Original Research Article

Use of systemic doxycycline as an adjunct to initial periodontal therapy in mild to moderate generalized periodontitis: A randomized clinical trial

Abstract

Background: Antibiotics like doxycycline can show an anti-bacterial effect which can reduce the bacterial load and promote healing in patients with chronic periodontitis.

Aim: To evaluate the use of doxycycline as an adjunct to initial periodontal therapy in mild to moderate periodontitis.

Materials and Methods: Randomized controlled clinical trial was done on 24 patients. Plaque index score, bleeding on probing, periodontal pocket depth and attachment loss was evaluated at six-week and twelve-week intervals after treatment with systemic doxycycline along with deep scaling and placebo medication with deep scaling. Data obtained was analyzed using SPSS software version 22. T-test was used to compare results between the two groups.

Results: Independent T-test shows statistically significant reduction in plaque index score, bleeding on probing, periodontal pocket depth at six-week interval in doxycycline group as compared to the control group with deep scaling alone. There was a statistically significant gain in the attachment level at six-week interval in doxycycline group than initial periodontal therapy alone. This result was not statistically significant at the twelve-week interval.

Conclusion: The study shows doxycycline as a good adjunct to initial periodontal therapy; however, more studies are required to obtain strong evidence.

Keywords: Antibiotics, doxycycline, periodontitis , periodontology

UNDER PEER REVIEW

Introduction

Periodontal disease involves inflammation of the supporting structures of the teeth caused by the accumulation of the plaque and long term buildup of the calculus[(1)]. Periodontitis can be an

aggressive type which follows an acute course or can be associated with long term improper oral hygiene called chronic periodontitis[2]. Along with improper oral hygiene as the primary cause, systemic and genetic diseases are other most common causes of periodontal and gingival diseases[3]. Irrespective of the cause, an initial periodontal therapy always involves the removal of the plaque and calculus to reduce the inflammation in the periodontal tissue[4].

The initial periodontal therapy includes cleaning of the plaque from the root surface and calculus deposits found in the deep pockets. The principle behind the initial periodontal therapy is to reduce a major bacterial load which can promote healing of the surrounding tissues[5]. Initial periodontal therapy is known to reduce probing depths and gingival inflammation, hence it is always considered as a fine line of treatment in the management of periodontal disease[6]. A study by Saito et al has also shown that initial periodontal therapy largely improves the quality of life of patients with periodontitis in Japan[7].

Doxycycline belongs to the class of tetracycline antibiotics which are known to have an antibacterial action[8]. In oral tissues, doxyclines are known to alternate the host response by inhibition of the enzymes and cytokines. It also halts the osteoclastic activity which aids in the tissue regeneration and healing response[9]. Hence the use of doxycycline can be a good added benefit to reduce the inflammation in patient's periodontal disease. A broad spectrum of antibacterial activity can be achieved using doxycycline which provides coverage against gram positive as well as gram negative microbes effectively aids in managing periodontal disease[10]. A study by Stoller et al has shown that use of doxycycline is known to maintain a high concentration in periodontal pockets for 7 days as compared to other antimicrobials[11]. Another study by Golub et al has also shown anti-inflammatory property of doxycycline in addition to the antibacterial property[12].

The benefits of systemic doxycycline can be used along with the traditional method of the reduction of bacteria by scaling and root planing. A low degree of evidence is available which has used doxycycline along with scaling and root planing procedures in the management of periodontal disease[13-15]. Hence, the present study aims to evaluate the use of systemic doxycycline as an adjunct to the initial periodontal therapy and deep scaling procedures.

Materials and Methods

The present study follows a randomized controlled study design. The present study was carried out in a private dental clinic in Palestine.

UNDER PEER REVIEW

Patients between the age group of 28 to 60 years who required treatment for generalized periodontitis were included in the present study. Prior informed consent was obtained from all the participants after explaining the nature of the study design of the present study. The patient included in the study required to have at least ten teeth requiring periodontal treatment and at least four teeth with periodontal pockets with probing depth greater than 5 mm.

