ORIGINAL ARTICLE

# Prevention of dry socket in mandibular 3rd molars with single preoperative oral dose of metronidazole and amoxicillin compared to conventional therapy

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## Abstract

**Objective:** To compare the efficacy of metronidazole and amoxicillin as preoperative single dose treatment with conventional therapy in prevention of dry socket.

**Methods:** A double blind randomized controlled trial was conducted at the oral and maxillofacial surgery OPD at DUHS, Karachi. Patients attending and requiring surgical extraction of madibular 3rd molar during October 2018 till April 2019 were randomly divided into 3 groups. Ethical approval was taken from Institutional Review Board of DUHS, Karachi. Informed consent was also taken from patients. First group was given single preoperative oral dose of 400mg metronidazole one hour before extraction, second group was treated with single oral dose of 500mg amoxicillin an hour before tooth extraction, and both of the groups were given painkillers postoperatively. Third group was given 500mg of Amoxicillin BD, 400mg of metronidazole and painkillers postoperatively. Every group had a follow-up on fifth postoperative day.

**Results:** Dry socket was reported among patients 19(8.4 %), among them 4 were males and 15 were females. Chi-square test was used to calculate the p-value (0.066). Results of the present trial were statistically insignificant. Incidence of dry socket in amoxicillin group was 3 (5.5%), in metronidazole was 4 (7.5) and in conventional therapy group was 12(16%).

**Conclusion:** Present trial was not effective in preventing the occurrence of dry socket by means of single preoperative oral dose of metronidazole and amoxicillin compared to conventional therapy. However, clinically percentage of occurrence of dry socket was higher in conventional group compared to amoxicillin and metronidazole group.

**Keywords:** Dry socket, metronidazole, amoxicillin, mandibular 3rd molars, class 2 impaction. (JPMA 71: 585; 2021)

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## Introduction

Dry socket is a painful condition, which occurs after tooth extraction, between third to fifth postoperative days and can last for up to three weeks.[1] It happens due to delayed healing of extraction wound, which is either because of early dislodgment or lack of formation of blood clot. Dry socket is characterized by moderate to severe pain in and adjacent to the tooth-extracted area, along with bad breath and unpleasant taste.[1] Clinically it appears as a hollow socket lacking the blood clot with inflamed boundaries and whitish bone seen within the socket.[2] Putrid odour and intense pain that radiates to the ear and neck can also be noticed.[3]

The term Dry socket was described for the very first time in 1896 by an American dentist J. Young Crawford.[4-6] Various terms since then have been used to label the condition, such as Alveolar osteitis, localized osteitis, postoperative alveolitis, alveolitis sicca dolorosa, septic dry socket, necrotic socket, localized osteomyelitis and fibrinolytic alveolitis. Most accurate is fibrinolytic alveolitis introduced by Brin as it reveals its etiological theory.[5]

Predisposing factors of dry socket can be divided into two categories, patient dependent and non-patient dependent. Patient dependent factors are age, gender (more common in females), smoking status, oral contraceptive, poor oral hygiene, type of the tooth, previously infected tooth, recurrent spitting and rinsing after extraction and replacing dressing gauze frequently.[7,8] Non-patient depending factors can be, duration of extraction, type of extraction (surgical or non-surgical), excessive amount of local anaesthesia used and vasoconstrictor present within local anaesthesia. Vasoconstrictor in local anaesthesia is linked to dry socket because of producing ischaemia and fibrinolytic activities.[9,10]

Microbes are also associated with occurrence of dry socket, for example, trepenoma denticola, streptococcus, alpha and beta haemolyticus.[6] Location of tooth plays a major role in incidence of dry socket, as it is more common in mandible than in maxilla; and as we go

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posterior in the oral cavity, chances of dry socket increases hence mandibular third molar is the most common site for incidence of dry socket.[11]

Rate of occurrence of dry socket after extraction of impacted third molar is about 25-30%.[12] Lower third molar is the most frequently impacted tooth and its prevalence ranges from 16.7% to 68.6%.[13] Incidence of dry socket ranges from 5% to 20% worldwide.[6] Whereas 13.8% was reported in Pakistani population.[5] Thus the aim of this study was to prevent the incidence of dry socket among surgically extracted mandibular 3rd molars.

## Methods

Double blind randomized controlled trial of 225 sample size was calculated by using OpenEpi, one sample proportion with 95% confidence interval 5% marginal error[13]. Data collection was done by non-probability consecutive sampling method from the patients requiring surgical extraction of mandibular 3rd molar with Pell and Greogry's class II impaction[14], at the outpatient department of oral and maxillofacial department of Dow University of health sciences from October 2018 till April 2019.

