

CLINICAL EVALUATION OF NON-SURGICAL PERIODONTAL THERAPY WITH AND WITHOUT SYSTEMIC ADMINISTRATION OF ANTIBIOTICS IN CHRONIC PERIODONTITIS PATIENT: A RANDOMISED CONTROLLED TRIAL

Periodontology

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ABSTRACT

This study was done to clinically evaluate the effect of non-surgical periodontal therapy with or without systemic administration of antibiotic in chronic periodontitis patients. A total of 120 mild to moderate chronic generalised periodontitis patients with probing pocket depth from 4 to 7 mm were randomly divided into three equally sized groups. Patients in Group A treated with scaling and root planing alone; in Group B and Group C the systemic use of amoxicillin (500mg x 3 times daily) and metronidazole (400mg x 3 times daily) were prescribed for 3 and 7 days respectively as an adjunct to scaling and root planing. Pocket depth, clinical attachment level, bleeding on probing and full mouth plaque scores were assessed at baseline, 2 weeks and 6 weeks post treatment. This study represents significantly better clinical outcomes, i.e. Probing pocket depth (PD) reduction and clinical attachment level (CAL) gain, following the adjunctive use of amoxicillin plus metronidazole to scaling and root planing compared to the treatment with scaling and root planing alone. The adjunctive use of amoxicillin plus metronidazole with scaling and root planing for 3 days is enough to gain improvement in clinical outcomes; so that the long-term use of antibiotic that causes unnecessary microbial resistance can be avoided.

KEYWORDS

Amoxicillin; Metronidazole; Non-Surgical Periodontal Treatment.

BACKGROUND

Periodontal treatment aims at reduction in the sub gingival oral biofilm, including pathogenic species, to achieve homeostasis [1]. Most forms of periodontal disease can be successfully treated by a regimen that includes mechanical removal of the supra- and sub gingival bacterial deposits and the institution of careful self-performed plaque control measures [2]. The reduction in the supra- and sub gingival oral biofilm, is mainly accomplished by mechanical removal of the bacterial deposits from the tooth surfaces, i.e. via scaling and root planing (SRP) [1].

However, bacteria residing in root concavities, dentin tubules or within soft tissues are not easily reached with mechanical instrumentation, and therefore SRP rarely leads to complete elimination of the sub gingival biofilm [3]. So, to overcome these limitation, the adjunctive use of antibacterial agents (antibiotics and antiseptics) may be considered [4].

A large variety of antibiotics (AB) has indeed been investigated as possible adjunct to SRP [5]. Dosage and duration of the prescribed antibiotic regime vary greatly in the literature [6].

At present, it remains unknown whether a short-term (e.g. 3 days) administration of AMX + MET as adjunct to non-surgical periodontal therapy may provide additional benefits to scaling and root planing (SRP) alone. Thus, the aim of this study was to evaluate the potential effect of 3- or 7-day systemic administration of AMX and MET as adjunct to SRP over SRP alone during non-surgical periodontal therapy in patients with chronic periodontitis.

MATERIAL AND METHODS

SUBJECT SELECTION

The hypothesis to be tested in this randomized controlled clinical trial was that "the systemic use of AMX and MET administered for 3 or 7 days as adjunct to SRP leads to superior clinical results compared with SRP alone" [1]. Sample size calculation was performed before starting the study. A total of 60 subjects were selected for the study with 20 subjects per treatment group, from the outpatient Department of Periodontology and Implantology, Institute of Dental Sciences, Bareilly, Uttar Pradesh between January 2017 and March 2017. Signed written informed consent was obtained from every individual after

explaining the procedures and the outcomes of treatment in their vernacular language.

