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Comparative evaluation of efficacy of adjunctive use of azithromycin and ciprofloxacin with scaling and root planning and scaling & root planning alone in the treatment of chronic periodontitis: a clinico microbiological study

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ABSTRACT

Background and aims: The present study was envisaged to compare the efficacy of Adjunctive use of Azithromycin and Ciprofloxacin with Scaling and Root Planning and Scaling & Root Planning alone in the treatment of Chronic Periodontitis. **Materials and methods:** Forty five subjects with chronic periodontitis were randomly selected and divided into three groups as follows. Group 1: scaling and root planning without any systemic antibiotics (SRP alone). Group 2: scaling and root planning with systematic administration of ciprofloxacin (SRP+CIPRO). Group 3: scaling and root planning alone with systemic administration of azithromycin (SRP+AZM). Periodontal parameters comprising of plaque index, bleeding index, probing pocket depth, clinical attachment level and microbiological parameters comprising of spirochete count and BANA test scores were assessed at base line and six weeks after completion of periodontal therapy for subjects in all the three groups. **Results:** The reduction in post-treatment scores as compared to pre-treatment scores of plaque index, bleeding index, pocket depth, clinical attachment levels and spirochete count was highly significant in all the groups ($p<0.01$). BANA hydrolysis is a reliable marker of periodontal disease as it has proved to be a suitable test for detection of spirochetes. **Conclusion:** The judicious use of systemic antibiotics in the treatment of chronic periodontitis may provide an additional benefit in the clinical outcome compared to SRP alone.

Keywords: Chronic periodontitis, BANA hydrolysis test, Ciprofloxacin and Azithromycin, scaling and root planing.

Introduction

Periodontal disease is among the infectious disease caused by micro-organisms that colonize the tooth surfaces at or below the gingival margins which lead to the destruction of the periodontal ligament and alveolar bone that surrounds the teeth thus causing loss of attachment to the tooth. Analysis of these periodontal pathogens is becoming an important aspect of diagnosis and treatment of periodontal diseases [1]. Periodontal diseases, now recognized as bacterial infections, elicited by a complex of bacterial species, that interact with the host tissue cells, and release an array of cytokines, chemokines and mediators leading to the destruction[1,2].

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Diagnostic tools are based upon enzymes diagnostic markers in order to identify specific periodontopathic bacteria, so as to enforce preventive and therapeutic measures toward disease control[1].The most comprehensive of these early studies implicated Porphyromonas gingivalis and spirochetes as the species and bacterial types that could be statistically associated with periodontal disease. Grossi investigated attachment and alveolar bone loss including the presence of subgingival P. gingivalis and T. forsythia. Socransky and Haffajee found the BANA positive species T. denticola, P. gingivalis, and T. forsythia have the highest prevalence. The Albandar used DNA probes to assess the relationship between the plaque flora and EOP and found that there was no relationship between A. actinomycetemcomitans and disease progression, but the BANA species, P. gingivalis and T. denticola were significantly associated with loss of attachment[3]. BANA-Enzymatic test™ kit is a rapid and reliable chair side diagnostic test, which can be

performed in about 15 min time, that can give information about the presence of three of the putative pathogens in subgingival plaque samples, that is, Porphyromonas gingivalis, Treponema denticola and Tannerella forsythia, shares unique ability of hydrolyzing the trypsin substrate. Loesche et al. studied a strong relationship between a BANA positive reaction and high levels of plaque spirochetes [1].Mechanical debridement is a highly demanding procedure with some limitations, such as the inability to access deep pockets, surface irregularities and furcation areas. Because of the infectious nature of periodontitis, the rationale for using adjunctive antimicrobial agents is to eradicate or reduce the numbers of pathogenic bacteria in deep pocket, root furcations and concavities or those residing at or within the periodontal tissues at the biofilm gingival interface. Adjunctive antimicrobial agents can be delivered either systemically or locally. Systemically delivery has the potential advantage of reaching pathogens widely distributed in the oral cavity as compared to local delivery. Herrera stated that in specific situations such as patients with deep pockets or with progressive 'active' disease or with specific profiles, use of adjunctive systemic antimicrobial could be clinically relevant[4].Hence, this study was aimed to compare the efficacy of adjunctive use of azithromycin with scaling and root planning (SRP), the adjunctive use of ciprofloxacin and SRP, and SRP alone in the treatment of chronic periodontitis with the help of BANA-Enzymatic test and by the microbiological examination.