Participants who did not give their consent for participation were excluded from the study. Additionally, those patients who underwent periodontal treatment during the last six months were not included in the study. Patients who used medicated mouthwashes were also excluded from the study. Since the present study focuses on generalized periodontitis, any patient with tendency to localized periodontitis was excluded from the study. Presence of aetiology of systemic diseases and risk factors like smoking was not considered while enrolling the participants in the study.

General oral hygiene instructions were given to all the patients before the procedure was started. A baseline data of plaque index, bleeding on probing, periodontal pocket depth and gingival recession was noted by the examiner. Three days after the baseline data was noted, deep scaling procedures were carried out using ultrasonic and manual scalers by the operator. Oral prophylaxis was done to remove the residual stains after the scaling procedure. Curettes were used when the subgingival calculus could not be accessed by the ultrasonic scaler tips alone. Full mouth deep scaling was completed on the same single day.

The patient to administer systemic doxycycline was randomly assigned using a sequence of random numbers. The allocated treatment group and the control group were concealed in the envelope to avoid bias in the study. The operator opened the envelope on the day of treatment after the deep scaling and gave systemic doxycycline or placebo as indicated by the sequence mentioned in the envelope. A bottle containing twenty pills was given to the patient and told to take one pill every day for the next three weeks. In the test group, pills contained 100 mg Doxycycline. A follow up visit was planned at six-week and twelve-week intervals.

The observer was blinded about the intervention group and control group and examined the plaque index, bleeding on probing, periodontal pocket depth and gingival recession. After obtaining the parameters at six weeks, the outcome data was obtained by the observer after another six weeks (twelve weeks after scaling session).

All the data obtained was noted in a spreadsheet and the data was analyzed using SPSS software version 22. The mean values were calculated of plaque index score, bleeding on probing score, probing depth and gingival recession at baseline, 6-week interval and 12 week interval.

UNDER PEER REVIEW

Independent T-test was used to compare the difference in the two groups at 6 week interval and 12 week interval. P-value is considered significant less than 0.05.

Results

The present study had a total of 43 patients included between the age group of 28-60 years. However, seven patients reported that they did not take the prescribed medication for various reasons. Another twelve patients did not report for the follow up visits at six week and twelve week and were excluded from the study. The data of 24 patients was analyzed which were divided into the intervention and placebo group. Table 1 gives the age-wise distribution of the population included in the study.

Table 2 shows mean and standard deviation of the recorded plaque index, bleeding on probing, and pocket depth at baseline, six week follow up interval and twelve week follow up interval. The Paired T-test shows that there was a significant difference between the baseline measures and measures at six-week and twelve-week interval of plaque index, bleeding on probing and pocket depth measures for both the groups ($p<0.05$). T test showed that the doxycycline group had more reduction in plaque index score and bleeding on probing that traditional treatment at six week follow up and twelve week follow up. However, this result was not statistically significant ($p>0.05$). The doxycycline group showed statistically significant reduction in the pocket depth than the traditional treatment group at six-week follow up ($p<0.05$). This result was not statistically significant at the twelve-week follow up.

Table 3 shows that gain in the attachment between the two treatment modalities. The results of the T-test showed that the doxycycline group had statistically significant gain in the attachment than traditional treatment at six-week intervals ($p<0.05$). However, in spite of more gain in attachment in the doxycycline group at twelve-week follow up, this result was not statistically significant ($p>0.05$).

Discussion

Systemic antibiotics have been used as an adjunct to the traditional periodontal treatment of scaling and root planing procedure with the sole aim of providing higher concentration of the antibiotics to the diseased site[16,17]. Studies by Chiu show that sub antibacterial doses of doxycycline increases its concentration in the gingival crevicular fluid[18]. Hence the present

UNDER PEER REVIEW

study was conducted with an aim to evaluate the effectiveness of doxycycline as an adjunct to traditional periodontal therapy.

The results of the study show that treatment with systemic doxycycline shows better outcome in reducing the plaque, bleeding on probing and pocket depth as compared to deep scaling alone. These results are similar to those obtained in another study by Eickholz et al which showed that scaling and root planing along with doxycycline provides greater reduction of bleeding on probing, periodontal pocket depth[19]. Another study by Salvi and co-workers showed that no improvement in the bleeding on probing and pocket depth in patients treated with doxycycline and deep scaling procedures[20]. This can be due to differences in the method of administration of doxycycline. Systematic review by Tan et al have shown reduction in pocket depth with the use of local doxycycline[21].

