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Effect of Systemically Administered Amoxicillin and Metronidazole in the Treatment of Chronic Periodontitis

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ABSTRACT

Introduction: Nonsurgical periodontal therapy reduces periodontal inflammation, but complete removal of toxin and bacterial deposits is not always possible. Thus, adjunctive therapeutic strategies like use of systemic amoxicillin and metronidazole have evolved.

Objective: To evaluate effect of systemically administered amoxicillin and metronidazole in the treatment of chronic periodontitis.

Methods: A pretest post-test study was conducted from February 2021 to November 2021 in Department of Periodontics and Oral Implantology at Peoples Dental College and Hospital after ethical clearance from Institutional Review Committee of PDCH. Thirty-six patients with chronic periodontitis were recruited through convenient sampling. The patients were assigned into two groups meeting the criteria of at least six teeth with probing pocket depth 5-7 mm. Group A received scaling and root planing and Group B received adjunctive systemic Amoxicillin and Metronidazole three times daily for seven days. Clinical parameters were evaluated at one month, three months and six months post-treatment. Data were analysed in SPSS v.20.

Results: Mean values of pocket depth (PD), clinical attachment level (CAL), plaque index (PI) and gingival index (GI) were reduced significantly after treatment in both treatment groups with more clinical improvement in adjunctive systemic amoxicillin and metronidazole. However, on intergroup comparison, clinical attachment level and plaque index was not significantly reduced.

Conclusions: The findings of the current study showed significant improvements in both groups compared with baseline. Thus, adjunctive systemic amoxicillin and metronidazole provide better results than scaling root planing alone.

Keywords: Antinfective agents; amoxicillin; chronic periodontitis; metronidazole; nonsurgical periodontal therapy; therapeutic use.

INTRODUCTION

Periodontitis is an infectious disease resulting from bacterial inflammation.[1] It is progressive and episodic in nature. If not treated, the resulting loss of attachment structures can ultimately lead to tooth loss. Bacterial plaque is a primary etiologic factor of periodontitis, although environmental[2] behavioral[3] and genetic[4] factors also contribute to the disease progression.

Nonsurgical periodontal therapy is considered as a "gold standard" of periodontal therapy.[5] However, studies have shown that nonsurgical periodontal therapy alone is unable to completely eradicate the bacterial deposits and toxins from the root surface and periodontal pocket.[1] Thus, numerous adjunctive therapeutic strategies have evolved, such as systemic amoxicillin and metronidazole.

Amoxicillin is a broad spectrum amino-penicillin derivative, effective against both strains of bacteria by its mechanism of cell wall synthesis inhibition.[6] Metronidazole is effective against anaerobic gram-negative microorganism. Mechanism of action of metronidazole is disruption of deoxyribonuclic acid and inhibition of nucleic acid synthesis.[7]

The combination of Metronidazole and Amoxicillin was first introduced in periodontology by Van Winkelhoff et al.[8] Combination of amoxicillin and metronidazole has been demonstrated to have synergistic bactericidal effect against complex microbiology of periodontal disease.[9] Thus, aim of the study is to evaluate effect of systemically administered amoxicillin and metronidazole in the treatment of chronic periodontitis.

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METHODS

A pretest post-test study (non-randomized trial) was done to evaluate the effect of systemically administered amoxicillin and metronidazole in the treatment of chronic periodontitis visiting the Department of Periodontics and Oral implantology at Peoples Dental College and Hospital (PDCH), Sorhakhutte, Kathmandu, Nepal from February 2021 to November 2021. Patients were recruited by convenience sampling method. Ethical approval was obtained from Institutional Review committee of PDCH (Ref. 19.2077/78). Informed consent was obtained from the patients.

Sample size was computed using the formula

$$N = 2[(Z\alpha+Z\beta)^2 s^2/d^2]$$

Where, z_α = 1.96 at 95% confidence level; z_β = 1.65 at 95% power according to reference article by Berglundh et. al.[9] d = Mean difference of probing pocket depth = 0.4 s = Variability, standard deviation of probing pocket depth = 0.3;15 per group. Adding 20% of expected dropout 15+3 = 18 per group.

The sample comprised of systemically healthy with untreated chronic periodontitis patient of age 35 - 55 years, who had minimum 20 teeth in both jaws. Minimum six teeth were selected for study exhibiting probing pocket depth 5-7 mm, Clinical Attachment Level: 2-4 mm, Plaque index 1-2, Gingival index 1-2.

