

Comparative evaluation of adjunctive antibiotics given post periodontal flap surgery

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ABSTRACT

Background: Antibiotics are known to improve clinical parameters in patients with periodontitis, so they should be capable of enhancing the surgical treatment outcome by improving clinical parameters when given adjunctively following periodontal flap surgery. **Methods:** Thirty subjects with moderate to severe periodontitis were randomly divided into three groups: Group I: 10 patients without antibiotic prescription after flap surgery, Group II: 10 patients prescribed with metronidazole 400 mg t.i.d. for 14 days, and Group III: 10 patients prescribed with doxycycline 200 mg o.d. as booster dose followed by successive doses of 100 mg o.d. for 21 days. Plaque index (PI), gingival index (GI), pocket probing depth (PPD), and clinical attachment level (CAL) were recorded at baseline, 2 weeks, and 2 months. The mean values and standard deviation values for each parameter were calculated using analysis of variance. Group comparison was done using paired *t*- and unpaired *t*-tests. **Results:** Reduction in PI, GI, PPD, and CAL after 2 weeks and 3 months from baseline in all the three groups was seen; intergroup comparison showed more reduction in PPD and GI and more gain in CAL in Groups II and III after 3 months when compared with Group I. No statistical difference was seen between Groups II and III. **Conclusion:** Within the limits of this study, it can be concluded that antibiotic administration as an adjunct to conventional flap surgery helps in improving clinical parameters.

Keywords: Antibacterial agents, chronic periodontitis, oral surgical procedures, periodontal attachment loss

Introduction

The goal of periodontal therapy is to alter or eliminate microbes and contributing risk factors.^[1] Mechanical debridement may fail to remove pathogens because of their location in subepithelial gingival tissue, crevicular epithelial cells, altered cementum and radicular dentinal tubuli, subgingival hard deposits, furcations, and so on complicating adequate instrumentation. Moreover, pathogens frequently colonize and translocate from nonperiodontal sites to periodontal crevices.^[2]

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Many studies showed that administration of metronidazole, metronidazole + amoxicillin, and doxycycline improves clinical parameters,^[3,4] reduces pocket depths,^[5,6] and gains in attachment in patients with periodontitis.^[5-7]

Hence, this study is intended to evaluate and compare efficacy of different antibiotics in improving treatment outcomes following flap surgery.

Materials and Methods

A total of 30 subjects of both sexes with chronic periodontitis requiring periodontal flap surgery were selected randomly from the outpatient Department of Periodontology. The ethical clearance for the study was provided by an institutionally approved ethical committee.

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Inclusion criteria: Systemically healthy patients between 25 and 55 years of age with moderate chronic periodontitis with plaque index (PI) score and gingival index (GI) score ≤ 2 , persistent probing depth ≥ 5 mm and ≤ 7 mm, and clinical attachment loss ≥ 3 mm and ≤ 5 mm after nonsurgical periodontal therapy in a minimum of three teeth of any quadrant.

Exclusion criteria: (1) Patients who required regenerative or resective osseous surgery were excluded from the study. (2) Female patients who were pregnant or on breastfeeding. Current smokers were excluded from the study.

Thirty patients fulfilling the above-mentioned criteria were randomly divided into three groups: Group I: 10 patients without any antibiotic prescription after flap surgery, Group II: 10 patients prescribed with metronidazole 400 mg thrice daily for 14 days^[8] after routine periodontal flap surgery, and Group III: 10 patients prescribed with doxycycline 200 mg as booster dose for 1 day followed by successive doses of 100 mg once daily for 21 days^[3] after routine periodontal flap surgery. A written consent was signed and detailed case history was recorded.