Materials and Methods

Fourty five (45) patients with in age range of 25-55 years of both the sex will be selected from the Out Patient Department of Periodontology and Implantology, D J College of Dental Science And Research, Modinagar, after the approval of the ethical committee of the DJ College Of Dental Science And Research, Modinagar, Utter Pradesh. Each patient was given a detailed verbal and written description of the study. They were required to sign an informed consent for to commencement of the study. Patients had to fulfil the following inclusion criteria:- age group of 25-55 years having at least 24 natural teeth, free from relevant allergies and systemic diseases, who have not received any surgical/non-surgical periodontal therapy or any antibiotic therapy for past 6 months, and chronic generalized periodontitis with a probing depth >5mm will be present. Patients who are excluded with a known or suspected allergy to the ciprofloxacin and azithromycin, aggressive periodontitis, using tobacco in any form, having habit of alcoholism and Immunocompromised patients.

45 subjects were selected on basis of inclusion criteria were categorized into three treatment groups. After subject selection 15 patients were randomly assigned to one of the three groups based on the treatment method.

- Group 1 (SRP alone) n =15, scaling and root planning without any systemic antibiotics.
- Group 2 (SRP+CIPRO) n=15, scaling and root planning with systematic administration of ciprofloxacin 500mg, BID for 8 days.
- Group 3 (SRP+AZM) n=15, scaling and root planning alone with systemic administration of azithromycin 500mg, OD for 3 days.

Clinical Assessments: The following clinical parameters were recorded for subjects in all the three groups:- Plaque index, Bleeding Index, Probing pocket depth, Clinical attachment level.

Clinical procedure:- On the first visit, detailed case history including clinical parameters [plaque index, gingival bleeding index, probing pocket depth, clinical attachment level (with the help of UNC-15 probe to the nearest millimeter)], and subgingival plaque sample were taken. This was followed by a comprehensive phase I therapy which included patient education and motivation, plaque control, scaling and root planning. Complete phase 1 therapies were performed and in the test groups, sites were treated with SRP, followed by medication of ciprofloxacin and azithromycin, whereas in the control group, sites were treated with SRP alone. The patients were recalled after 6 weeks and these measurements (GBI, PD, PI, CAL) and sub gingival plaque sample were repeated.

Microbiological examination sample collection

Sub gingival plaque was collected from 4-6 most diseased tooth sites using a sterile curette. Thereafter, the curette tip was vigorously agitated in a test tube containing 0.5 ml of Sorensen buffer solution at pH of 7.2, and placed for 20 s in a vortex mixer to get a homogenous plaque suspension and stored at -200C till dark field microscopic examination. Sub gingival plaque sample was taken at baseline and after 6 weeks in all 3 groups for microbiological examination.

Dark field microscopic examination

A 10 µL of plaque suspension was placed on to a glass slide and examined less than 10 x magnification of dark field microscope for evaluation of spirochetes. When viewed under dark field microscope, spirochetes are elongated motile, flexible bacteria twisted spirally along the long axis and seen as a shiny spiral structure with dark background.

Enzyme assay (BANA hydrolysis test):- specimen collection and preparation

Remove a BANA test strip from the bottle. Record the patient's name and date in the spaces on the BANA test strip.

Remove subgingival plaque for sampling. Use a curette to obtain subgingival plaque from the apical third of any deep pocket.

Each sample was applied on the reagent matrix affixed to the lower portion of the strip in a location corresponding to the number of the tooth where the specimen was taken. Apply the specimen to the lower test pad on a BANA Test strip.Before taking another specimen, wiping the curette on a clean cotton gauze pad to prevent carry-over of plaque.

After all desired sites have been sampled and transferred, moisten the upper pad of the test strip with distilled water on a cotton swab. The pad should be just moist, not wet. Too much water can dilute the blue colour over a larger area, possibly making it too faint to see, and being interpreted as a false negative result.

