Original Study

COMPARISON OF THE EFFECT OF PENICILLIN-METRONIDAZOLE AND CLINDAMYCIN IN THE TREATMENT OF FACIAL ABSCESSES AT EMAM KHUMEINI HOSPITAL IN AHVAZ : SUB-CLINICAL TRIAL

Raeisian S,[1] Raeisi S,[2] Azimi G,[3] Moradpoor H[4]

1. Assistant professor, Department of Oral and Maxillary Surgery, School of Dentistry, Ahvaz University of Medical Sciences, Iran.
2. Assistant Professor, Department of Prosthodontics, School of Dentistry , Kermanshah University of Medical Sciences, Iran.
3. Dentist, Department of Oral and Maxillary Surgery, School of Dentistry, Ahvaz University of Medical Science, Iran.
4. Assistant professor, Department of Prosthodontics, School of Dentistry, Kermanshah University of Medical Sciences, Iran.

ABSTRACT

Aim: The maxillofacial region due to the specific anatomical location exposed to different infections. The aim of this study was to investigate the effect of penicillin & metronidazole and clindamycin on the treatment of facial abscesses in Ahvaz.

Materials & Method: This descriptive-analytic study was performed on patients referred to the hospital during the years 2016 to 2017 with diagnosis of head and face abscess. Patients were randomly divided into two groups of penicillin & metronidazole recipients and clindamycin receiving groups. Blood samples were taken from patients for ESR and CRP tests. After 3 days, 5 days and 7 days, patients were re-tested. Finally, the data were analyzed by SPSS software.

Results: According to the results, in the women receiving penicillin-metronidazole, the decrease in ESR on the third day was statistically significant ($p<0.02$) compared to clindamycin receiving women. The effect of penicillin-metronidazole on the reduction of infection in women was more than men, and the decrease in ESR in women on day 3 was statistically significant ($p<0.01$). In women receiving penicillin-metronidazole, the reduction in CRP on the fifth day was significantly ($p<0.02$) higher than that of clindamycin receiving women.

Conclusion: According to the results of this study, antibiotics can be used to control odontogenic infections. The efficacy of penicillin-metronidazole and clindamycin in treatment of maxillofacial abscesses was different in men and women. But these drugs generally reduced the risk of adenocarcinoma in men and women.

Introduction

The head and neck are very important both in terms of beauty and proximity to sensitive areas of the body. This area is the site of a large number of infections, including local infections or infections occurring in the adjacent areas,[1-3] due to its unique anatomical position. Abscess refers to localized collection of pus due to tissue reaction against pus-producing agents and microorganisms such as bacteria or external agents. The collection of pus in any part of the body can usually lead to swelling and inflammation around it. The oral cavity abscess begins due to infection or tooth decay. Although gingivitis and dental infection can be due to inappropriate health conditions and lack of proper care, and tooth, diseases or treatments that weaken the immune system, autoimmune disorders, diabetes and chemotherapy also play a role in this regard.[4,5] Since the oral environment is in contact of with various microorganisms, this site is the most common area of maxillofacial infection. The maxillofacial area is the site where various infections occur due to it's the specific anatomical location. Some infections observed in this area have dental-jaw origin and others are related to distant organs and limbs and still others are skin infections. Due to the contact of the oral environment with various microorganisms, the head and neck is the site of many infections.[1] Teeth are the most common source of maxillofacial infection.[3] Various treatments, including I & D, tooth extraction, antibiotics and RCT are needed for the treatment of maxillofacial abscesses. One or more of the treatments are carried out together depending on the patient's conditions. One of the ways to treat an abscess is to use antibiotics. Penicillin, amoxicillin, clindamycin, metronidazole, ciprofloxacin, ceftriaxone, tetracycline and erythromycin are used in the treatment of dental-facial abscess.[6,7] The criteria for selecting appropriate antibiotics include having a limited range of effects to prevent development of various types of resistant ones, the ability to reduce the incidence of additional infections, having less toxicity by maintaining the drug's dosage effectiveness and lower risk of allergies and side effects. The aim of the present study was to investigate the effect of penicillin, metronidazole and clindamycin on the treatment of facial abscesses in Ahvaz.