PI (Silness and Loe), GI (Loe and Silness), pocket probing depth (PPD; millimeters), and clinical attachment level (CAL; millimeters) were measured at baseline, 2 weeks after phase I therapy, and after 2 months following periodontal surgery.^[9]

Methods

Presurgical protocol

- On first visit, baseline recording of all parameters was done and they were further moved for phase I therapy [Figures 1a, 1d, 1g and 2a, 2d, 2g]

- Thorough scaling and root planning was performed and oral hygiene instructions were given
- After 2 weeks, second recording of parameters was done [Figures 1b, 1e, 1h and 2b, 2e, 2h]
- Systemically healthy patients with persistent probing depths ≥ 5 mm and ≤ 7 mm and CAL ≥ 3 mm and ≤ 5 mm in at least three teeth in a quadrant, PI and gingival indices ≤ 2 , and those not requiring any regenerative or osseous resective surgery were subjected to periodontal flap surgery in a specially prepared surgical room setup. Hence, a quadrant site which fulfils inclusion criteria was subjected to conventional flap surgery
- All the patients were subjected to routine blood investigations.

Surgical procedure

All personnel assigned in the operating room practiced standard presurgical procedures. Preprocedural mouth rinse with 10 mL of 0.2% chlorhexidine was done. Proper barrier methods were used. Conventional flap surgery was carried out in the selected quadrant. Postsurgical instructions were given.

In Group I, patients were not prescribed with any antibiotic, Group II patients were prescribed metronidazole 400 mg three times a day for 14 days, and Group III patients were prescribed doxycycline 100 mg twice a day as a loading dose and 100 mg once daily thereafter for 21 days. Nonsteroidal anti-inflammatory drug (ibuprofen 400 mg + paracetamol 325 mg) twice daily for a minimum of 3 days was prescribed for all the three groups after surgery. After 7 days, removal of periodontal packs and sutures was done. After 1 month, reinforcement of oral hygiene instructions was done. After 3 months, third recording of all clinical parameters was done [Figures 1c, 1f, 1i and 2c, 2f, 2i].

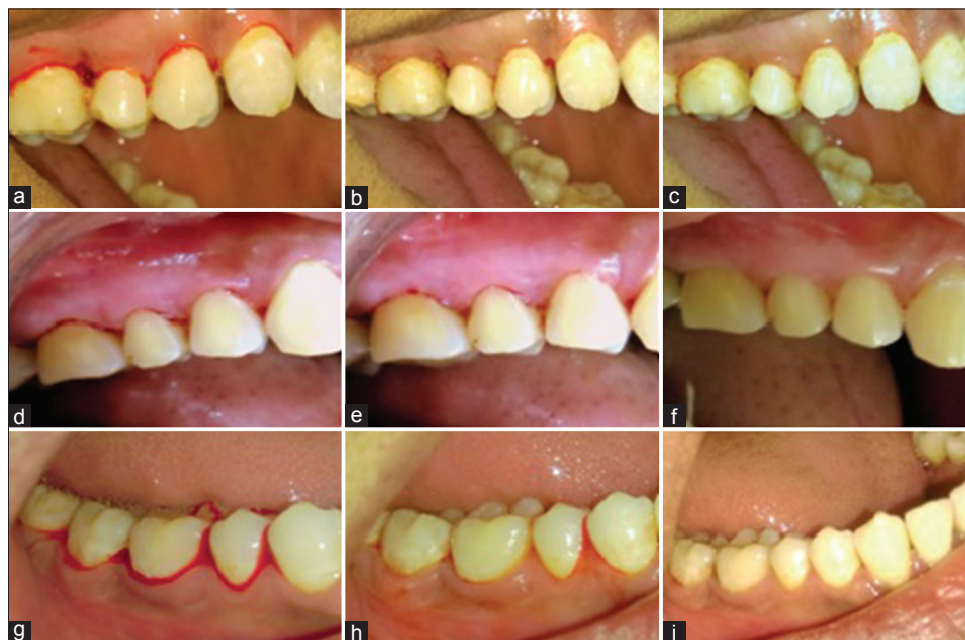


Figure 1: Gingival index for Group I: (a) baseline, (b) 2 weeks, and (c) 3 months; Group II: (d) baseline, (e) 2 weeks, and (f) 3 months; and Group III: (g) baseline, (h) 2 weeks, and (i) 3 months (original)

Statistical analysis

Statistical analyses of the entire data were performed using SPSS 16 software program. The mean values and standard deviation values for each parameter included were calculated using analysis of variance. Intergroup comparison and intragroup comparison were done using paired *t*-test and unpaired *t*-test, respectively. *P* values from all statistical tests were presented, but were considered statistically significant at $P \leq 0.05$ and highly significant at $P \leq 0.001$.