The reagent strip was folded at the crease mark so that the upper and lower matrices meet.

The reagent strip was then placed into one of the two top slots of the BANA-Zyme processor and heated for 15 min at 55°C ± 5°C.

The processor cycle begins when the indicator light comes on. Incubation is complete when the bell sounds.

The lower portion of the test strips was separated from the upper strip and discarded.

Evaluate the BANA Test results by comparing the upper, salmon-colored reagent pad with the sample chart on the BANA Test bottle label. Subgingival plaque sample was taken at baseline and after 6 weeks for all 3 groups. Record the results for each plaque sample as either negative, weakly positive or positive. The result of the test in each subject was noted and recorded.

BANA test Scoring 5,6

•Negative - 0

•Weak Positive – 1

•Positive- 2

The result of the test in each subject was noted and recorded.

Statistical Analysis

The results of the study were subjected to statistical analysis by ANOVA and Pearsons correlation coefficient.

Results

Plaque index, bleeding index, probing pocket depth and clinical attachment levels were assessed at base line and 6 weeks after the completion of periodontal therapy for all the subjects. Table 7-12 describes the intergroup comparison of change in probing depth, CAL, plaque index, gingival bleeding index between the three groups at 6 week intervals from the baseline. At 6 weeks interval there was a reduction in the probing depth, CAL, plaque index, gingival bleeding index in all the three groups i.e Group I, II and III respectively and the intergroup difference between the three groups was statistically significant when analyzed using One Way ANOVA. When the post Hoc LSD analysis was done it was found that reduction in the probing depth, CAL, plaque index, gingival bleeding index scores at 6 weeks interval was statistically significant between Group I and Group II, Group I and Group III, however the difference between the Group II and Group III was statistically non-significant. The intra-group comparison between the two time intervals i.e baseline and 6 weeks was statistically significant for Group I, Group II and Group III. Table 1-6 shows Intragroup comparison of Group I (Scaling and Root-planning) between the different intervals shows that there is significant reduction in mean scores of Probing depth, CAL, plaque index, gingival bleeding index at baseline, 6 week. Intra group comparison of Group II (Scaling and Root-Planning + Ciprofloxacin) between the different intervals shows that there is significant reduction in mean scores of Probing depth, CAL, plaque index, gingival bleeding index at baseline, 6 week. Intra group comparison of Group III (Scaling and Root-Planning + Azithromycin) between the different intervals shows that there is significant reduction in mean scores of Probing depth, CAL, plaque index, gingival bleeding index at baseline, 6 week. Thus, it shows that Scaling and Root-Planning with Azithromycin and Ciprofloxacin is efficient in reducing Probing depth, CAL, plaque index, gingival bleeding index.

Table 1: Intra group comparison of change in probing depth scores between the different intervals- baseline, 6 weeks

	Groups	Baseline	6 Week	P value	Significance
Probing Depth	Group I	5.13±0.32	3.76±0.46	0.001	Significant
	Group II	5.23±0.32	3.42±0.32	0.001	Significant
	Group III	5.36±0.35	3.60±0.35	0.001	Significant

Table 2: Intra group comparison of cal index scores between the different intervals- baseline, 6 weeks

	Groups	Baseline	6 Week	P value	Significance
CAL	Group I	3.05±0.59	1.75±0.57	0.001	Significant
	Group II	3.22±0.27	1.37±0.27	0.001	Significant
	Group III	3.10±0.19	1.32±0.19	0.001	Significant

Table 3: Intra group comparison of plaque index scores between the different intervals- baseline, 6 weeks

	Groups	Baseline	6 Week	P value	Significance
Plaque Index	Group I	2.00±0.15	1.13±0.10	0.001	Significant
	Group II	2.00±0.14	0.91±0.18	0.001	Significant
	Group III	1.97±0.10	0.92±0.15	0.001	Significant

Table 4: Intra group comparison of gingival bleeding index scores between the different intervals- baseline, 6 weeks