Materials & Method

This descriptive-analytic study was carried out on patients referred to Imam Khomeini Educational Hospital in Ahvaz in 2016-2017 who were diagnosed with abscesses in the head and face regions.

The inclusion criteria included having surface and deep abscesses in the head and face that require surgical treatment.

The exclusion criteria included the use of non-steroidal anti-inflammatory drugs (NSAIDs) and systemic antibiotics over the past two months. The information of the admitted patients will be collected using a two-part questionnaire; The first part relates to the patient's demographic information, including age, gender, type of underlying disease (diabetes, chemotherapy, etc.), history of oral and diseases and infections, rate of referral to the dentist, oral and dental health level. The second part relates to the patient's medical information. The patient is responsible for the location of the infection, the cause (teeth number), the

type of treatments performed (antibiotics, salt detergents and dental treatments).

The patients were later randomly divided into two groups of 20; metronidazole-penicillin groups and clindamycin group in such way that patients in both groups will be homogenous in terms of gender distribution and age categories. Before being divided into each group, the CRP and ESR blood sample will be prepared from them and a the same test will be carried out again when the patients received medication 3 days, 5 days and 7 days later. Metronidazole-penicillin recipients will receive 500 mg of metronidazole 3 times every 8 hours and penicillin G will be given every 6 hours depending on the patient's weight. Clindamycin recipients also received the drug (600 mg) every 8 hours.

After collecting the required data, all the information correlation will be analyzed by the statistical analysis. SPSS ver. 22 was used to analyze the statistical data. Descriptive statistics and analytical statistics were used by ANOVA. The significance level was considered to be $p \leq 0.05$.

Results

The present study was performed on 40 patients with head and neck abscesses. Patients included 19 males (47%) and 21 females (53%). The metronidazole-penicillin group consisted of 9 men (45%) and 11 women (55%). The clindamycin group also consisted of 10 men (50%) and 10 women (50%). The results of the present study revealed that the infectious agents in the metronidazole-penicillin group were observed in 18 men's teeth and 17 women's teeth. The same infectious agents in the clindamycin group were seen in 13 men's teeth and 14 women's teeth. Thus, the number of infectious agents was lower in the clindamycin group. [Figure.1]

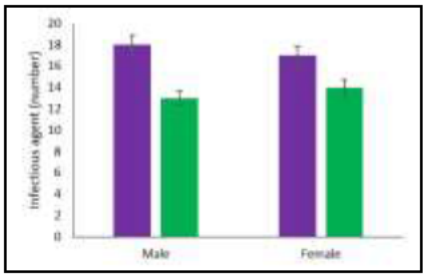

Figure 1: Infectious agent in the two groups receiving clindamycin and metronidazole-penicillin.

Figure. 2 shows the effects of penicillin-metronidazole and clindamycin antibiotics on the treatment of facial abscess in men and women based on changes in erythrocyte sedimentation rate (ESR) on days 3, 5 and 7. ESR levels on days 3, 5 and 7 clindamycin-treated men were lower than penicillin-metronidazole-treated ones, but there was no statistically significant reduction in ESR level ($p>0.05$). However, in penicillin-metronidazole-treated women, the ESR reduction in the day 3 was significantly higher than clindamycin-treated women ($p<0.02$). However, there were no significant changes in the ESR levels on days 5 and 7.

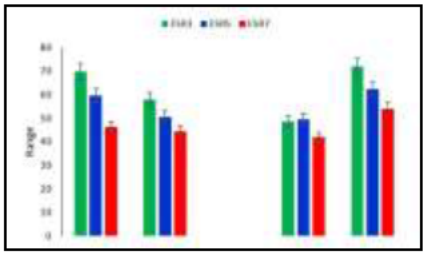

Figure 2: The effect of penicillin-metronidazole and clindamycin on the treatment of facial and body abscess in men and women based on changes in ESR on days 3,5and 7.

Figure. 3 shows the effect of penicillin-metronidazole on the treatment of facial abscess in men and women based on changes in ESR levels on days 3, 5 and 7. The results lead us to the conclusion that the effect of penicillin-metronidazole drugs were more effective in reducing infections in women than men and significant reduction was seen in the ESR level in women on day 3 ($P < 0.01$); however, there were no significant changes in the ESR levels on days 5 and 7. This figure shows that the ESR level on days 3, 5 and 7 decreased in both groups of women and men, but the rate was lower in women.