Results

All the patients returned regularly for the maintenance program, without any dropouts. None of the patients belonging to Groups I, II, and III developed any allergy or unfavorable response to the drug, requiring discontinuation.

Comparison was done at two levels:

1. Intergroup comparison of mean values of each parameter in all the three groups
2. Intragroup comparison of mean values of each parameter after 2 weeks and 3 months from baseline in all the three groups.

I. Intergroup comparison

1. Plaque index

On comparing the mean values for Group I and Group II, Group I and Group III, and Group II and Group III, PI at 2 weeks and 3 months from baseline was found to be insignificant [Table 1, Graph 1].

2. Gingival index

On comparing the mean values for Group I and Group II, GI at 2 weeks was found to be highly significant and more in Group II when compared with Group I ($P = 0.001$), but at baseline and 3 months GI was found to be insignificant. On comparing the mean values for Group I and Group III, GI at 2 weeks was found to be significantly more in Group III when compared with Group I ($P = 0.031$), whereas at baseline and 3 months GI between the two groups was found to be insignificant. On comparing the mean values for Group II and Group III, GI at baseline, 2 weeks, and 3 months were found to be insignificant [Table 2, Graph 1].

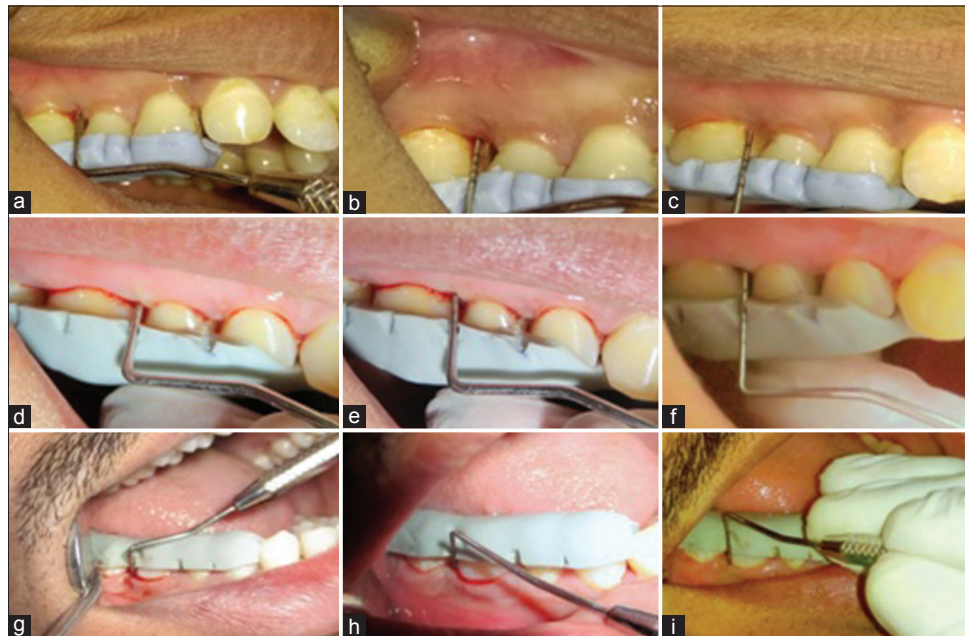


Figure 2: Pocket depth for Group I: (a) baseline, (b) 2 weeks, and (c) 3 months; Group II: (d) baseline, (e) 2 weeks, and (f) 3 months; and Group III: (g) baseline, (h) 2 weeks, and (i) 3 months (original)