Patients were selected according to the inclusion and exclusion criteria. For randomization, patients were asked to take one folded paper from the box containing chits with alphabets a, b and c, hence participants were divided into 3 groups containing 75 group members. After explaining the purpose of study and its associated benefits and risks, consent was obtained from the patients. Ethical approval was obtained from institutional review board of DUHS, Karachi. Trial is registered on http/clinicaltrial.gov NCT03992144.

Mandibular third molars with class II impaction, both genders, aged between 18 to 40 years were included in the trial. Whereas smokers, alcoholic patients, pregnant and nursing mothers, those taking anticoagulant, oral contraceptives, already taking antibiotics, with renal or hepatic dysfunction, allergic to antibiotics and reluctant to participate were excluded from the trial.

All patients were operated by R2 postgraduate trainee of oral and maxillofacial surgery department, under local anaesthesia, inferior alveolar and long buccal nerves were anaesthetised. Ward's incision was given with scalpel, number 5 blades. Flap was elevated and osteotomy and/or tooth sectioning was done depending on the case. Round and fissured burs were used to remove the bone with low speed micromotor straight hand piece. Normal saline was used as coolant and irrigating solution. After extraction of the tooth, socket was irrigated and flushed with normal saline. Sutures were given with 3-0 silk material and a roll of sanitized gauze was placed over the extraction socket and patients were asked to bite on it for at least 40 minutes. One of the groups had received conventional therapy (amoxicillin 500mg twice a day, 400mg metronidazole 8 hourly for five days and painkiller three times a day for first 48 hours and then SOS), second group was treated with pre-operative single oral dose of metronidazole 400mg an hour before extraction and painkiller 3 times per day for next 48 hours and then SOS. Third group was given preoperative single oral dose of 500mg of amoxicillin one hour before extraction and painkiller 3 times per day for first 48hours and then SOS. Post-operative instructions were given to the patients both verbally as well as in written form. On fifth post-operative day patients were examined with naked eye under the light of dental unit. Those diagnosed with dry socket were treated with alveogel after irrigating and flushing the socket with normal saline.

For Statistical Analysis, data was analyzed in SPSS 24 software. Frequency and percentage was calculated for categorical variables (gender, reason for extraction, location of the tooth and treatment provided). Mean ± standard deviation was calculated for numerical variables (age and duration). Stratification was done for age, gender, reason for extraction, treatment provided. For post stratification chi-square test was applied at 95% confidence interval on categorical variables. The P-value $\leq$ 0.05 was considered as statistically significant.

## Result

Out of 225 patients, 221 completed the trial. Males were 67(30%) and females were 158(70%). Dry socket was reported in 19(8.4%) patients. Out of 19 patients, 4 were from amoxicillin group, 3 were from metronidazole whereas 12 were from conventional therapy group. P-

**Table-1:** Clinical and demographic characteristics of the patients among study groups.

| | Amoxicillin N (75) % | Metronidazole N (75) % | Conventional N (75) % |
|---|---|---|---|
| **Age (years)** Mean ±SD | 29.64 ±7.04 | 29.79±6.34 | 31.25±7.01 |
| 18 to 25 years | 26 | 23 | 19 |
| 25.1 to 35 years | 30 | 38 | 33 |
| 35.1 to 40 years | 19 | 14 | 23 |
| **Duration (minutes)** Mean ±SD | 28.57±3.82 | 29.09±3.67 | 29.43±3.091 |
| **Gender** | | | |
| Male | 20 (29.9) | 21(31.3) | 26(38.8) |
| Female | 55 (34.9) | 54(34.2) | 49(31) |
| **Reason for extraction** | | | |
| Caries | 55(73.3) | 61(81.3) | 47(62.7) |
| Pericoronitis | 20(26.7) | 14(18.7) | 28 |

**Table-2:** Frequency of dry socket among the study groups.

| Dry socket | Amoxicillin N (%) | Metronidazole N (%) | Conventional N (%) |
|---|---|---|---|
| Yes | 3(5.5) | 4(7.4) | 12(16) |
| No | 70(93.3) | 70(93.3) | 62(82.6) |
| Lost | 2(2.6) | 1(1.3) | 1(1.3) |
| Total | 75 | 75 | 75 |
| P-value | 0.437 | 0.126 | 0.385 |