To be included in the study, subjects had to fulfill following criteria:

- 60 systemically healthy patients with age group 18 to 60 years
- ≥ 20 natural teeth present in the oral cavity distributed in all four quadrants
- Patient with mild to moderate chronic generalised periodontitis i.e. with probing pocket depth ranges from 4 to 7 mm along with radiographic sign of generalised bone loss

Exclusion criteria were as follows:

- Systemic or local use of antibiotics within the previous 3 months
- Patient undergone any periodontal therapy within the previous 12 months
- Patient allergic to amoxicillin and metronidazole
- Patient with head and neck radiation therapy
- Patient with smoking and alcohol consumption habit
- Pregnant and lactating women
- Patient with infectious or heart diseases that need prophylactic administration of AB before dental treatment
- Patient with liver diseases

TREATMENT PROTOCOL

This study was a randomized controlled clinical trial. All subjects enrolled in the study were randomly divided into following three treatment groups: Sub gingival scaling and Root Planing alone (Group A, n = 40), Sub gingival scaling and Root Planing + amoxicillin (500 mg TID 3 days) + metronidazole (400 mg TID 3 days; Group B, n = 40) and Sub gingival scaling and Root Planing + amoxicillin (500 mg TID 3 days) + metronidazole (400 mg TID 7 days; Group C, n = 40).

At baseline (i.e. prior to Sub gingival scaling and Root Planing), at 2 and 6 week post treatment assessment of the clinical parameters i.e. Probing pocket depth [were recorded at six sites per tooth to the nearest millimetre using a periodontal probe (UNC 15)], Clinical attachment level [the reference point for the CAL measurements was considered the cement-enamel junction (CEJ); if the CEJ had been modified by restorative treatment, then the reference point was considered the most apically located margin of the restoration], Gingival bleeding index (Ainamo & Bay 1975) and Full mouth plaque scores (O'Leary et al. 1972) was performed. 0.05 value was considered to be statistically

In particular, all pockets ranging from 4 to 7 mm [7] were scaled and root planed to the bottom of the pocket with ultrasonic instruments and Gracey curettes (Hu Friedy, Chicago, IL, USA), under local anaesthesia. At the end of the SRP sessions, clinician allocated the patients to one of the three treatment groups according to the randomization protocol, gave their medications and instructed them on how to take them.

Patients were recalled at 2 weeks, and 6 weeks after completion of Sub gingival scaling and Root Planing and the clinical parameters i.e. probing pocket depth, clinical attachment level, gingival bleeding index, and full mouth plaque scores were recorded accordingly.

The statistical data were obtained and then transferred into a statistical software program (SPSS statistics version 21). Comparisons within the groups between the various time points were performed using Repeated measures ANOVA and Friedman test. Comparisons between the groups were performed using Oneway ANOVA and Kruskal Wallis ANOVA tests. $P \leq 0.05$ value was considered to be statistically significant.

RESULTS

146 patients were screened for inclusion in the study. Of those, 21 were excluded for not meeting the inclusion criteria and six declined to participate. Of the remaining 125 patients who began the study, five were lost to follow-up, leaving 120 patients who completed the study with 40 patients in each group. The patients tolerated the treatment regimen well without any complications or complaints.

(Table 1) shows the demography of the subjects and the pre-test means of the clinical parameters. No statistically significant differences in means between the three groups were noted at baseline. The Group C included older subjects (mean age 36.45), and had more GBI score (mean of 2.15) and FMPS (mean of 3.50) preoperatively than the other two groups.

TABLE-1 DEMOGRAPHIC DISTRIBUTION AND PRE-TEST MEANS

VARIABLES	Group A	Group B	Group C
No. OF PATIENTS	40	40	40
MALE%	55	50	60
FEMALE%	45	50	40
	Mean± SD	Mean± SD	Mean± SD
AGE	33.65±10.085	34.05±8.413	36.45±9.816
PPD	3.45±0.21	3.46±0.27	3.51±0.21
CAL	3.43±0.23	3.41±0.24	3.48±0.28
GBI	1.65±0.88	2.00±0.92	2.15±0.81
FMPS	3.35±0.59	3.35±0.67	3.50±0.51

PPD, probing pocket depth; CAL, clinical attachment level; GBI, gingival bleeding index; FMPS, full mouth plaque scores

The clinical parameters registered at baseline, 2 weeks and 6 weeks are presented in (Table 2). No statistical differences were observed among the groups at baseline for any of the evaluated parameters ($p > 0.05$). At 2 and 6 weeks, all investigated parameters demonstrated statistically significant improvements compared to baseline in all treatment groups. At both 2 and 6 weeks, statistically significantly greater improvements ($p < 0.05$) in the two antibiotic groups i.e. Group B and Group C compared to Group A were observed (Table 2).