Table 1: Comparison of mean values of plaque index between Group I and Group II, Group I and Group III, and Group II and Group III at baseline, 2 weeks, and 3 months (original)

Plaque index	Group I Mean±SD	Group II Mean±SD	<i>P</i>	Group I Mean±SD	Group III Mean±SD	<i>P</i>	Group II Mean±SD	Group III Mean±SD	<i>P</i>
Baseline	2.14±0.34	2.43±0.35	0.076	2.14±0.34	2.35±0.28	0.147	2.43±0.35	2.35±0.28	0.588
2 Weeks	1.23±0.07	1.38±0.15	0.012*	1.23±0.07	1.30±0.26	0.392	1.38±0.15	1.30±0.26	0.436
3 Months	1.11±0.09	1.04±0.10	0.114	1.11±0.09	1.14±0.25	0.733	1.04±0.10	1.14±0.25	0.253

SD: standard deviation. *Significant ($P \leq 0.05$)

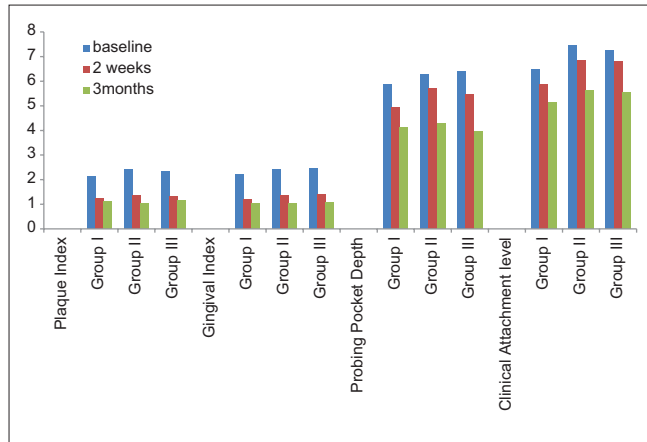
3. Pocket probing depth

On comparing the mean values for Group I and Group II, PPD after 2 weeks was found to be significantly more in Group II ($P = 0.008$), but at baseline and 3 months PPD was found to be insignificant. On comparing the mean values for Group I and Group III, PPD at 2 weeks was found to be significantly more in Group III ($P = 0.028$), but comparing between the mean values at baseline and 3 months PPD was found to be insignificant. On comparing the mean values for Group II and Group III, PPD at

baseline, 2 weeks, and 3 months was found to be insignificant [Table 3, Graph 1].

4. Clinical attachment level

On comparing the mean values for Group I and Group II, CAL at 2 weeks was found to be significantly more in Group II ($P = 0.017$), but at baseline and 3 months CAL was found to be insignificant. On comparing the mean values for Group I and Group III, CAL at 2 weeks was found to be significantly more in Group III ($P = 0.015$), but at baseline and 3 months CAL was found to be insignificant. On comparing the mean values for Group II and Group III, CAL at baseline, 2 weeks, and 3 months was found to be insignificant [Table 4, Graph 1].



Graph 1: Intergroup comparison of mean plaque index, gingival index, pocket probing depth, and clinical attachment level at baseline, after 2 weeks, and after 3 months between all three groups (original)

II. Intragroup comparison

In this category, the comparison of values for each parameter was done within every group. The mean value of each parameter was compared between baseline and 2 weeks, baseline and 3 months, and 2 weeks and 3 months.

1. Plaque index

On intragroup comparison, the mean difference values of PI when compared after 2 weeks from baseline and after 3 months from baseline for Group I, Group II, and Group III were found to be highly significant [Table 5, Graph 2].