The present study shows significant gain in attachment at six-week interval in treatment with systemic doxycycline. This gain was not significant at the twelve-week interval. Similar results were obtained in a study by Al Hulami et al[15]. The present study evaluates the clinical signs alone. However further studies can be conducted to check the reduction in the bacterial load of the pocket.

The results of doxycycline having an added benefit along with initial periodontal treatment can be variable as per different studies. A systematic review can be beneficial to give the evidence based treatment protocol of the use of doxycycline as an adjunct to deep scaling procedure in generalized periodontitis.

Conclusion

The present study shows doxycycline as a good adjunct in managing bleeding on probing, reduction in the plaque index and pocket depth than deep scaling alone. The present study also showed significant gain in attachment at six-week intervals with doxycycline paired with deep scaling. However, these results were insignificant at the twelve-week interval. This study shows that doxycycline can act as an adjunct to scaling and polishing procedure to show significant improvement in clinical signs and symptoms of periodontitis.

UNDER PEER REVIEW

References

1. Machtei EE, Christersson LA, Grossi SG, Dunford R, Zambon JJ, Genco RJ. Clinical criteria for the definition of "established periodontitis." J Periodontol. 1992 Mar;63(3):206–14.

2. Armitage GC, Cullinan MP. Comparison of the clinical features of chronic and aggressive periodontitis. Periodontol 2000. 2010 Jun;53:12–27.

3. Hajishengallis G. Immunomicrobial pathogenesis of periodontitis: keystones, pathobionts, and host response. Trends Immunol. 2014 Jan;35(1):3–11.

4. Renvert S, Persson GR. A systematic review on the use of residual probing depth, bleeding on probing and furcation status following initial periodontal therapy to predict further attachment and tooth loss. J Clin Periodontol. 2002;29 Suppl 3:82–9; discussion 90–1.

5. Takamatsu N, Yano K, He T, Umeda M, Ishikawa I. Effect of initial periodontal therapy on the frequency of detecting Bacteroides forsythus, Porphyromonas gingivalis, and Actinobacillus actinomycetemcomitans. J Periodontol. 1999 Jun;70(6):574–80.

6. Claffey N, Loos B, Gantes B, Martin M, Egelberg J. Probing depth at re-evaluation following initial periodontal therapy to indicate the initial response to treatment [Internet]. Vol. 16, Journal of Clinical Periodontology. 1989. p. 229–33. Available from: http://dx.doi.org/10.1111/j.1600-051x.1989.tb01646.x

7. Saito A, Hosaka Y, Kikuchi M, Akamatsu M, Fukaya C, Matsumoto S, et al. Effect of initial periodontal therapy on oral health-related quality of life in patients with periodontitis in Japan. J Periodontol. 2010 Jul;81(7):1001–9.

8. Saivin S, Houin G. Clinical pharmacokinetics of doxycycline and minocycline. Clin Pharmacokinet. 1988 Dec;15(6):355–66.

9. Emingil G, Gürkan A, Tervahartiala T, Hernandez M, Özgül S, Sorsa T, et al. Adjunctive Effects of a Sub-Antimicrobial Dose of Doxycycline on Clinical Parameters and Potential Biomarkers of Periodontal Tissue Catabolism. Dent J [Internet]. 2019 Jan 20;7(1). Available from: http://dx.doi.org/10.3390/dj7010009

10. Crout RJ, Lee HM, Schroeder K, Crout H, Ramamurthy NS, Wiener M, et al. The "cyclic" regimen of low-dose doxycycline for adult periodontitis: a preliminary study. J Periodontol. 1996 May;67(5):506–14.

UNDER PEER REVIEW

11. Stoller NH, Johnson LR, Trapnell S, Harrold CQ, Garrett S. The pharmacokinetic profile of a biodegradable controlled-release delivery system containing doxycycline compared to systemically delivered doxycycline in gingival crevicular fluid, saliva, and serum. J Periodontol. 1998 Oct;69(10):1085–91.