**Table-3:** Frequency of occurrence of dry socket among the study groups with respect of age and gender.

| | | Dry socket | | |
|---|---|---|---|---|
| | Gender | Yes | No | Lost |
| Amoxicillin | Male | 0 | 19 | 1 |
| | Female | 3 | 51 | 1 |
| Metronidazole | Male | 0 | 20 | 1 |
| | Female | 4 | 50 | 0 |
| Conventional | Male | 4 | 21 | 1 |
| | Female | 8 | 41 | 0 |
| **Amoxicillin** | Age years | | | |
| | 18 to 25 | 0 | 25 | 1 |
| | 25 to 35 | 2 | 28 | 0 |
| | 35 to 40 | 1 | 17 | 1 |
| **Metronidazole** | Age years | | | |
| | 18 to 25 | 0 | 23 | 0 |
| | 25 to 35 | 3 | 34 | 1 |
| | 35 to 40 | 1 | 13 | 0 |
| **Conventional** | Age years | | | |
| | 18 to 25 | 3 | 16 | 0 |
| | 25 to 35 | 6 | 27 | 0 |
| | 35 to 40 | 3 | 19 | 1 |

value calculated was 0.066, considered statistically insignificant. Mean of age and duration, number of males and females and reasons for extraction among the study groups are mentioned in Table-1.

In amoxicillin group, dry socket was reported in 3 (5.5%) patients, all three patients in which dry socket occurred were females. In metronidazole group, dry socket was found in 4 (7.4%) patients, who were also females. In conventional therapy group, dry socket was reported in 12 (16%) patients, in which 8 were females and 4 were males as mentioned in Table-2 and 3.

## Discussion

To the best of our knowledge, this is the only clinical trial which has compared the role of single preoperative oral dose of antibiotics with conventional therapy among Pakistani population. The results of the present trial were insignificant statistically. However, in conventional therapy group, dry socket was found among 12 patients, where as in Amoxicillin groups and Metronidazole group, dry socket was reported in 3 and 4 patients, respectively.

Prevention of dry socket is more effective than its treatment.[11] It is considered as one of the most common postoperative complication that occurs after surgical removal of lower third molars.[12]

Third Molar is the last tooth to erupt in everyone irrespective of racial differences in the eruption sequence. This late eruption is one of the major etiological factors for this tooth to be most commonly impacted. Jaw size, facial growth and size of the tooth varies among different cultures and populations. These factors are also essential for eruption pattern, status of impaction and agenesis seen in third molars.[13] Impaction of teeth is often associated with problems like pericoronitis, periodontitis, cysts, root resorption and can also damage the adjacent tooth.[14]

In routine practice, antibiotics are prescribed after tooth extraction to prevent postoperative complication, whereas some studies have suggested that risk of developing complications after extraction of tooth are minimal to permit antibiotics.[6] There is still controversy about routine usage of systemic antibiotics for prevention of infectious and inflammatory conditions concomitant with the extraction of tooth.[15,16] There is no justification for prescribing antibiotics after third molar extraction; current evidence questions the benefits of routine prophylactic antibiotic therapy after third molar extraction.[17]

Results of the present trial were supported by a double blind randomized controlled trial based on 150 patients, to observe the need of oral antibiotic in prevention of dry socket. Study group of 75 patients received amoxicillin and metronidazole for five postoperative days and other group was given placebo. A total of 21 were reported with postoperative complications. It was concluded that postoperative antibiotics were not significantly effective in prevention of postoperative complications.[10] Similar results were found in present trial, clinically. Nonetheless, it was reported that for patients with high chances of dry socket, postoperative antibiotics are advisable for five days.[18] However, in present trial, occurrence of dry socket in patients, provided with 5 days postoperative antibiotics was higher, comparatively.[12]

In contrast with the results of present trial, another study observed preoperative role of single oral dose of metronidazole to prevent dry socket. Single preoperative oral dose of metronidazole, 30 minutes before extraction was given to 135 patients, while 135 patients were given placebo. Dry socket was reported in 13 cases (4.8%). Out

of 13 patients, 6 were from metronidazole group and 7 from placebo group. No significant effect of metronidazole was reported in prevention of dry socket.[19] It was also reported in another study that single preoperative dose of metronidazole was not effective in prevention of dry socket.[20] However, in their study, students and staff members did the extraction of third molars whereas in present study post graduate residents of oral and maxillofacial department have done the extractions. Level of dental practitioner was different among the studies, which could probably be the reason for differences in results. Type of classification of lower third molar impaction was not mentioned in the studies,[5,6] although in present study, class 2 impaction of lower third molar was studied. Mean age of the patients in previous studies were 24-25 years and 23-24 years,[19,20] whereas in present study, mean age of the patients was 30-33 years. In previous study, single dose of metronidazole was given 30 minutes and 45 minutes before extraction,[19,20] where as in present study, metronidazole was given an hour before extraction. Level of dental practitioner, mean age and type of impaction might also be the reason for the difference among present and previous studies.