Table 2: Comparison of mean values of gingival index between Group I and Group II, Group I and Group III, and Group II and Group III at baseline, 2 weeks, and 3 months (original)

Gingival index	Group I	Group II	P	Group I	Group III	P	Group II	Group III	P
	Mean±SD	Mean±SD		Mean±SD	Mean±SD		Mean±SD	Mean±SD	
Baseline	2.21±0.36	2.41±0.41	0.263	2.21±0.36	2.45±0.30	0.131	2.41±0.41	2.45±0.30	0.831
2 Weeks	1.19±0.10	1.36±0.09	0.001*	1.19±0.10	1.42±0.30	0.031†	1.36±0.09	1.42±0.30	0.553
3 Months	1.02±0.10	1.02±0.15	0.939	1.02±0.10	1.09±0.15	0.553	1.02±0.15	1.09±0.15	0.293

SD: standard deviation. †Highly significant ($P \leq 0.001$). *Significant ($P \leq 0.05$)

Table 3: Comparison of mean values of pocket probing depth in Group I and Group II, Group I and Group III, and Group II and Group III at baseline, 2 weeks, and 3 months (original)

Pocket probing depth	Group I	Group II	P	Group I	Group III	P	Group II	Group III	P
	Mean±SD	Mean±SD		Mean±SD	Mean±SD		Mean±SD	Mean±SD	
Baseline	5.85±0.42	6.29±0.79	0.138	5.85±0.42	6.41±0.75	0.055	6.29±0.79	6.41±0.75	0.733
2 Weeks	4.92±0.59	5.70±0.58	0.008*	4.92±0.59	5.47±0.43	0.028*	5.70±0.58	5.47±0.43	0.341
3 Months	4.13±0.61	4.28±0.47	0.547	4.13±0.61	3.97±0.45	0.509	4.28±0.47	3.97±0.45	0.149

SD: standard deviation. *Significant ($P \leq 0.05$)

Table 4: Comparison of mean values of clinical attachment level in Group I and Group II, Group I and Group III, and Group II and Group III at baseline, 2 weeks, and 3 months (original)

Clinical attachment level	Group I	Group II	P	Group I	Group III	P	Group II	Group III	P
	Mean±SD	Mean±SD		Mean±SD	Mean±SD		Mean±SD	Mean±SD	
Baseline	6.49±0.85	7.47±1.23	0.054	6.49±0.85	7.24±0.81	0.059	7.47±1.23	7.24±0.81	0.628
2 Weeks	5.88±0.70	6.83±0.90	0.017*	5.88±0.70	6.81±0.85	0.015*	6.83±0.90	6.81±0.85	0.970
3 Months	5.15±1.03	5.61±0.95	0.307	5.15±1.03	5.55±0.45	0.269	5.61±0.95	5.55±0.45	0.859

SD: standard deviation. *Significant ($P \leq 0.05$)

2. Gingival index

On intragroup comparison, the mean difference values of GI when compared after 2 weeks and 3 months from baseline for Group I, Group II, and Group III were found to be highly significant ($P = 0.00$). When compared after 3 months from 2 weeks' values of GI for Group I, Group II, and Group III, the values of Group I and Group II were found to be highly significant ($P = 0.00$), whereas the values for Group III were significant [Table 6, Graph 2].

3. Pocket probing depth

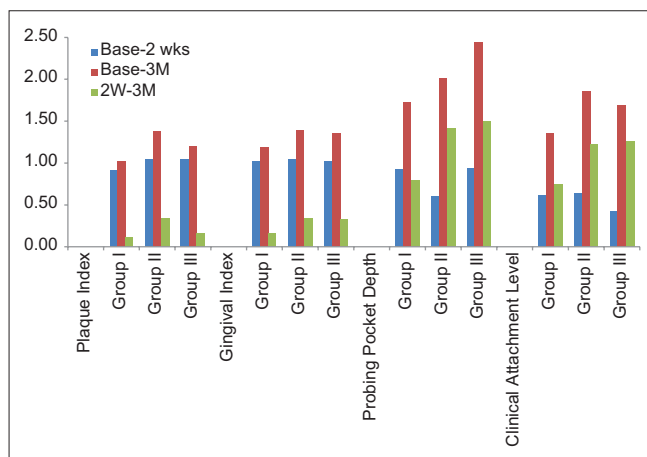
On intragroup comparison, the mean difference values of PPD when compared after 2 weeks from baseline, and 3 months from baseline between 2 weeks and 3 months for Group I, Group II, and Group III were found to be highly significant [Table 7, Graph 2].