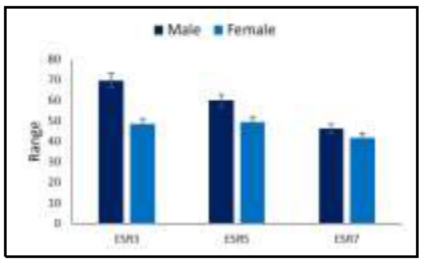

Figure3. The effect of penicillin-metronidazole on the treatment of facial abscess in men and women based on changes in ESR levels on days 3, 5 and 7.

According to the results observed in Figure 4, it can be concluded that clindamycin was more effective in reducing the infection rate in men than that women; however, it was not statistically significant ($p>0.05$). The same figure shows that the ESR level decreased in both men and women on the days 3, 5 and 7, but the reduction rate was higher in men, although not statistically significant.

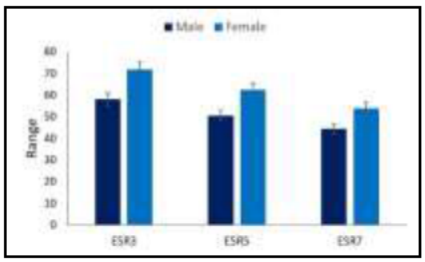

Figure 4: Effect of clindamycin on the treatment of facial abscess in men and women based on changes in ESR levels on days 3, 5 and 7.

Figure 5 shows the effect of penicillin-metronidazole and clindamycin on the treatment of facial abscess in men and women was based on the changes in C-reactive protein (CRP) levels on days 3, 5 and 7. CRP levels decreased in penicillin-metronidazole-treated men than those receiving clindamycin on days 3, 5 and 7, but this reduction was not statistically significant (p>0.05). However, the CRP level reduction in penicillin-metronidazole-treated women was significantly higher than clindamycin-treated women on the day 5 (P<0.02). However, however, there were no significant changes in the CRP levels on days 3 and 7.

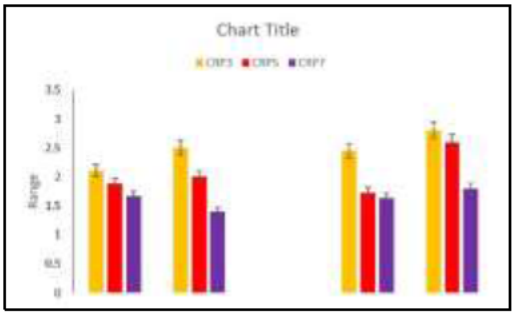

Figure 5: The effect of penicillin-metronidazole and clindamycin on the treatment of facial abscess in men and women based on changes in CRP levels on days 3, 5 and 7.

Figure 6 shows the effect of penicillin-metronidazole on the treatment of facial abscess in men and women based on changes in the CRP level on days 3, 5 and 7. Regarding the results illustrated in this figure, it can be concluded that the penicillin-metronidazole drug had equal effect in reducing the infection in men and women and there was no significant difference between both groups in terms of changes in CRP levels.

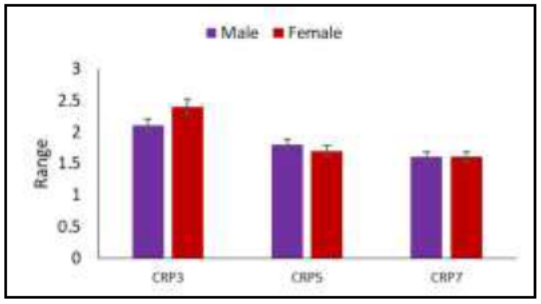

Figure 6: The effect of penicillin-metronidazole on the treatment of facial abscess in men and women based on changes in the CRP level on days 3, 5 and 7.

According to the results of Fig. 7, it can be concluded that clindamycin was more effective in reducing the infection rate in men than women, but it was not statistically significant (p>0.05). It is seen in this figure that CRP levels decreased in both groups of men and women on days 3, 5 and 7, but the decrease was higher in men, although it was not statistically significant.

