socket was covered with a sterilized gauze roll, while the patient was instructed to bite on it for at least 40 minutes.

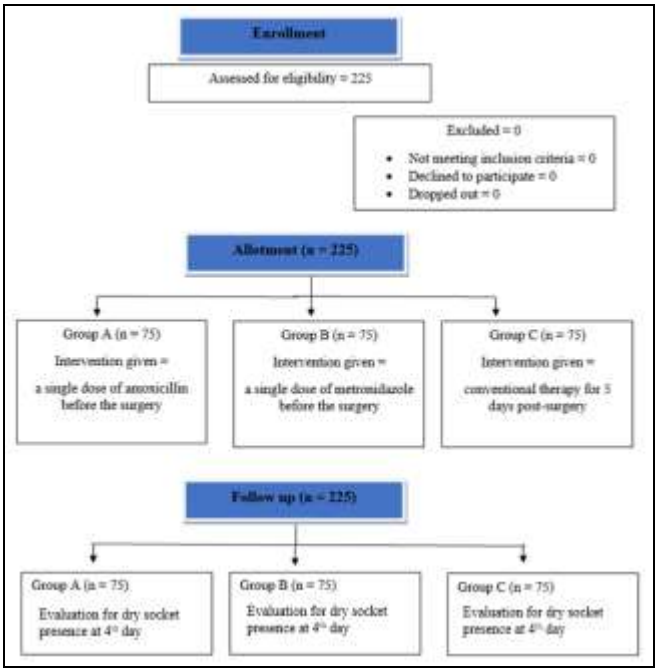

Figure: Patient Flow Diagram

Out of the three Groups, the first Group received a single preoperative oral dose of 500 mg Amoxicillin an hour prior to extraction and a painkiller three times a day for the first 48 hours, then SOS. The second

Group was given a single preoperative oral dose of 400 mg Metronidazole one hour before the extraction and a painkiller three times daily for the first 48 hours, then SOS. The third Group received conventional therapy (500 mg of Amoxicillin twice daily, 400 mg of Metronidazole every eight hours, for five days, and a painkiller thrice daily for the first 48 hours, followed by SOS). After the surgery, both written and verbal instructions were provided to the patients. All patients were examined visually under the dental unit light on the 4th postoperative day. Alveogyl was used to treat the patients diagnosed with dry socket, following irrigation and flushing of the socket with normal saline.

Statistical analysis was done using statistical package for social sciences (SPSS) version 27. Descriptive statistics were applied: frequencies and percentages were calculated for categorical variables (gender, tooth location, reason for extraction, and treatment received), while mean and standard deviation (SD) were calculated for the numerical variable (age). Stratification of patients was carried out by age, gender, treatment Group, and reason for extraction to control for potential confounding. The Chi-square test was applied to assess associations between categorical variables and the presence of dry socket. When expected cell counts were less than 5, Fisher's Exact test was used as it provides a more accurate significance level for small sample sizes in contingency tables. A *p*-value of <0.05 was considered statistically significant, and all tests were performed with a 95% confidence interval.

RESULTS

A total of 225 patients included in the study had a mean age of 32.89±10.50 years, with 132(58.67%) males and 93(41.33%) females. The reason for extraction, as reported by the patients, was attributed to either pericoronitis in 131 patients (58.22%), caries in 77 patients (34.22%), damage to the adjacent second molar in 12 patients (5.33%), or orthodontic treatment in 5 patients (2.22%).

The demographic and clinical profile of 225 patients among three study Groups—Amoxicillin, Metronidazole, and Conventional treatment is indicated in Table-I. The mean age of the patients varied from around 30 to 34 years among Groups. Male subjects outnumbered females in each Group by a small margin. The most frequent reasons for extraction were pericoronitis and caries, with some variation in frequency between treatment Groups.

Table-I: Demographic and Clinical Parameter details of the Patients belonging to the three Groups (n=225)

Variables	Groups		
	Group-1 n=75	Group-2 n=75	Group-3 n=75
Age (years), Mean±SD	34.03±9.73	34.29±11.72	30.37±9.73
18 to 24 years, n(%)	12.00(16.00)	20.00(26.67)	26.00(34.67)
25 to 35 years, n(%)	32.00(42.67)	22.00(29.33)	26.00(34.67)
36 and above years, n(%)	31.00(41.33)	33.00(44.00)	23.00(30.67)
Gender			
Male, n(%)	41.00(54.67)	46.00(61.33)	45.00(60.00)
Female, n(%)	34.00(45.33)	29.00(38.67)	30.00(40.00)
Reasons for extraction			
Pericoronitis , n(%)	50.00(38.17)	40.00(30.53)	41.00(31.29)
Caries, n(%)	17.00(22.08)	31.00(40.26)	29.00(37.66)
Damage to Second Molar, n(%)	5.00(41.67)	4.00(33.33)	3.00(25.00)
Orthodontic Treatment, n(%)	3.00(60.00)	0.00(0.00)	2.00(40.00)