12. Golub LM, Goodson JM, Lee HM, Vidal AM, McNamara TF, Ramamurthy NS. Tetracyclines Inhibit Tissue Collagenases: Effects of Ingested Low-Dose and Local Delivery Systems. J Periodontol. 1985 Nov;56 Suppl 11S:93–7.

13. Deo V, Gupta S, Bhongade ML, Jaiswal R. Evaluation of subantimicrobial dose doxycycline as an adjunct to scaling and root planing in chronic periodontitis patients with diabetes: a randomized, placebo-controlled clinical trial. J Contemp Dent Pract. 2010 May 1;11(3):009–16.

14. Machion L, Andia DC, Lecio G, Nociti FH Jr, Casati MZ, Sallum AW, et al. Locally delivered doxycycline as an adjunctive therapy to scaling and root planing in the treatment of smokers: a 2-year follow-up. J Periodontol. 2006 Apr;77(4):606–13.

15. Al Hulami H, Babay N, Awartani F, Anil S. The effect of locally delivered doxycycline as an adjunctive therapy to scaling and root planing in smokers. Saudi Dent J. 2011 Jul;23(3):143–8.

16. Nandan B, Barman Roy D, Pant VA, Gupta V, Bhaduria U, Kaur H, et al. Comparative Evaluation of Cost-Effectiveness, Clinical and Microbiological Parameters of Systemic Antibiotics Versus Local Drug Delivery in Aggressive Periodontitis. Cureus. 2022 Jan;14(1):e20985.

17. Golub LM, Lee HM, Stoner JA, Sorsa T. Subantimicrobial-dose doxycycline modulates gingival crevicular fluid biomarkers of periodontitis in postmenopausal osteopenic women. Journal of [Internet]. 2008; Available from: https://aap.onlinelibrary.wiley.com/doi/abs/10.1902/jop.2008.070623

18. Chiu S-C. The Effect of Subantimicrobial Dose Doxycycline of Gingival Crevicular Fluid Inflammatory Mediators in Diabetic Patients. University of Minnesota; 2006. 206 p.

19. Eickholz P, Kim T-S, Bürklin T, Schacher B, Renggli HH, Schaecken MT, et al. Non-surgical periodontal therapy with adjunctive topical doxycycline: a double-blind randomized controlled multicenter study [Internet]. Vol. 29, Journal of Clinical Periodontology. 2002. p. 108–17. Available from: http://dx.doi.org/10.1034/j.1600-051x.2002.290204.x

20. Salvi GE, Mombelli A, Mayfield L, Rutar A, Suvan J, Garrett S, et al. Local antimicrobial therapy after initial periodontal treatment. J Clin Periodontol. 2002 Jun;29(6):540–50.

21. Tan OL, Safii SH, Razali M. Clinical Efficacy of Single Application Local Drug Delivery and Adjunctive Agents in Nonsurgical Periodontal Therapy: A Systematic Review and Network Meta-Analysis. Pharmaceutics [Internet]. 2020 Nov 12;12(11). Available from: http://dx.doi.org/10.3390/pharmaceutics12111086

UNDER PEER REVIEW

Table 1: Age wise distribution of participants included in the study

Age Group	Participants
28-35	4
36-42	5
43-47	2
48-53	7
54-60	6

Table 2: Plaque index, bleeding on probing and pocket depth of deep scaling alone (A) and doxycycline as an adjunct (B)

Parameters	Groups	Baseline data(Mean±SD)	Six weeks (Mean±SD)	Twelve weeks (Mean±SD)
Plaque index	A	1.23±0.28	0.33±0.12	0.31±0.03
	B		0.25±0.19	0.21±0.12
BOP	A	0.44±0.18	0.13±0.03	0.19±0.02
	B		0.13±0.017	0.12±0.01
Pocket Depth	A	5.46±0.22	3.68±0.41	3.32±0.26
	B		3.30±0.52	3.22±0.65

Table 3: Gain of attachment of two groups at six-week and twelve-week interval

UNDER PEER REVIEW

Groups	Six-week interval (Mean±SD)	Twelve-week interval (Mean±SD)
A	1.86±0.19	2.14±0.05
B	2.16±0.32	2.24±0.44

255

256

UNDER PEER REVIEW