Teeth with grade II, III mobility (Millers classification 1938) of quantifying teeth, Grade II, III, IV furcation involvement (Glickman's classification 1953), patient with medical disorders that require prophylactic coverage, patient with known hypersensitivity to amoxicillin and metronidazole, pregnancy and lactating mother, systemic disease that could affect the outcome or progression of periodontal therapy (diabetes, liver disease, hypertension), teeth with crown, bridges, orthodontic appliances, and implant, smokers, alcoholics, and drug abusers, patient who had received professional surgical and non-surgical periodontal therapy six months prior to initiation of study, consumption of drugs known to affect periodontal status (antibiotic, anti-inflammatory, anticonvulsant, immunosuppressant, or calcium channel blocker) within the past six months), periapical alteration of teeth and third molars were excluded in this study.

After selection of the subjects, impressions of the respective arches were taken with alginate, cast was made. An individual occlusal stent was fabricated of self-curing resin to create fixed landmarks and to standardise the location of periodontal probe. The occlusal stent was prepared to cover the occlusal surface of tooth being treated, as well as the occlusal surfaces of at least one adjacent tooth in mesial and distal direction.

Proper history taking and clinical examination was done. Patient education motivation and detailed oral hygiene instructions were given. Patients were motivated to perform proper brushing technique (Modified Bass) prior to the commencement of the study. Before treatment, each patient was thoroughly explained about the nature, risks, and benefits of the clinical procedure.

Patients falling under the inclusion criteria were chosen conveniently as a sample and divided into two equal groups. Every odd number of subjects were allotted in group A and even number of subjects were allotted into group B. Patient falling under group A were treated with scaling and root planing alone. Patient falling under group B were treated with adjunctive systemic Amoxicillin and Metronidazole.

In first visit supragingival scaling was done with ultrasonic device in both groups. One week after scaling patient was recalled for subgingival scaling and root planing with the help of ultrasonic device followed by Gracey curettes under application of local anaesthesia. After completion of scaling and root planing patients in group A received scaling root planing alone. In group B patients received a combination of systemic Amoxicillin 500 mg and Metronidazole 400 mg three times daily for seven days.

All patients were advised not to drink alcoholic beverages while using the medication. Oral hygiene instructions were repeated in every appointment. Patient were reevaluated at one month, three months and six months for all the clinical parameters.

Data were entered, cleaned, and coded in Microsoft Excel Sheet 2016. Data were then transported to IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA) for further analysis. Independent t-test was done for the intergroup comparison of

probing depth, clinical attachment level, plaque index and gingival index. Paired t-test was done for the intragroup comparison of probing depth, clinical attachment level, plaque index and gingival index. Level of significance was set at p-value ≤ 0.05.

RESULTS

The mean age of the study participants was 43.4±4.94 in group A and 42.1±5.36 in group B with minimum of 36 years and maximum of 54 years. Gender wise distribution of study participants showed that majority were females 19 (52.77%) and 17 (47.23%) were male

Among the study participants, there was a statistically significant difference in mean probing depth and clinical attachment level at baseline, one month, three months and six months (Table 1). Among the study participants, there was a statistically significant difference in mean clinical attachment level at baseline, one month, three months and six months.

The difference in mean probing depth between group A and group B was not found to be statistically significant at baseline (P value = 0.95). However, there was a statistically significant difference in mean probing depth between group A and group B (Table 2) at one month, three months and six months with the mean probing depth lesser in group B than in group A in all the cases.

The intergroup comparison of clinical attachment level of the study participants (Table 2) at baseline, one month, three months and six months of intervention. The difference in mean clinical attachment level between group A and B was not found to be statistically significant at baseline, one month, three months, and six months.

Table 1: Intragroup comparison of probing depth and clinical attachment level.

Probing depth (mm)							
Group	Probing depth mean		SE	t value	95% Confidence Interval		P value
					Lower bound	Upper bound	
A	Baseline	1 month	0.303	3.881	0.533	1.819	< 0.001
		3 months	0.296	5.876	1.113	2.369	< 0.001
		6 months	0.320	3.482	0.437	1.798	0.003
B	Baseline	1 month	0.253	8.845	1.709	2.779	< 0.001
		3 months	0.241	11.859	2.356	3.376	< 0.001
		6 months	0.248	11.121	2.237	3.284	< 0.001
Clinical Attachment Level (in mm)							
Group	Clinical attachment level		SE	t value	95% Confidence Interval		P value
					Lower bound	Upper bound	
A	Baseline	1 month	0.212	3.565	0.307	1.210	< 0.001
		3 months	0.219	4.787	0.586	1.519	< 0.001
		6 months	0.244	3.438	0.322	1.359	0.003
B	Baseline	1 month	0.143	7.911	0.831	1.435	< 0.001
		3 months	0.176	8.946	1.209	1.956	< 0.001
		6 months	0.185	8.304	1.152	1.936	0.001

Table 2: Intergroup comparison of probing depth and clinical attachment level.