	Groups	Baseline	6 Week	P value	Significance
Gingival Bleeding	Group I	87.53±5.84	22.53±5.52	0.001	Significant
	Group II	88.40±5.43	12.53±2.77	0.001	Significant
	Group III	87.33±6.81	04.87±2.29	0.001	Significant

Table 5: Intra group comparison of BANA index scores between the different intervals- baseline, 6 weeks

	Groups	Baseline	6 Week	P value	Significance
BANA Scores	Group I	1.48±0.24	0.48±0.15	0.001	Significant
	Group II	1.58±0.05	0.28±0.04	0.001	Significant
	Group III	1.59±0.05	0.29±0.04	0.001	Significant

Table 6: Intra group comparison of spirochete scores between the different intervals- baseline, 6 weeks

	Groups	Baseline	6 Week	P value	Significance
Spirochete Scores	Group I	35.53±2.92	11.53±2.41	0.001	Significant
	Group II	36.80±2.67	5.26±2.71	0.001	Significant
	Group III	36.26±2.84	6.00±2.64	0.001	Significant

Table 7: Inter group comparison of probing depth between the three groups Post hoc analysis of intergroup comparison

Dependent Variable	GROUP	(J) GP	Mean Difference (I-J)	Std. Error	Sig.	Significance
Probing Depth	GROUP I	Group II	-7.95	2.031	0.001	Significant
		Group III	-6.03*	2.031	0.005	Significant
	GROUP II	Group I	7.95*	2.03143	0.001	Significant
		Group III	1.91	2.03143	0.351	Non-significant
	GROUPIII	Group I	6.03*	2.03143	0.005	Significant
		Group II	-1.91	2.03143	0.351	Non-significant

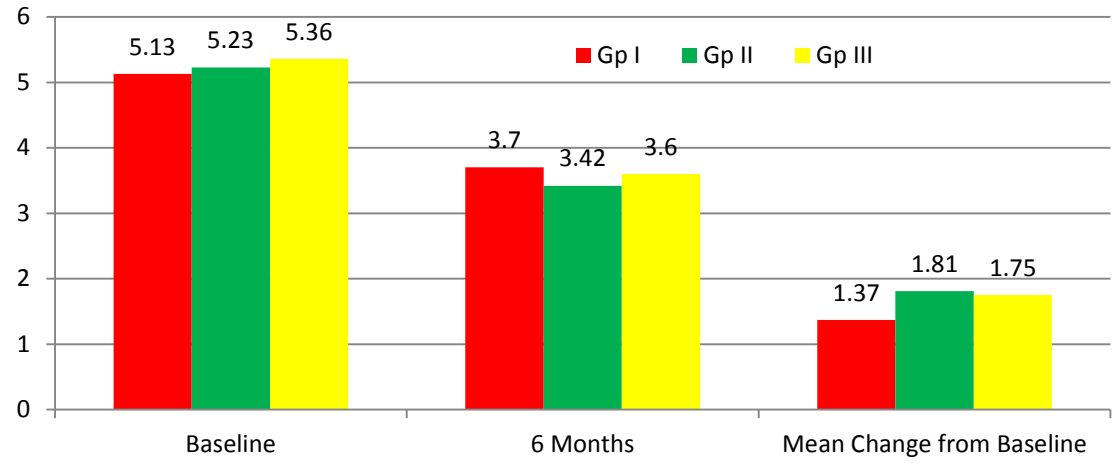

Fig. 1: Intergroup comparison of probing depth scores between three interval for group I , group II & group III

Table 8: Inter group comparison of cal between the three groups Post hoc analysis of intergroup comparison

Dependent Variable	(I) GP	(J) GP	Mean Difference (I-J)	Std. Error	Sig.	Significance
CAL	Group I	Group II	-13.47*	2.15458	0.001	Significant
		Group III	-13.49*	2.15458	0.001	Significant
	Group II	Group I	13.47*	2.15458	0.001	Significant
		Group III	-0.023	2.15458	0.992	Non-significant
	Group III	Group I	13.49*	2.15458	0.001	Significant
		Group II	0.023	2.15458	0.992	Non-significant
*. The mean difference is significant at the 0.05 level.						