While a maximum frequency of dry socket was noted in the control Group (14.5%), following the Amoxicillin (5.8%) and Metronidazole (6.3%) Groups, the variation was not statistically significant (p=0.162) (Table-II). This implies that although patients treated with a single preoperative dose of either Amoxicillin or Metronidazole had fewer instances of dry socket than those administered postoperative antibiotics, the reduction witnessed was not significant enough to establish a statistically protective effect. Most patients in each of the three Groups did not suffer from dry socket (>84%), which means that the cumulative risk remained low irrespective of the antibiotic regimen.

Table II: Frequency of Dry Socket Frequency among the Patients in all three study Groups (n=225)

Dry Socket	Group-1 n=75	Group-2 n=75	Group-3 n=75	*p*-value
Presence, n(%)	4.00(5.80%)	3.00(6.30%)	10.00(14.50%)	0.162
Absence, n(%)	68.00(92.30%)	71.00(94.50%)	63.00(84.00%)	
Loss, n(%)	3.00(4.00%)	1.00(1.40%)	2.00(2.00%)	

No statistically significant differences in the dry socket distribution by gender, age, and reason for extraction between the three study Groups were noted (p>0.05) (Table-III). Females (20%) had a higher rate of dry socket than males (8.9%) in the conventional therapy Group, whereas lower and equal rates were noted in the antibiotic Groups. Younger patients (18–24 years) in the control Group had a greater prevalence (15.4%), while antibiotic Groups had uniformly low rates in all ages. For reasons of extraction, caries was more often associated with dry socket in the control Group (17.2%) than pericoronitis (9.8%). Conversely, few were seen in the antibiotic Groups no matter the reason for extraction. These results indicate that while differences were not statistically significant, preoperative antibiotics were linked with fewer instances of dry sockets among subGroups when compared to standard therapy.

Table-III: Distribution of Dry Socket Frequency across Study Groups by Age, Gender, and Reason of Extraction (n=225)

Groups	Dry Socket				*p*-value (Fischer's exact test)
	Factors	Presence n(%)	Absence n(%)	Loss n(%)	
	Gender				
Group-1	Male	1(2.44)	38(92.68)	2(4.88)	0.441
	Female	3(8.82)	30(88.24)	1(2.94)	
Group-2	Male	2(4.26)	43(93.48)	1(2.12)	0.698
	Female	1(3.45)	28(96.55)	0(0)	
Group-3	Male	4(8.89)	39(86.67)	2(4.44)	0.213
	Female	6(20)	24(80)	0(0)	
	Age years				
Group-1	18 to 24	1(8.33)	10(83.33)	1(8.33)	0.853
	25 to 35	1(3.125)	30(93.75)	1(3.125)	
	36 and above	1(3.125)	29(90.625)	1(3.125)	
Group-2	18 to 24	1(5)	19(95)	0(0)	0.449
	25 to 35	0(0)	21(95.5)	1(4.5)	
	36 and above	2(5.88)	31(93.94)	0(0)	
Group-3	18 to 24	4(15.38)	22(84.6)	0(0)	0.410
	25 to 35	3(12)	21(84)	2(8)	
	36 and above	3(13.04)	20(86.96)	0(0)	
	Reason for Extraction				
Group-1	Pericoronitis	2(50)	47(94)	1(20)	0.421
	Caries	2(11.76)	14(82.35)	1(5.88)	
	Damage to second molar	0(0)	4(80)	1(20)	
	Orthodontic Treatment	0(0)	3(100)	0(0)	
Group-2	Pericoronitis	2(5)	37(92.5)	1(2.5)	0.873
	Caries	1(3.23)	30(96.77)	0(0)	
	Damage to second molar	0(0)	4(100)	0(0)	
	Orthodontic Treatment	0(0)	0(0)	0(0)	
Group-3	Pericoronitis	4(9.76)	36(87.80)	1(2.44)	0.878
	Caries	5(17.24)	23(79.31)	1(3.45)	
	Damage to second molar	1(33.33)	2(66.67)	0(0)	
	Orthodontic Treatment	0(0)	2(100)	0(0)	

DISCUSSION

This study suggested that the numerical frequency of dry socket was lesser with prophylactic antibiotics (5.8% in the Amoxicillin Group and 6.3% in the Metronidazole Group) than with the conventional therapy (14.5%); although there was no significant difference (p=0.162) observed. Likewise, gender, age and reason for extraction subGroup analyses also demonstrated no statistically important association (p>0.05), that is, they were not substantial factors for the risk of developing dry socket in the study population.

