Short-Term Clinical and Microbiological Effects of Systemic Ornidazole vs. Metronidazole in the Treatment of Generalized Chronic Periodontitis Patients

K Jaswal, J Dixit, A Jain

Citation

K Jaswal, J Dixit, A Jain. *Short-Term Clinical and Microbiological Effects of Systemic Ornidazole vs. Metronidazole in the Treatment of Generalized Chronic Periodontitis Patients*. The Internet Journal of Dental Science. 2008 Volume 8 Number 1.

Abstract

Background: The purpose of this study was to evaluate and compare the clinical and microbiological effects of systemic ornidazole (ORN) and metronidazole (MET) in sites with/without scaling and root planning (SRP) in generalized chronic periodontitis patients.Methods: Ramfjord 6 teeth with total of 192 sites in 40 systemically healthy patients suffering from generalized chronic periodontitis with pocket depth ≥ 5mm and no SRP in previous 3 months were included. Patients were randomly placed into three groups (Gp I= SRP + ORN and MET given orally, Gp II= only ORN and MET given orally, Gp III= SRP+ placebo given orally). A total of 120 gingival crevicular fluid samples were collected randomly. The gingival scores (GS), probing depth (PD) scores, bleeding on probing (BOP), counts of spirochetes (SPI), gram positive cocci (GPC), gram positive bacilli (GPB), gram negative cocci (GNC) and gram negative bacilli (GNB) were evaluated at pretreatment (day 0), and post treatments (day 14 and 28 day).Results: Results revealed that SRP alone did bring some reduction in GS, PD and BOP scores but extent of reduction in all three clinical parameters was significantly less as compared to ORN/MET + SRP groups. The ORN and MET both showed similar and comparatively higher improvement in clinical parameters as compared to ORN and MET alone and placebo. Microbiological findings also indicated that ORN and MET also led to similar and comparatively higher gradual decrease in counts of SPI, GNC and minimal decrease in GNB from baseline onwards to the end of study, which was replaced by increase in population of GPC and GPB. The improvement of ORN and MET was found to be similar, clinically and microbiologically.Conclusions: TheORN andMET combined with SRP showed beneficial shifts in bacterial population associated with substantial clinical improvements. Study found both ORN and MET equally effective adjunct in treatment of generalized chronic periodontitis.

INTRODUCTION

Periodontal diseases are caused by a number of micro-organisms consisting mainly of gram negative anaerobic bacteria which are often referred to as indicator microorganisms or key pathogens and have been implicated in initiation and progression of periodontal disease. Suppression or elimination of these key pathogens has been suggested as the main treatment goal [1]. Treatment of periodontal diseases has been based largely on conventional management, oral hygiene procedures with scaling and root planing and periodontal surgery.

Conventional therapy has been found to be effective for majority of patients. However, in some individuals periodontal breakdown continues despite careful attention to conventional therapy. This is due to persistent infection by invasive subgingival bacteria. In such cases systemic antimicrobial agents can serve as useful adjuncts for eradicating invasive periodontal pathogens. Recent evidence however, suggests bacterial specificity that especially incriminates anaerobic bacteria and thus suggests a role for anaerobically directed antimicrobial therapy. The drugs so far used to treat periodontal diseases include tetracycline [2], clindamycin [3], erythromycin [4], metronidazole [5], tinidazole [6], ornidazole [7] and others. The group nitroimidazole (metronidazole, ornidazole etc.) is specifically anti-anaerobically directed and is therefore indicated as anaerobes are implicated in the pathogenesis of periodontitis.

To our knowledge, no study has compared the efficacy of systemic ORN and MET, thus a short-term study was conducted to compare the effectiveness of these in generalized chronic periodontitis patients. We hypothesized that ORN and MET in combination with SRP may be

equally and more effective than ORN and MET alone and placebo, clinically and microbiologically.

MATERIALS AND METHODS

A short term clinical trial was conducted on 40 patients in age group of 18-42 years, with evidence of generalized chronic periodontitis attending the post-graduate clinic of the department of Periodontics, CSM Medical University, Lucknow in collaboration with Department of Microbiology, CSM Medical University.

Inclusion Criteria - Systemically healthy patients with generalized chronic periodontitis having probing depth > 5 mm with moderate to severe gingivitis and without scaling and root planning within the previous 3 months.

Exclusion Criteria - Patients with smoking or tobacco chewing habits, alcoholics and drug abusers, use of antibiotics and antioxidants prior 3 months, pregnant or lactating mothers, mobile and carious teeth.

Patients completed medical history form and were given information about the aim of trial as well as written consent was taken before the start of trial. The patients were randomly placed into three groups on the basis of treatment executed. Group I and II were further sub-divided into two subgroups as Group Ia– Drug A (MET + SRP), Group Ib– Drug B (ORN + SRP), Group IIa– Drug A (MET only), Group IIb– Drug B (ORN only). The Group III were treated with- Drug C or placebo (Glucose + SRP). There were eight subjects in each group.

CLINICAL PARAMETERS

Clinical examination was done in each patient at base line i.e. day 0 and 14, 28 days post treatment. According to the Ramfjord [8] 6 teeth (16, 21, 24, 36, 41 & 44) per patient were considered for clinical examination i.e. total 48 teeth/192 sites. The clinical parameter, GS was estimated by Gingival Index [9] , while BOP by Papillary Bleeding Index [10] . The PD was measured by using a standard periodontal probe (UNC-15) with rounded end and diameter of 0.4mm. All clinical evaluations were performed by the same periodontist.