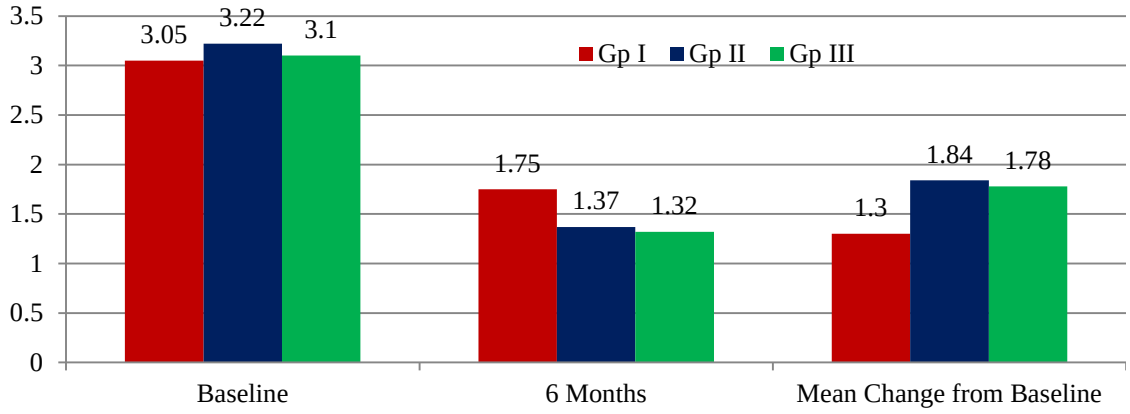

Fig. 2: Intergroup comparison of cal scores between three interval for group I, group II & group III

Table 9: Inter group comparison of plaque index between the three groups Post hoc analysis of intergroup comparison

Dependent Variable	(I) GP	(J) GP	Mean Difference (I-J)	Std. Error	Sig.	Significance
Plaque Index	Group I	Group II	-10.88*	2.95775	0.001	Significant
		Group III	-10.17*	2.95775	0.001	Significant
	Group II	Group I	10.88*	2.95775	0.001	Significant
		Group III	0.712	2.95775	0.811	Non-significant
	Group III	Group I	10.176*	2.95775	0.001	Significant
		Group II	-0.712	2.95775	0.811	Non-significant
*. The mean difference is significant at the 0.05 level.						

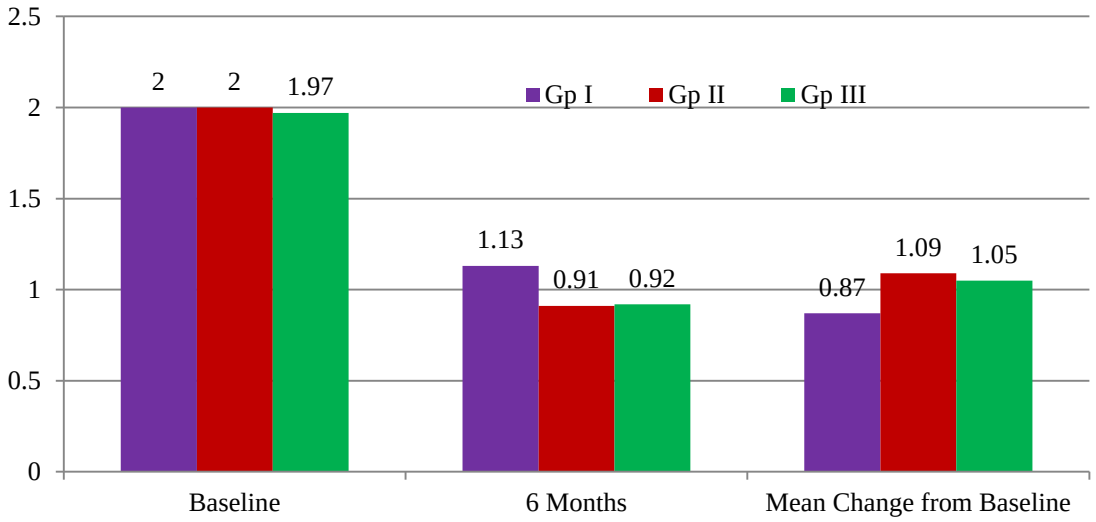

Fig. 3: Intergroup comparison of plaque index between scores three interval for group I, group II & group III