4. Clinical attachment level

On intragroup comparison, mean difference values of CAL for Group I, Group II and Group III when compared after 2 weeks and 3 months from baseline were found to be highly significant ($P = 0.00$). Also when mean difference values were compared after 3 months from 2 weeks, value for Group I was found significant ($P = 0.01$) whereas values for Group II and Group III were highly significant ($P = 0.00$) [Table 8 and Graph 2].

Discussion

Although mechanical debridement usually results in significant improvement in periodontal health, some patients or some sites within an individual patient's mouth do not respond as well as anticipated, as it may fail to remove pathogenic organisms because of their location in subepithelial gingival tissue (*Aggregatibacter actinomycetemcomitans*), crevicular



Graph 2: Intragroup comparison of mean difference in plaque index, gingival index, pocket probing depth, and clinical attachment level from baseline to 2 weeks, baseline to 3 months, and 2 weeks to 3 months in all three groups (original)

epithelial cells (*A. actinomycetemcomitans*, *Peptostreptococcus micros*, *Prevotella intermedia*, and *Porphyromonas gingivalis*), collagenous substrata (*P. gingivalis*), altered cementum and radicular dentinal tubuli, subgingival hard deposits or furcations, or other anatomic features complicating adequate instrumentation.^[10]

Table 5: Intragroup comparison of plaque index after 2 weeks and 3 months from baseline in Group I, Group II, and Group III

Plaque index	Group I		Group II		Group III	
	Mean±SD	P	Mean±SD	P	Mean±SD	P
Baseline and 2 weeks	0.91±0.38	0.00†	1.05±0.31	0.00†	1.05±0.34	0.00†
Baseline and 3 months	1.02±0.39	0.00†	1.38±0.39	0.00†	1.20±0.46	0.00†
2 Weeks and 3 months	0.11±0.09	0.00†	0.34±0.22	0.00†	0.16±0.34	0.09

SD: standard deviation. †Highly significant

Table 6: Intragroup comparison of gingival index after 2 weeks and 3 months from baseline in Group I, Group II, and Group III

Gingival index	Group I		Group II		Group III	
	Mean±SD	P	Mean±SD	P	Mean±SD	P
Baseline and 2 weeks	1.02±0.36	0.00†	1.05±0.42	0.00†	1.03±0.34	0.00†
Baseline and 3 months	1.19±0.35	0.00†	1.39±0.34	0.00†	1.35±0.41	0.00†
2 Weeks and 3 months	0.17±0.14	0.00†	0.34±0.16	0.00†	0.33±0.33	0.01*

SD: standard deviation. †Highly significant ($P \leq 0.001$). *Significant ($P \leq 0.05$)

Table 7: Intragroup comparison of pocket probing depth after 2 weeks and 3 months from baseline in Group I, Group II, and Group III

Pocket probing depth	Group I		Group II		Group III	
	Mean±SD	P	Mean±SD	P	Mean±SD	P
Baseline and 2 weeks	0.93±0.78	0.00†	0.60±0.26	0.00†	0.94±0.45	0.00†
Baseline and 3 months	1.72±0.85	0.00†	2.01±0.62	0.00†	2.44±0.80	0.00†
2 Weeks and 3 months	0.79±0.63	0.00†	1.41±0.39	0.00†	1.50±0.42	0.00†

SD: standard deviation. †Highly significant ($P \leq 0.001$)

Table 8: Intragroup comparison of clinical attachment level after 2 weeks and 3 months from baseline in Group I, Group II, and Group III