These results are partially consistent with Khooharo *et al.,* who showed significantly lower frequency of dry socket by only 1.6% after combined preoperative medication with Amoxicillin and Metronidazole compared to 8.2% in the control Group (p<0.05).[12] The lack of statistical significance in their study compared with ours may be related to the combination of therapy, larger sample size, and more homogeneous population of patients (only patients with pericoronitis requiring removal of an impacted third molar) whereas our patient population was more heterogeneous. Gazal *et al.,* reported low rates of dry socket of 3.6% in the co-amoxiclav Group, 5.3% in the Amoxicillin Group, and 6.2% in the Metronidazole Group, all significantly less than in the placebo arm (p<0.05).[13] Our results show the same pattern for Metronidazole and Amoxicillin, although this is not statistically significant, presumably because of missing clavulanic acid and because the postoperative instructions and follow-up period were not similar.

Lupi *et al.,* and Menon *et al.,* reported that prophylactic antibiotics, particularly Amoxicillin and Amoxicillin-clavulanate, can both decrease the risk of infections and dry socket following surgery. Menon et al. found that those prescribed Amoxicillin exhibited a relative risk (RR) decrease of 0.43 (95% CI 0.28–0.65) for the development of dry socket,[14,15] which is contrary to our non-significant outcome and this study. This finding could be due to small sample size, power constraints, or single-dose regimens in their series compared to prolonged, postoperative courses in ours. Also, Octavi Camps-Font *et al.,* in a network meta-analysis, reported that systemic antibiotics were associated with a significant decrease in the dry socket; the ORs (odds ratios) were between 0.30 and 0.50, depending on the type of antibiotic and timing.[16] Our single preoperative doses are at the lower limit of efficacy in comparison with the longer duration and/or combined regimens evaluated in their study. The methodological differences, including nonspecific standardization of surgical technique, could explain why our overall dry socket rate was higher at 7.56%, in contrast to the 3-5% range reported in their study.

De Angelis *et al.,* highlighted that the statistical efficacy of antibiotics is different depending on surgical complexity and patient risk profile. Within their systematic review, trials employing antibiotics demonstrated a pooled risk reduction of 39% for dry socket (p<0.05), particularly in >20-minute procedures or those involving bone removal.[17] As our research involved patients of mixed complexity but did not record operative time, this variable may have contributed to outcome variation and statistical power. Sologova *et al.,* were able to conclude that antibiotic prophylaxis had a 4.1% mean reduction of postoperative infections (p<0.01) in 11 trials.[18] But also recognized, dry sockets were inconsistently reported and more often than not statistically significant in a single report, comparable with ours.

In a recent study, Majid (2025) concluded that although antibiotics seem to decrease the frequency of dry socket (mean reduction of 3–5%), the evidence is weak and not uniformly statistically significant, referencing high heterogeneity between trials.[19] Our research adds to this uncertainty by demonstrating non-significant but clinically apparent reductions in dry socket in prophylactic antibiotic Groups. Lodi *et al.,* demonstrated antibiotic use led to a statistically significant decrease in infection rates (RR 0.54; 95% CI: 0.41–0.72), but dry socket reduction evidence was weaker (RR 0.83; 95% CI: 0.56–1.23), indicating probable benefit but not absolute statistical proof,[20] in comparison to our results. Lastly, Murthi *et al.,* reported a dry socket frequency of 6.1% without the routine use of antibiotics, which is similar to our overall frequency of 7.56%.[21] This again indicates that although prophylactic antibiotics might decrease risk of dry socket slightly, their absolute effect size might not always be statistically significant, particularly in smaller or more diverse patient populations.

LIMITATION OF STUDY

Factors like surgical time, trauma during extraction and extent of bone removal were not standardized or documented, introducing possible confounders that may influence outcomes. Secondly, the study population was limited to mesioangular impactions with Class I ramus relationship; limiting generalizability to other types of impactions. Lastly, the postoperative follow-up duration was relatively short with dry socket assessment being limited to postoperative day 4, whereby, late-onset cases may have been missed.

CONCLUSION

This study reported no statistically significant difference in the prevention of dry socket in patients who had taken either a single preoperative oral dose of Amoxicillin or Metronidazole in comparison to those who underwent conventional therapy. However, frequency rate of dry socket in the conventional therapy Group was greater than the Groups that received a single oral dose of Amoxicillin and Metronidazole, prior to surgery.

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Authors' Contribution

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

SS & SUK: Data acquisition, data analysis, critical review, approval of the final version to be published.

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

SN & HA: 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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