In a meta-analysis, it was concluded that prophylactic use of Amoxicillin does not significantly reduce the risk of infection and dry socket after third molar extraction.[21] Same results were concluded in a clinical trial where class 1 and class 2 of impacted third molars were studied.[22] Whereas in present trial out of 225, 3 cases of dry socket were found in Amoxicillin group. In present study, lower third molar of class 2 impaction of Pell and Gregory were studied, however, Class 1 and class 2 classification American Society of anaesthesiologist (ASA) were included in previous study.[22]

In present trial, majority of the patients were females (158) whereas males were 67. One of the reasons for this gender predominance could be the exclusion of smokers from present trial. Patients in which dry socket was reported, females were 15 and 4 were males. The gender predominance cannot be related to the incidence of dry socket, as the number of males and females were unequal.

With reference to age, an increase in the incidence of dry socket with increasing age was reported in a study,[23] with an increased likelihood of 1.9 times per year.[24] This fact could be attributed to a slower metabolism, delayed healing and a weaker immune system.[11,24] It was recommended that surgical extraction of impacted mandibular third molars should be conducted before 24 years of age, because of possibility of postoperative problems is higher in elder patients.[24] In present trial, mean age of the patients was 30.2 ± SD 6.81.

When comparison was done between the groups, difference between Metronidazole and Amoxicillin was insignificant as 3 (5.5%) among amoxicillin and 4 (7.4%) from metronidazole group showed the signs of dry socket, whereas in conventional therapy group 12 (16%) patients were reported with dry socket.

## Conclusion

Mandibular third molar is the most commonly impacted tooth, and its extraction is a common dental procedure. It is a common practise to prescribe antibiotics for 5 days after extraction of the tooth. However, in order to decrease the drug and bacterial resistant practitioner must carefully consider the use of antibiotics. According to the findings of the present trial, it was concluded that prevention of dry socket by means of single preoperative oral dose of metronidazole and amoxicillin compared to conventional therapy was statistically insignificant. However, the rate of occurrence of dry socket among conventional therapy group was higher than the preoperative single oral dose of Metronidazole and Amoxicillin.

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## References

1. Al-Belasy FA. The relationship of shisha (water pipe) smoking to postextraction dry socket. J Oral Maxillofac Surg. 2004; 31:10-4.
2. Gbotolorun OM, Dipo-Fagbemi IM, Olojede AO, Ebigwei S, Adetoye JO. Are systemic antibiotics necessary in the prevention of wound healing complications after intra-alveolar dental extraction? Int J Oral Maxillofac Surg. 2016; 31:1658-64.
3. Supe NB, Choudhary SH, Yamyar SM, Patil KS, Choudhary AK, Kadam VD. Efficacy of alvogyl (Combination of Iodoform+ Butylparaminobenzoate) and zinc oxide eugenol for dry socket. Ann Maxillofac Surg. 2018; 8:193-9.
4. Inamdar MN, Chauhan R, Mapare SA, Goswami RP, Goswami Y, Khadri SF. Prevention of Dry Socket using Chlorhexidine Gel and Ornidazole Gel in Impacted Mandibular Third Molar: A Comparative Randomized Prospective Study on 30 Patients. J Intl Oral Health. 2015; 1:7:41.
5. Claesson L, Lundberg I. Dry socket-prevalence and risk factors in a Pakistani population. Odontologiska Institutionen, Karolinska Institutet.
6. Kaur J, Raval R, Bansal A, Kumawat V. Repercussions of intraalveolar placement of combination of 0.2% chlorhexidine & 10 Mg metronidazole gel on the occurrence of dry sockets-A randomized control trial. J Clin Exp Dent. 2017; 9:e284-8.
7. Reaaquena-Calla S, Funes-Rumiche I. Effectiveness of intra-alveolar chlorhexidine gel in reducing dry socket following