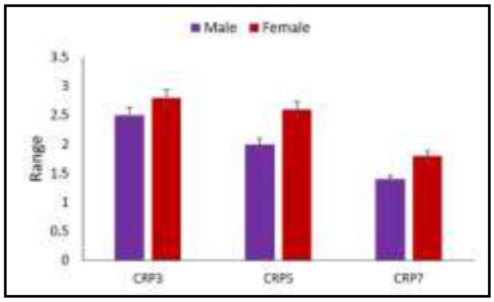

Figure7: Effect of clindamycin on the treatment of facial abscess in men and women based on changes in the CRP level on days 3, 5 and 7.

Discussion and Conclusion

Today, it is known that various types of periodontal diseases, such as abscess, are caused by bacterial infection. In addition to treatments such as Insicion & Drain, tooth extraction, antibiotic prescription and RCT, the use of antibiotics is one of the ways to treat maxillofacial abscesses. Antibiotics used in the treatment of abscess include penicillin, amoxicillin, clindamycin, metronidazole, ciprofloxacin, ceftriaxone, tetracycline and erythromycin.[6,7] To have high effectiveness in treating an abscess, antibiotics should have the following characteristics: Having a limited spectrum effect to prevent the development of resistant bacteria, ability to reduce the incidence of additional infections, having less toxicity by maintaining the dose effectiveness of the drug, lower risk of allergy and fewer side effects.[1-3] Therefore, the aim of the present research was to evaluate the types of maxillofacial abscesses and the effects of penicillin-metronidazole and clindamycin on the treatment of facial abscesses in the city of Ahvaz, Iran as well as to measure its relationship with underlying factors. The results revealed that the infectious agent in the metronidazole-penicillin group was higher than that of the clindamycin recipient group. In other words, more teeth were affected by the development of odontogenic abscess in the metronidazole-penicillin group. Greene *et al*. also showed in their study that teeth are the most common source of maxillofacial infection, and odontogenic infections can be transformed into life-threatening events and are generally related to the patient's safety status.[3] In this study, two ESR and CRP tests were used to diagnose infections and inflammation associated with maxillofacial abscess. The ESR test shows the degree of body inflammation by examining the red blood cell sedimentation. The presence of certain proteins, which are called acute phase proteins and immunoglobulin in the blood and increase under inflammation conditions, cause the red blood cells to precipitate more rapidly.[8,9] The results of the present research showed that the ESR level in clindamycin-treated men was lower than that of penicillin-metronidazole recipients on days 3, 5 and 7, but it was not statistically significant. However, the ESR reduction rate in the penicillin-metronidazole-treated women was significantly higher than that of clindamycin-treated women on day 3.