Probing depth (mm)						
Probing depth mean	Group	Mean±SD	t value	95% Confidence Interval		P value
				Lower Bound	Upper Bound	
Baseline	A	5.72±0.54	- 0.060	- 0.30	0.302	0.952
	B	5.71±0.56				
1 month	A	4.5±1.2	- 3.433	- 0.379	0.203	< 0.001
	B	3.1±1.2				
3 months	A	4.0±1.1	- 3.01	- 0.340	0.112	< 0.002
	B	2.8±1.2				
6 months	A	4.8±0.6	- 6.0	- 0.509	0.206	< 0.001
	B	2.9±1.1				

Clinical attachment level (mm)						
Clinical attachment level mean	Group	Mean±SD	t value	95% Confidence Interval		P value
				Lower Bound	Upper Bound	
Baseline	A	3.23±0.49	1.43	- 0.84	0.49	0.15
	B	3.44±0.34				
1 month	A	2.4±0.78	- 7.5	- 0.67	0.31	0.45
	B	2.3±0.67				
3 months	A	2.2±0.81	- 1.3	- 0.87	0.18	0.19
	B	1.8±0.74				
6 months	A	2.4±0.48	- 2.07	- 1.04	- 0.10	0.06
	B	1.9±0.74				

Table 3: Intergroup comparison of plaque index of the study participants at baseline, one month, three months and six months of intervention.

Plaque index	Group	Mean±SD	t value	95% Confidence Interval		P value
				Lower Bound	Upper Bound	
Baseline	A	1.8±0.42	0.00	- 0.30	0.30	1
	B	1.8±0.46				
1 month	A	1.03±0.49	- 0.6	- 0.37	0.20	0.54
	B	0.95±0.34				
3 months	A	0.9±0.29	- 0.9	- 0.34	0.1	0.33
	B	0.8±0.37				
6 months	A	1.55±0.47	- 0.8	- 0.5	0.2	0.39
	B	1.35±0.56				

Table 4: Intergroup comparison of gingival index of the study participants at baseline, one month, three months and six months of intervention.

Gingival index	Group	Mean±SD	t value	95% Confidence Interval		P value
				Lower Bound	Upper Bound	
Baseline	A	1.98±0.41	- 0.12	- 0.28	0.29	0.9
	B	1.97±0.43				
1 month	A	1.17±0.43	- 8.2	- 0.5	0.01	< 0.005*
	B	0.96±0.38				
3 months	A	1.10±0.39	- 4.6	- 0.77	- 0.3	< 0.001*
	B	0.5±0.26				
6 months	A	1.3±0.45	- 4.2	- 0.8	- 0.3	< 0.001*
	B	1.1±0.37				

DISCUSSION

The primary etiologic agent in periodontitis is bacterial plaque. It is well established that meticulous scaling and root planing in conjunction with a patient's proper plaque control can control periodontitis. However, this therapy occasionally fails due to recolonisation and invasion of the pockets by certain micro-organisms or inadequate mechanical therapy in areas inaccessible to periodontal instruments.[10]

The aim of the present study was to evaluate the effect of systemic amoxicillin and metronidazole administered immediately after completion of full-mouth scaling and root planing in patients with chronic periodontitis. Clinical attachment level, probing pocket depth, plaque index and gingival index was considered to evaluate periodontal status at baseline, one month, three months and six months.

Whenever the pocket depth is more than five mm, scaling and root planing becomes progressively less effective.[11] This has led to the development of alternative or adjunct treatment that provide added benefits along with scaling and root planing.

The results of present study demonstrated statistically significant improvement for both the treatment groups, when intragroup comparison of plaque index, gingival index, pocket depth and clinical attachment level was done at baseline, one month, three months and six months. Result of intergroup comparison showed statistically significant reduction in probing pocket depth, and gingival index. However, clinical attachment level and plaque index was not statistically significant. But clinical improvement was seen at one month, three months and six months in patients with adjunctive systemic amoxicillin and metronidazole compared to SRP alone.

Immediately after completion of scaling and root planing adjunctive systemic amoxicillin and metronidazole was administered in group B patient because scaling and root planing alter the biofilm and systemic antibiotics are more effective against species growing on planktonic state than species growing in biofilm.[12] So, in the present study systemic amoxicillin and metronidazole was given immediately after scaling and root planing. Similarly, Loesche et al. 1994[13] found that the administration of antibiotics immediately after last session of scaling and root planing provide better clinical outcome than administration of antibiotics at the first scaling session.