TABLE- 2 BETWEEN GROUP COMPARISON 2 AND 6 WEEKS POSTOPERATIVELY

VARIABLES	GROUP A	GROUP B	GROUP C	p value 1-2	p value 1-3	p value 2-3
PD 2 weeks	3.41±0.23	3.23±0.30	3.24±0.20	0.06	0.61	0.01*
PD 6 weeks	3.39±0.23	3.19±0.30	3.20±0.20	0.02*	0.81	0.00*
CAL 2 weeks	3.37±0.24	3.19±0.24	3.21±0.26	0.15	0.59	0.02*
CAL 6 weeks	3.37±0.25	3.17±0.27	3.19±0.25	0.03*	0.61	0.00*
GBI 2 weeks	0.75±0.55	0.55±0.60	0.45±0.60	0.21	0.51	0.00*

GBI 6 weeks	0.75±0.44	0.05±0.22	0.20±0.41	0.00*	0.46	0.01*
FMPS 2 weeks	2.00±0.32	1.85±0.37	1.90±0.31	0.36	0.43	0.00*
FMPS 6 weeks	2.40±0.60	2.05±0.39	2.30±0.47	0.07	0.08	0.03*

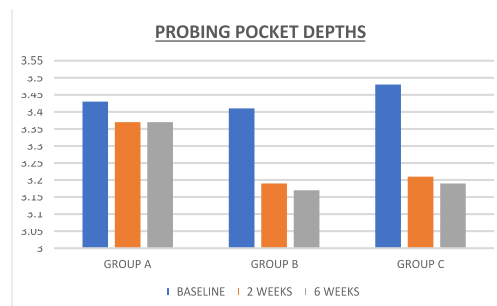
PPD- probing pocket depth; CAL- clinical attachment level; GBI- gingival bleeding index; FMPS- full mouth plaque scores

In particular, at 6 weeks, average Pocket Depth reduction in the Group A (3.39±0.23) was significantly smaller compared to the 3day (3.19±0.30) or the 7-day Antibiotic regime (3.20±0.20) groups. Significantly larger CAL gains were also recorded in Groups B and C (3.17±0.27 and 3.19±0.25, respectively) compared to the control group (3.37±0.25) at 6 weeks (Table 2). Statistically significantly greater PD reductions ($p < 0.05$) were obtained at 6 weeks in the two Antibiotic groups as compared with the control group (Table 2). Also, statistically significantly higher CAL gains ($p < 0.05$) were obtained in both the groups (Group A, Group B) compared with the control group at 6 weeks (Table 2).

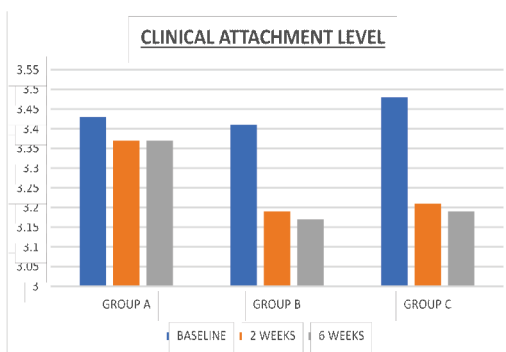
Statistically significant reduction in probing pocket depth, gain in clinical attachment level and reduction in gingival bleeding index score at 6 week postoperatively were seen in Group B as compared to Group A. No statistically significant reduction in full mouth plaque score were seen in same group comparison at 6 weeks postoperatively (Table 2).

There were statistically significant differences were seen between Group B and Group C both at 2 and 6 weeks postoperatively of probing pocket depth reduction (3.18±0.30 and 3.24±0.20, respectively), clinical attachment level gain (3.29±0.27 and 3.38±0.25, respectively), gingival bleeding score reduction (0.05±0.22 and 0.20±0.41, respectively) and full mouth plaque score reduction (2.05±0.39 and 2.30±0.47, respectively) (Table 2).

Maximum difference in probing pocket depth reduction from baseline to 6 weeks can be seen in group 2 as per graph represents in Graph 1 whilst maximum difference in clinical attachment gain from baseline to 6 weeks can be seen in Group B as per the bar diagram in Graph 2.