The results also show showed that CRP levels in the male recipients of penicillin-metronidazole were lower than those receiving clindamycin on days 3, 5 and 7, but this reduction was not statistically significant. However, the CRP showed significant reduction in penicillin-metronidazole-treated women as compared to clindamycin-treated women on day 5. Therefore, clindamycin may be more effective than penicillin-metronidazole in the treatment of odontogenic abscess in men; however, penicillin metronidazole had more effectiveness than clindamycin in women. Since there has been no study on the effectiveness of penicillin-metronidazole and clindamycin on the basis of gender, the different effects of these drugs in men and women can be attributed to gender, hormone differences and different drug metabolism in different genders. Odontogenic infections are commonly caused by several types of aerobic and anaerobic microbes, since there is a complex population of microorganisms in the oral cavity. However, the population of anaerobic bacteria is generally higher than that of aerobic ones.[10] Since bacteria play an important role in odontogenic infections, the antibiotics are used for therapeutic and preventive reasons.[11] Antimicrobials should never be used as an alternative to drainage of the infection or debridement and should only be used as an additional treatment.[12] Timely and pre-surgical treatment of odontogenic infections by using antimicrobials can shorten the course of infection and reduce the risks associated with abscess.[13] As mentioned above, penicillin-metronidazole and clindamycin were also used in the present study for the treatment of odontogenic abscess. Penicillin is one of the least dangerous antibiotics and undoubtedly causes fewer complications than other antimicrobial agents.[14] Metronidazole is a bactericidal antibiotic and has an effect on anaerobic bacteria.[15] When used in combination with other antibiotics, metronidazole can be effective against actinomycetemcomitans.[16,17] Metronidazole is also effective against anaerobic bacteria such as porphyromonas gingivalis and patella intermedia.[18] Clindamycin is a bacteriostatic antibiotic. It has limited use due to its serious side effects. It is used to treat staphylococcal infections.[19,20] The results of the present study showed that the penicillin-metronidazole was more effective in reducing the infection rate in women than men and the ESR level was reduced more significantly in women than men on day 3. However, the results showed that clindamycin led to a significantly higher reduction in infection rate in males than females, but was not statistically significant. The present study also investigated the effect of penicillin-metronidazole on the reduction of infection in women and men and the results showed no significant difference between the two groups in terms of changes in CRP levels. Also, the results of investigating the effect of clindamycin showed that CRP levels decreased in both male and female groups on days 3, 5 and 7, but the decrease was higher in males, although not statistically significant. Therefore, it can be concluded that the drugs prescribed in this study had different effectiveness in terms of gender. Other studies have shown that clindamycin has a wide range of mechanism of action. It is possible to compare its effectiveness with penicillin in treating odontogenic infections.[21] The use of clindamycin led to successful outcomes when treatment with other therapeutic agents failed.[22] The broad spectrum of clindamycin effects with high clinical efficacy of clindamycin in the treatment of odontogenic infections has introduced this drug as an alternative to penicillin v.[21,23] Today, it has been evident that the number of microorganisms, which are resistant to common antibiotics used in the treatment of odontogenic infections, has doubled in the last 15 years. Similarly, Herrera *et al*. showed that beta-lactamase-producing bacterial species (as a factor involved in the antibiotic resistance) are present in 87% of patients with periodontitis.[24] Also, Bresco *et al*. have reported that bacteria are resistant to metronidazole (50%), erythromycin (39%) and erythromycin (33%) in bacterial odontogenic infections.[25] Therefore, the different effectiveness of the drugs prescribed in the present study can be attributed to the drug resistance of bacteria in various patients. Another point to be taken into account during drug administration is the side effects of drugs. The most important side effect of penicillin G, is the reaction to hypersensitivity, especially the local/ systemic anaphylaxis.[26] The disadvantages and side effects of clindamycin include diarrhea, abdominal discomfort, nausea, vomiting, antibiotic-induced colitis, exanthem, jaundice and changes in responses to liver tests, reduction of blood neutrophils, eosinophilia, agranulocytosis, and blood platelet counts.[27] The results of the current study lead to the conclusion that antibiotics are essential to control odontogenic infections. Penicillin-metronidazole and clindamycin showed different effectiveness in the treatment of maxillofacial abscess in men and women. However, these drugs generally reduce the odontogenic infections in men and women, and such drugs should be prescribed according to their side effects and the level of patients' allergy. It is also essential to achieve a correct understanding of the course of the disease, the microbiology of odontogenic infection and the pharmacokinetics of antibiotics for successful treatment.

Acknowledgement

The authors of this article would like to express their gratitude to Jondishapur University of Medical Sciences for their material and spiritual assistance.

References

1. Braham RL, Morris ME. Text book of pediatric dentistry. 2nd ed. Baltimore: Williams & Wilkins; 1990. P. 327, 421-22.
2. Regezi JA, Sciubba JJ, Pogrel MA. Atlas of oral and maxillofacial pathology. Saunders. 2000.
3. Green AW, Flower EA, New NE. Mortality associated with odontogenic infection! Br dent J. 2001;190(10):529-530.
4. Wei S, Hyman R. Pediatric dentistry-scientific foundations and clinical practice. CV Mosby Company, St Louis. 1982:640-51.