Plasma half-life of amoxicillin and metronidazole is six to eight hours. Based on this principle systemic amoxicillin 500 milligrams three times daily and metronidazole 400 milligrams three times daily was given in present study. Lopez et al.[14] demonstrated that one week course of systemic administration of metronidazole plus mmoxicillin as only therapy in patient with moderate to advanced adult periodontitis was effective in arresting progression of periodontal disease. This is in accordance with the present study.

Berglundh et al. 1998[9] found effect of systemic administration of metronidazole and amoxicillin as an adjunct to mechanical therapy resulted in an improvement of the periodontal conditions (reduction of BOP, PPD and CAL gain), elimination of putative periodontal pathogen such as Aggregatibacter *actinomycetemcomitans*, Porphyromonas. *gingivalis* and Previtella. *intermedia*. Proving combined mechanical and systemic antibiotic therapy was more effective than mechanical therapy alone. This is in accordance to the present study.

Winkel et al. 2001[15] demonstrated that use of systemic antibiotics significantly decreased bleeding index, clinical attachment level and probing pocket depth. However, dosages used in the present study was different from the other studies done by Berglundh[9], Winkel[15], Ehmke[16]. The dosage of amoxicillin and metronidazole in the present study was 500 milligrams and 400 milligrams respectively. While other studies used amoxicillin and aetronidazole 375 milligrams and 250 milligrams respectively. Pocket depth could have possibly been reduced in present study by three mechanisms i.e., reduction in inflammation, establishment of a long junctional epithelium and reorganization of collagen, all of which would influence probe penetration.[17]

Clinical attachment gain more in group B patients could have possibly been due to reduction of local level of proinflammatory cytokines. Offenbacher et al. 1986[18] Demonstrated that PGE_2 found in GCF could use as a predictor for periodontal attachment loss. Systemic amoxicillin and metronidazole reduce the level of PGE_2 level in GCF indicating reduced risk for further attachment loss. Similarly, Ribeiro et al.

2009[19] reported that significant reduction of IL-1 in both scaling root planing alone and in adjunctive systemic antibiotics. Result was in accordance with the present study.

As a clinical outcome variables plaque index and gingival index were used. Analyses for clinical outcome showed that gingival index was statistically significant in group B compared to Group A at one month, three months and six months. There was no significant difference between group A and group B with respect to full mouth plaque index suggesting that both treatments were equally effective to reduce plaque index. Systemic antibiotic therapy does not significantly affect supragingival plaque accumulation. Reduction in dental plaque depends mostly on patient's oral hygiene efforts.

Systemic antibiotic therapy is ineffective against gingival inflammation related to supragingival plaque but may help gingivitis caused by susceptible subgingival microorganism.[20] Result of present study is in accordance with Studies done by Lopez et al.[14] ,which showed metronidazole and amoxicillin therapy for eight days can reduce subgingival level of P. gingivalis and less gingival bleeding for up to 12 months compared with placebo.

Berglund et al.[9] Showed that subgingival scaling together with systemic amoxicillin and metronidazole for 14 days caused more suppression of P. gingivalis for 12 months than SRP alone. Similarly, Silva et al. 2011[21] showed that patient treated with adjunctive systemic Amoxicillin and Metronidazole significantly reduced the levels and proportions of all red complex pathogens and significantly greater beneficial changes in the microbial profile in comparison to SRP alone. Similarly, systematic review done by Teughels et al.[22] revealed that amoxicillin plus metronidazole was the best additional treatment in the non-surgical treatment of chronic periodontitis. Further, Zhao et al.[23] concluded that full mouth scaling and root planning adjunct to high drug dose (500/500 milligrams) of amoxicillin and metronidazole showed a significant and stable improvement on 6 months follow up period.

In the present study benefits also could have been better if an antibiotic sensitivity and microbiological test had been done with samples of subgingival biofilm prior to selecting the antibiotic. Also benefit could have been better if both groups were treated with different group of antibiotics.

All the clinical parameters reduced significantly from baseline to six months in both the groups. Probing pocket depth and gingival index was significantly reduced in group B compared to group A. Higher improvements in the clinical parameters in Group B as compared to Group A was seen. Hence, Chronic periodontitis patients achieved significantly better clinical improvement and more stable results when treated with systemic amoxicillin and metronidazole as an adjunct to scaling and root planing.

CONCLUSIONS

Within the limit of this study, the data from this study indicates positive effects in improving clinical parameters for patients treated with systemic amoxicillin and metronidazole. Hence, further research in this area with a larger sample size along with microbiological study are required to obtain a more accurate result regarding the effect of adjunctive systemic amoxicillin and metronidazole in the treatment of chronic periodontitis.

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