GRAPH 2 – CLINICAL ATTACHMENT LEVEL AT BASELINE, 2 WEEKS & 6 WEEKS



DISCUSSION

This study has evaluated the clinical outcomes following non-surgical periodontal therapy in conjunction with adjunctive amoxicillin plus metronidazole administered systemically for 3 or for 7 days compared with scaling and root planing alone in patients with generalized mild to moderate chronic periodontitis.

The results of this study showed that both, a 3- or 7-days antibiotic regimen as adjunct to scaling and root planing exhibited superior clinical results than those obtained by scaling and root planing alone. The main outcome variable in this study was the difference in the number of pockets with probing pocket depth 4 to 7 mm and the clinical attachment level, between baseline and 6 weeks after treatment.

Likewise, several studies have previously investigated the effect of antibiotics as adjunct to non-surgical periodontal treatment in various treatment protocols by using as endpoint the number of sites of specific depths (Arweiler et al 2014) [8]. Other studies have chosen mean full-mouth PD or CAL as endpoint for evaluating the efficacy of various antibiotic regimens (Feres M et al 2002, Silva M. P. et al 2011) [5, 9].

Comparable improvements after SRP combined with antibiotic regimen have been reported by Feres et al. However, the antibiotic regimen in that study was substantially different from herein, i.e. metronidazole (400 mg TID) and amoxicillin (500 mg TID) for 14 days. Interestingly, their results after 1 year are comparable with the results obtained after 6 months in the 3 or 7 days Antibiotic regimens of the present study [5].

In study done by Varela V. M in 2011, maximum difference in clinical attachment gain from baseline to 6 weeks can be seen with amoxicillin (500mg) + metronidazole (250mg) for 10 days. The antibiotic regimen was different from herein but the result showed a similar improvement in relation with the reduction in pocket depth and the gain in clinical attachment level in comparison with the present study [9].

Moreover shallow sites showing limited improvements even after treatment compared to deeper sites in terms of numerical values are likely to significantly dilute the effect observed in deeper sites, which are actually in need for further treatment [10, 11].

The present results are in accordance with the study done by Varela et al [9], Feres et al [5] that represents significantly better clinical outcomes, i.e. Probing pocket depth (PD) reduction and clinical attachment level (CAL) gain, following the adjunctive use of amoxicillin plus metronidazole to scaling and root planing compared to the treatment with scaling and root planing alone.

Regarding the aspect of antibiotics administration duration, several studies have shown that resistant microbial strains can appear de novo when low-drug doses are prescribed for long-term infections [12]. Therefore, in several areas of general medicine antibiotic administration in high dosage and for shorter intervals has been evaluated for various infections [13].

According to Vogelmann & Craig [14] it is important that the antibiotics is given in an adequate (minimum) bactericidal dose for an adequate (minimum) length of time. The present study represents that the adjunctive use of amoxicillin plus metronidazole with scaling and root planing for 3 days showed statistically significantly better clinical outcomes compare with the adjunctive use of amoxicillin plus metronidazole with scaling and root planing for 7 days.

Furthermore to see whether there is any elimination or suppression of putative periodontal pathogens such as *A. actinomycetemcomitans*, *P. gingivalis*, *P. intermedia* which occur as a result of use of antibiotics as an adjunct with scaling and root planning a further evaluation with large sample size and examination of microbiological characteristics of periodontal disease is needed.

CONCLUSION

In conclusion, these findings have shown that in chronic periodontitis patients, scaling and root planing in conjunction with a 3- or 7-day systemic administration of amoxicillin and metronidazole may lead to significantly greater clinical improvements compared to scaling and root planing alone. The adjunctive use of amoxicillin plus metronidazole with scaling and root planing for 3 days is enough to gain improvement in clinical outcomes; so that the long term use of antibiotic that cause unnecessary microbial resistance can be avoided.