surgical extraction of lower third molars. A pilot study. J Clin Exp Dent. 2016; 8:e160-3.
8. Tek M, Akkas I, Toptas O, Ozan F, Sener I, Bereket C. Effects of the topical hemostatic agent Ankaferd Blood Stopper on the incidence of alveolar osteitis after surgical raaemoval of an impacted mandibular third molar. Niger J Clin Pract.2014; 17:75-80.
9. Agrawal A, Singh N, Singhal A. Oxidized cellulose foam in prevention of alveolar osteitis. IOSR J Dent Med Sci. 2012; 22; 26-8.
10. Khawaja NA. Incidence of dry socket in lower jaw at a teaching dental hospital. Pak Oral Dent J. 2006; 26:227-30.
11. Taberner-Vallverdú M, Sánchez-Garcés MÁ, Gay-Escoda C. Efficacy of different methods used for dry socket prevention and risk factor analysis: A systematic review. Med Oral Patol Oral Cir Bucal. 2017; 22:e750.
12. Babar A, Ibrahim MW, Baig NJ, Shah I, Amin E. Efficacy of intra-alveolar chlorhexidine gel in reducing frequency of alveolar osteitis in mandibular third molar surgery. J Coll Physicians Surg Pak. 2012; 1:91-4.
13. Agarwal A, Singh N, Singhal A. Oxidized cellulose foam in prevention of alveolar osteitis. IORS J Dent Med Sci. 2012; 22:26-8.
14. Hashemipour MA, Tahmasbi-Arashlow M, Fahimi-Hanzaei F. Incidence of impacted mandibular and maxillary third molars: a radiographic study in a Southeast Iran population. Med Oral Patol Oral Cir Bucal. 2013; 18:e140-5.
15. Franceschi F, Ojetti V, Gabrielli M, Petruzziello C, Tortora A, Gasbarrini G, et al. High dose amoxicillin-based first line regimen is equivalent to sequential therapy in the eradication of H. pylori infection. Eur Rev Med Pharmacol Sci. 2016; 20:297-300.
16. Rodrigues WC, Okamoto R, Pellizzer EP, dos Anjos Carrijo AC, de Almeida RS, de Melo WM. Antibiotic prophylaxis for third molar extraction in healthy patients: Current scientific evidence. Quintessence Int. 2015; 1:46-2.
17. Prajapati A, Prajapati A, Sathaye S. Benefits of not prescribing prophylactic antibiotics after third molar surgery. J. Maxillofa. Oral Surg. 2016; 1:217-20.
18. Olusanya AA, Arotiba JT, Fasola OA, Akadiri AO. Prophylaxis versus pre-emptive antibiotics in third molar surgery: a randomized control study. The Nigerian postgrad Med J. 2011; 18:105-10.
19. Ritzau M, Hillerup S, Branebjerg PE, Ersbol BK. Does metronidazole prevent alveolitis sicca dolorosa?: A double-blind, placebo-controlled clinical study. Intl J Oral Maxillofa Surg. 1992; 1:299-302.
20. Bergdahl M, Hedström L. Metronidazole for the prevention of dry socket after removal of partially impacted mandibular third molar: a randomised controlled trial. British J Oral Maxillofa Surg. 2004; 31:555-8.
21. Arteagoitia MI, Barbier L, Santamaría J, Santamaría G, Ramos E. Efficacy of amoxicillin and amoxicillin/clavulanic acid in the prevention of infection and dry socket after third molar extraction. A systematic review and meta-analysis. Med Oral Patol Oral Cir Bucal. 2016; 21:494-504.
22. Xue P, Wang J, Wu B, Ma Y, Wu F, Hou R. Efficacy of antibiotic prophylaxis on postoperative inflammatory complications in Chinese patients having impacted mandibular third molars removed: a split-mouth, double-blind, self-controlled, clinical trial. British J Oral Maxillofa Surg. 2015; 1; 416-20.
23. Hasheminia D, Moaddabi A, Moradi S, Soltani P, Moannaei M, Issazadeh M. The efficacy of 1% Betadine mouthwash on the incidence of dry socket after mandibular third molar surgery. J Clin Exp Dent. 2018; 10:e445-9.
24. Haraji A, Rakhshan V. Single-dose intra-alveolar chlorhexidine gel application, easier surgeries, and younger ages are associated with reduced dry socket risk. J Oral Maxillofa Surg. 2014; 1:259-65.
25. Jamil G, Syed M, Baber H, Abbas Z, Khalid M, Rehman SA. 3rd Molar variations via radiograph. Biol. 2017; 2; 1-6.