Table 10: Inter group comparison of gingival bleeding between the three groups Post Hoc Analysis of Intergroup Comparison

Dependent Variable	(I) GP	(J) GP	Mean Difference (I-J)	Std. Error	Sig.	Significance
Gingival Bleeding	Group I	Group II	-11.00*	.01576	0.000	Significant
		Group III	-20.00*	.01576	0.001	Significant
	Group II	Group I	11.50*	.01576	0.001	Significant
		Group III	-8.60*	.01576	0.001	Significant
	Group III	Group I	20.20*	.01576	0.001	Significant
		Group II	08.60*	.01576	0.001	Significant
*. The mean difference is significant at the 0.05 level.						

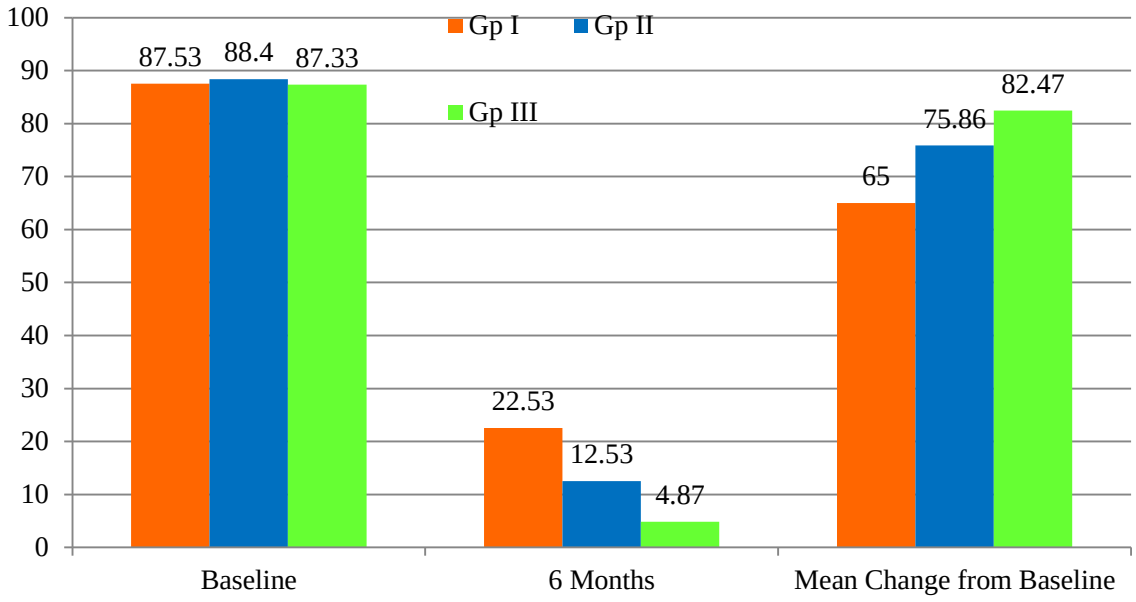

Fig. 4: Intergroup comparison of gingival bleeding index scores between three interval for group I , group II & group III

Table 11: Inter group comparison of BANA scores between the three groups

Dependent Variable	(I) GP	(J) GP	Mean Difference (I-J)	Std. Error	Sig.	Significance
Bana Scores	Group I	Group II	-13.72*	1.58811	0.001	Significant
		Group III	-13.370*	1.58811	0.001	Significant
	Group II	Group I	13.725*	1.58811	0.001	Significant
		Group III	0.355	1.58811	0.824	Non-significant
	Group III	Group I	13.37*	1.58811	0.001	Significant
		Group II	-0.355	1.58811	0.824	Non-significant
*. The mean difference is significant at the 0.05 level.						