Clinical attachment level	Group I		Group II		Group III	
	Mean±SD	P	Mean±SD	P	Mean±SD	P
Baseline and 2 weeks	0.61±0.33	0.00†	0.64±0.46	0.00†	0.42±0.26	0.00†
Baseline and 3 months	1.35±0.91	0.00†	1.86±0.53	0.00†	1.69±0.70	0.00†
2 Weeks and 3 months	0.74±0.79	0.01*	1.22±0.30	0.00†	1.26±0.73	0.00†

SD: standard deviation. †Highly significant ($P \leq 0.001$). *Significant ($P \leq 0.05$)

This study was designed to compare and evaluate the surgical treatment outcomes and the clinical parameters on adjunctive use of doxycycline and metronidazole after routine periodontal flap surgery.

On intragroup comparison, within Groups I, II, and III, there was significant reduction in PI and GI scores after 2 weeks and 3 months from baseline.

On intergroup comparison between Groups I and II, I and III, and II and III, there was no significant reduction in PI and GI scores at baseline, 2 weeks, and 3 months. The result that we have achieved is because of the reinforcement of oral hygiene instructions at regular intervals and satisfactory maintenance of oral hygiene by the patients. This showed that patients were compliant throughout the study in all the three groups. These results are in accordance with a study done by Mohan *et al.* in 2014 which compared doxycycline over amoxicillin and placebo and found no significant change in PI and GI between the three groups post surgery.^[11]

Soder *et al.* in 1999 had done a longitudinal clinical trial and found that nonsmoking patients who received metronidazole adjunctive to nonsurgical therapy showed significant improvement in inflammation and bleeding on probing than placebo group.^[9]

On intragroup comparison, within Group I there was a significant reduction in PPD and gain in CAL after 2 weeks and 3 months from baseline. These results after 2 weeks were thought to be obtained because of the complete removal of the supragingival plaque and calculus, and maintenance of oral hygiene by the patient. The results after 3 months were observed because of degranulation of remaining periodontal pockets, healing, and reinforcement of oral hygiene instructions.

Within Group II and Group III, there was a significant reduction in PPD and gain in CAL after 2 weeks and 3 months from baseline. These results were observed because of degranulation of remaining periodontal pockets, healing, and adjunctive use of metronidazole and doxycycline in Group II and Group III, respectively, which further has their action on the remaining tissue-invasive microorganisms that remain after surgical debridement of periodontal pockets.

On comparing PPD and CAL Group I with Group II and Group III, Group II and Group III showed significantly more reduction in PPD when compared with Group I after 3 months. This result is attributable to the fact that some tissue-invasive microorganisms, present subgingivally in periodontal pockets, cannot be completely removed by mechanical debridement. Hence, adjunctive use of metronidazole and doxycycline effectively reduced these tissue invasive microorganisms, thereby reducing PPD, hence gain in attachment level. These findings are similar to the studies done by Soder *et al.*,^[9] Loesche *et al.*,^[12] and Elter *et al.*^[5]

Studies conducted by Ng and Bissada^[3] and Mohan *et al.*^[11] showed similar results with the use of doxycycline.

There was no statistically significant difference between Group II and Group III for reduction in PPD after 3 months from baseline and 2 weeks.

Loesche *et al.* conducted a double-blind investigation in patients with elevated proportions or species of spirochetes in two or more plaque samples. They were randomly assigned to receive either metronidazole 250 mg thrice a day for first week or placebo after the completion of all debridement procedures. When the patients were reexamined 4–6 weeks later, patients in the metronidazole group exhibited a highly significant apparent gain in attachment levels relative to the patients without metronidazole.^[12]

Studies in which randomized controlled trials were conducted reported that selective antimicrobial agents when used as adjunctive to periodontal surgical procedures improved the periodontal parameters, whereas meta-analysis studies reported that adjunctively used systemic antimicrobials did not show statistically significant results. However, in this study, there was no significant difference in the clinical parameters such as PI and GI between antibiotic prescribed and no antibiotic groups, but there was significant improvement in PPD and CAL among groups prescribed with metronidazole and doxycycline than that of nonantibiotic groups.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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