REFERENCES

- 1) Cosgarea, R., Juncar, R., Heumann, C., Tristiu, R., Lascu, L., & Arweiler, N. et al. (2016). Non-surgical periodontal treatment in conjunction with 3 or 7 days systemic

- administration of amoxicillin and metronidazole in severe chronic periodontitis patients. A placebo-controlled randomized clinical study. *Journal Of Clinical Periodontology*, 43(9), 767-777. doi: 10.1111/jcpe.12559
- 2) Cobb, C. Nonsurgical pocket therapy; Mechanical. *Annals of Periodontology* 1996;1:443-90.
- 3) Carvalho, L., D'Avila, G., Leao, A., Goncalves, C., Haffajee, A., Socransky, S., & Feres, M. (2005). Scaling and root planing, systemic metronidazole and professional plaque removal in the treatment of chronic periodontitis in a Brazilian population II - microbiological results. *Journal Of Clinical Periodontology*, 32(4), 406-411. doi: 10.1111/j.1600-051x.2005.00720.x
- 4) Marsh, P. (2005). Dental plaque: biological significance of a biofilm and community life-style. *Journal Of Clinical Periodontology*, 32(s6), 7-15. doi: 10.1111/j.1600-051x.2005.00790.x
- 5) Feres, M., Haffajee, A., Allard, K., Som, S., Goodson, J., & Socransky, S. (2002). Antibiotic resistance of subgingival species during and after antibiotic therapy. *Journal Of Clinical Periodontology*, 29(8), 724-735. doi: 10.1034/j.1600-051x.2002.290809.x
- 6) Ribeiro, É., Bittencourt, S., Zanin, I., Bovi Ambrosano, G., Sallum, E., & Nociti, F. et al. (2009). Full-Mouth Ultrasonic Debridement Associated With Amoxicillin and Metronidazole in the Treatment of Severe Chronic Periodontitis. *Journal Of Periodontology*, 80(8), 1254-1264. doi: 10.1902/jop.2009.080403
- 7) Ronald M. Margolies Stages of periodontal diseases New York Comprehensive Dentistry 2009
- 8) Arweiler, N., Pietruska, M., Pietruski, J., Skurska, A., Dolińska, E., & Heumann, C. et al. (2014). Six-month results following treatment of aggressive periodontitis with antimicrobial photodynamic therapy or amoxicillin and metronidazole. *Clinical Oral Investigations*, 18(9), 2129-2135. doi: 10.1007/s00784-014-1193-6
- 9) Varela, V., Heller, D., Silva-Senem, M., Torres, M., Colombo, A., & Feres-Filho, E. (2011). Systemic Antimicrobials Adjunctive to a Repeated Mechanical and Antiseptic Therapy for Aggressive Periodontitis: A 6-Month Randomized Controlled Trial. *Journal Of Periodontology*, 82(8), 1121-1130. doi: 10.1902/jop.2011.100656
- 10) Silva, M., Feres, M., Oliveira Siroto, T., Silva Soares, G., Velloso Mendes, J., Faveri, M., & Figueiredo, L. (2011). Clinical and microbiological benefits of metronidazole alone or with amoxicillin as adjuncts in the treatment of chronic periodontitis: a randomized placebo-controlled clinical trial. *Journal Of Clinical Periodontology*, 38(9), 828-837. doi: 10.1111/j.1600-051x.2011.01763.x
- 11) Cionca, N., Giannopoulou, C., Ugolotti, G., & Mombelli, A. (2009). Amoxicillin and Metronidazole as an Adjunct to Full-Mouth Scaling and Root Planing of Chronic Periodontitis. *Journal Of Periodontology*, 80(3), 364-371. doi: 10.1902/jop.2009.080540
- 12) Lieberman, T., Michel, J., Aingaran, M., Potter-Bynoe, G., Roux, D., & Davis, M. et al. (2011). Parallel bacterial evolution within multiple patients identifies candidate pathogenicity genes. *Nature Genetics*, 43(12), 1275-1280. doi: 10.1038/ng.997
- 13) Joshi, J. (2011). Tuberculosis chemotherapy in the 21st century: Back to the basics. *Lung India*, 28(3), 193. doi: 10.4103/0970-2113.83977
- 14) Vogelmann, B., & Craig, W. (1986). Kinetics of antimicrobial activity. *The Journal Of Pediatrics*, 108(5), 835-840. doi: 10.1016/s0022-3476(86)80754-5