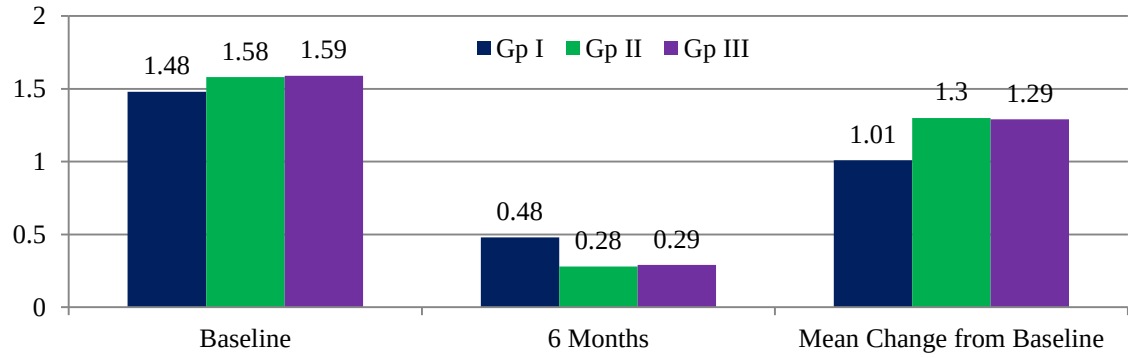

Fig. 5: Intergroup comparison of BANA scores between three interval for group I, group II & group III

Table 12: Inter group comparison of spirochete count between the three groups Post Hoc Analysis of Intergroup Comparison

Dependent Variable	(I) GP	(J) GP	Mean Difference (I-J)	Std. Error	Sig.	Significance
Spirochete Count	Group I	Group II	-18.295*	2.05623	0.001	Significant
		Group III	-16.082*	2.05623	0.001	Significant
	Group II	Group I	18.295*	2.05623	0.001	Significant
		Group III	2.213	2.05623	0.288	Non-significant
	Group III	Group I	16.08*	2.05623	0.001	Significant
		Group II	-2.21	2.05623	0.288	Non-significant

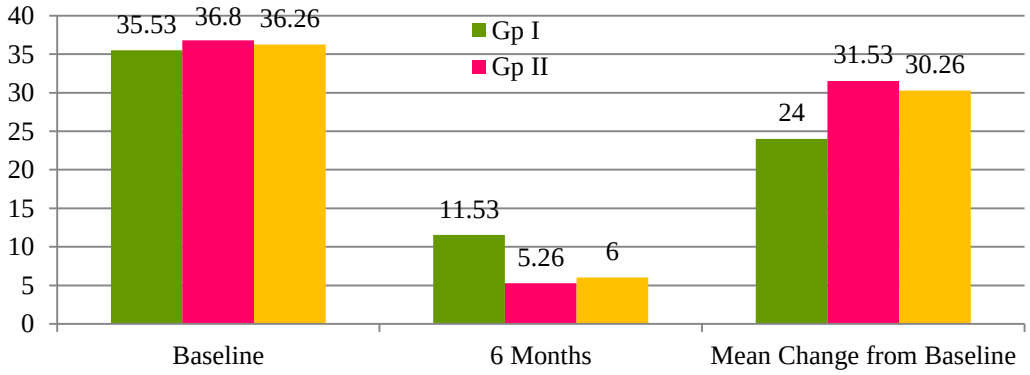

Fig. 6: Intergroup comparison of spirochete count between three interval for group i, group ii & group iii