5. Mitchell CS, Nelson MD Jr. Orofacial abscesses of odontogenic origin in the pediatric patient. Pediatr Radiol. 1993;23(6):432-434.
6. Sweetman SC. Martindle's Complete Drug Reference. 3rd ed. London: Pharmaceutical Press; 2002;149-150, 157-159, 239-240.
7. Peterson LJ, Ellis E, Hupp JR, Tucker MR. Contemporary oral and maxillofacial surgery. Mosby St. Louis, MO; 1988.
8. Danesh J, Collins R, Peto R, Lowe G. Haematocrit, viscosity, erythrocyte sedimentation rate: meta-analyses of prospective studies of coronary heart disease. Eur Heart J. 2000;21(7):515-520.
9. Black S, Kushner I, Samols D. C-reactive protein. J Biol Chem. 2004;279(47):48487-48490.
10. Sands T, Pynn BR, Katsikeris N. Odontogenic infections: Part two. Microbiology, antibiotics and management. Oral Health. 1995;85(6):11-14,17-21, 23.
11. Peedikayil FC. Antibiotics: use and misuse in pediatric dentistry. J Indian Soc Pedod and Prev Dent. 2011;29(4):282-287.
12. Pallasch TJ. Global antibiotic resistance and its impact on the dental community. J Calif Dent Assoc. 2000;28(3):215-233.
13. Fine DH, Hammond BF, Loesche WJ. Clinical use of antibiotics in dental practice. Int J Antimicrob Agents. 1998;9(4):235-238.
14. Gilman AG. Goodman and Gilman's the pharmacological basis of therapeutics. 1985.
15. Carranza DL, Jolkovsky SC. Clinical Periodontology. 10th Ed. Los Angeles, California: The C.V. Mosby Co. 2006; Chap52: 800-809.
16. Newman MG, Takei H, Klokkevold PR, Carranza FA. Carranza's clinical periodontology. 10th ed. St. Louis: Sunders, 2006:116-150, 840-845.
17. Eickholz P, Dannewitz B, Kim T-S. Antibiotics in Periodontal Therapy. Perio. 2005;2(4):235-251.
18. Greenstein G. The role of metronidazole in the treatment of periodontal diseases. J Periodontol. 1993;64(1):1-15.
19. Schlievert PM, Kelly JA. Clindamycin-induced suppression of toxic-shock syndrome-associated exotoxin production. J Infect Dis. 1984;149(3):471.
20. Ohlsen K, Ziebuhr W, Koller KP, Hell W, Wichelhaus TA, Hacker J. Effects of subinhibitory concentrations of antibiotics on alpha-toxin (hla) gene expression of methicillin-sensitive and methicillin-resistant Staphylococcus aureusisolates. Antimicrob Agents Chemother. 1998;42(11):2817-2823.
21. Sandor GK, Low DE, Judd P, Davidson RJ. Antimicrobial treatment options in the management of odontogenic infections. J Can Dent Assoc. 1998;64(7):508-514.
22. Lewis MA. Why we must reduce dental prescription of antibiotics: european union antibiotic awareness day. Br Dent J. 2008;205(10):537-538.
23. Peedikayil FC. Antibiotics in odontogenic infections-an update. J Antimicro. 2016;2(1):1-3.
24. Herrera D, van Winkelhoff AJ, Dellemijn-Kippuw N, Winkel EG, Sanz M. Beta-lactamase producing bacteria in the subgingival microflora of adult patients with periodontitis. A comparison between Spain and The Netherlands. J Clin Periodont. 2000;27(7):520-525.
25. Brescó-Salinas M, Costa-Riu N, Berini-Aytés L, Gay-Escoda C. Antibiotic susceptibility of the bacteria causing odontogenic infections. Med Oral Patol Oral Cir Bucal. 2006;11(1):e70-75.
26. Lewis MA, MacFarlane TW, McGowan DA. Antibiotic susceptibilities of bacteria isolated from acute dentoalveolar abscesses. J Antimicrob Chemother. 1989;23(1):69-77.
27. Azeh I, Gerber J, Wellmer A, Wellhausen M, Koenig B, Eiffert H, *et al*. Protein synthesis inhibiting clindamycin improves outcome in a mouse model of Staphylococcus aureus sepsis compared with the cell wall active ceftriaxone. Crit Care Med. 2002;30(7):1560-1564.

Corresponding Author

Dr. Hedaiat Moradpoor
Assistant professor,
Department of Prosthodontics,
School of Dentistry,
Kermanshah University of Medical Sciences,Iran.
Email Id: - h.moradpoor@gmail.com