Discussion

Periodontal diseases are bacterial infections characterized by inflammation and destruction of attachment apparatus, often leading to tooth loss. Traditional therapy for these Periodontal diseases has involved elimination or suppression of subgingival microbial complexes by mechanical debridement such as scaling and root planning or surgical procedures [7]. Scaling and root planning can eliminate most periodontitis associated bacteria, but the pathogens are present in the subgingival area which cannot be eliminated [8].Therefore adjunctive antimicrobial chemotherapy can improve the effectiveness of treatment in individuals with chronic periodontitis. Red complex microorganism and Actinobacillus actinomycetemcomitans are present in subgingival area and are difficult to eliminate by mechanical therapy alone. Both pathogens possess virulence factors that frustrate the host response and conventional therapeutic efforts by invading into the soft tissue wall of the pocket.9 Aa can invade epithelial cells and enter the underlying connective tissue, whereas Pg can invade epithelial cells and linger inside them.8 Their tendency to invade soft tissue makes them difficult to eliminate by scaling and root planning alone.10 Efforts to detect these periodontal pathogens in dental plaque have included microscopic measures, and BANA hydrolysis test. P. gingivalis, T. forsythia, and T. denticola possess a trypsin-like enzyme that can hydrolyze the synthetic trypsin substrate benzoyl DL-arginine-naphthylamide (BANA)[11].The presence of these organisms in subgingival plaque can be determined by the ability of the plaque to hydrolyze BANA using a 5-minute chair side assay[12].In microbiological examination, Dark field microscopy can detect number of microorganisms[1].Treponema palladium appear as a brightly illuminated objects against a dark background. They are identified by their typical morphology, size and movement. The organism moves slowly along their longitudinal axis accompanied by bending and twisting in the middle [13]. Matarazzo observed significant advantages in clinical and microbiological parameters by using antibiotics.14 Identification of periodontal pathogens by microbial testing in a clinical setting is generally limited to the main putative pathogens [15].

Keestra stated that, statistically no specific type of antibiotic was superior over another[16].Azithromycin and Ciprofloxacin has been evaluated extensively as an adjunct in the treatment of periodontal disease and useful in the treatment of periodontal disease and is more effective against certain Gram-negative bacteria, especially Actinobacillus actinomycetemcomins (Muller et al) P.gingivalis[17,18]. Improvement tends to be greater when antibiotics are administered (Haffajee, Mascarenhas, Oteo, Smith). They found improvements in clinical parameters (PD reduction and CAL gain), and reduction of benzoyl-DL-arginine naphthylamine (BANA) levels[17, 19].Studies have shown that the adjunctive use of systemic antibiotics provide a better clinical outcome, particularly in terms of pocket depth reduction and attachment level gain than SRP alone. Effects of three groups were assessed at baseline and 6 week after non-surgical periodontal therapy by means of a commercial BANA hydrolysis kit and by Microbiological examination. The mean change of three group changes from baseline to 6 week. When three groups were compared, there was statistical significant difference observed. Systemic antibiotic used in conjunction with scaling and root planning can offer an additional benefit over SRP alone in the treatment of periodontitis in term of clinical attachment level, pocket depth change, plaque index and reduced risk of additional CAL loss. The reduction in spirochete count and BANA scores was found to correlate positively with the reduction in BOP, pocket depths and CAL gain.Overall, the results of the present study indicate that the judicial use of systemic antibiotics in the treatment of chronic periodontitis patients may provide an additional benefit in the clinical outcomes compared to SRP alone due to greater reduction in spirochete count.

Conclusion

The Results were obtained on the basis of all clinical parameters. Microbiological examination comprising of spirochete count and BANA test scoring. The clinical and microbiological parameters were assessed in all the groups at baseline and after 6 week. A base line comparison of all the parameters between the three groups did not show any significant difference. Following periodontal therapy, the periodontal health in all the subjects improved remarkably as evidenced by good plaque control, maintenance of gingival health, significant reduction in GBI, probing pocket depth and gain in clinical attachment level. This was also accompanied by significant reductions in spirochete count and BANA scores in all the three groups. However, subjects in Group II (SRP+ AZM) and in Group III (SRP+CIP) showed a greater reduction in spirochete count, BANA score, pocket depth, gain in clinical attachment level gingival bleeding index, plaque index when compared to subjects in Group I (SRP alone) which was statistically significant. This study has shown that there is significantly greater reduction in spirochete count when antibiotics are used as adjuvants to scaling and root planning. Therefore, we conclude that while mechanical debridement is an essential component of periodontal therapy, judicious use of antibiotics provides an added advantage. BANA hydrolysis is an effective and reliable tool for detecting chronic periodontitis. Use of azithromycin and ciprofloxacin as adjuvant to conventional treatment for chronic periodontitis generally improves clinical and microbiological findings compared to conventional treatment alone.

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