DRUG PREPARATION

A total of 560 empty capsules of same size and colour were purchased (224 each for MET and ORN and 112 for placebo). A 400 mg of MET tablets and 500mg of ORN tablets were grounded into fine powder form and then filled into the each capsule. A total of 112 capsules were filled with glucose which served as placebo. These capsules were placed in three containers which were labeled A for MET, B for ORN and C for placebo by a third person making the study a double blind trial.

TREATMENT PROCEDURE

After completion of the baseline recordings of the clinical parameters, patients were subjected to respective treatments. Patients were instructed to take the drug A orally thrice daily at 8 hrs interval and drug B twice daily at 12 hrs interval for 7 days.

COLLECTION OF SAMPLE FOR MICROBIOLOGICAL ANALYSIS

Three samples of gingival crevicular fluid (GCF) were collected from the facial surface of selected teeth before the start of treatment, 14 and 28 days post treatment from each patient i.e. total of 120 GCF samples. A standard size (No. 15) paper point * was inserted in the periodontal pocket for 2 minutes then withdrawn and placed in sterile Eppendroff vial containing 1 ml of sterile normal saline. Samples were pooled and immediately taken to the department of microbiology for microbiological analysis.

MICROBIOLOGICAL ANALYSIS

Each sample was centrifuged at 3000 rpm and centrifuged deposit was suspended in 100µl saline. A 10 µl of this suspension was used for smear preparation. Minimum 5 fields in oil immersion were examined for bacterial count and their numbers were represented as percentage count. Gram's staining was used to identify and classify bacteria in two major groups- gram positive and gram negative. Staining of SPI was done by Fontana's method [11] . Smears were examined for presence of SPI, GPC, GPB, GNC and GNB.

*Meta, Biomed Co.Ltd.Korea.

STATISTICAL ANALYSIS

Scores of clinical parameters and microbiological findings were compared by two factor (treatments x days) analysis of variance (ANOVA) and their pair wise significance of mean difference were done by Newman Keuls post hoc test. Before performing ANOVA, homogeneity of variance testing were done by Cochran, Hartley and Bartlett test and groups (treatments x days) variance of all parameters were found to be homogeneous. Treatments effect on parameters were assessed by coefficients of simple linear regression

analysis, considering time (days) as independent variable and response (scores) the dependent variable. A probability value $p<0.05$ was considered to be significant. All statistical analysis was performed on STATISTICA ver. 7.1 (Stat Soft, Inc., USA).

RESULTS

The scores of clinical parameters and microbiological findings are used to evaluate the effectiveness of five modes of therapy, which were summarized in Table 1. In all treatments, mean scores of clinical parameters are comparatively high than the microbiological parameters and with time (days), GS, PD, BOP, SPI, GNC and GNB show decreasing trend while GPC and GPB the increasing trend and from baseline (day 0) the decrease/increase in scores were high at day 14 than day 28. On comparing mean between treatments, scores of all the parameters at day 0 did not differ significantly ($p>0.05$) i.e. found to be the same except GPC which showed significantly ($p<0.01$) high scores in treatment IIb and III than treatment Ia, Ib and IIa while at day 14 and day 28 scores of all the parameters in treatments Ia and Ib were found to be the same i.e. did not differ significantly ($p>0.05$) and were significantly ($p<0.01$) different from IIa, IIb and III. Similarly, comparing mean between days, scores of all the parameters in all the treatments differ significantly ($p<0.01$) at day 14 and day 28 from day 0 as well between day 14 and day 28 except GNB.

The regression coefficient (β) (Table 2) which indicates a rate of change (scores/day) showed that with time (days), treatments enhanced the scores of GPC and GPB significantly ($p<0.01$) while decreased the scores of GS, PD, BOP, SPI, GNC and GNB significantly ($p<0.01$) except GNB in which treatment IIb and III did not respond significantly ($p>0.05$).

Results also showed that the responses of treatments were higher in clinical than microbiological (Fig. 1). Among treatments, the effect of Ib was the maximum followed by Ia, IIb, IIa and III. Similarly, treatments decreased (improvement) the clinical parameter, GS the most and PD the least. In contrast, microbiological findings showed maximum decrease in SPI followed by GNC and GNB while GPC showed higher increase than GPB (Fig. 1). Treatment Ib which showed the maximum improvement, the improvement of it on GS, PD, BOP, SPI, GPC, GPB, GNC and GNB were found to be 1.3, 1.5, 1.6, 1.7, 2.0, 2.5, 2.3 and 1.9 times more respectively than the respective treatment III i.e. placebo (Table 3). The results found both ORN and MET in combination with SRP equally and more effective than other treatments.

Figure 1

Table 1. Summary (Mean ± SD) of clinical parameters and microbiological findings of generalized chronic periodontitis patients (n=8) treated with 5 different treatments.

Para-meters	Days	Treatments				
		Ia	Ib	IIa	IIb	III
Clinical						
GS	0	5.81 ± 3.52	5.88 ± 2.64	5.91 ± 2.95	5.93 ± 4.07	5.76 ± 3.74
	14	2.75 ± 3.63	2.60 ± 3.25	3.33 ± 2.33^{ab}	3.16 ± 2.39^{ab}	3.75 ± 2.88^{abcd}
	28	1.18 ± 0.83	1.10 ± 0.53	1.88 ± 2.30^{ab}	1.75 ± 2.83^{ab}	2.00 ± 1.41^{ab}
PD	0	9.35 ± 0.58	9.39 ± 0.45	9.68 ± 0.38	9.80 ± 0.41	9.41 ± 0.55
	14	7.23 ± 0.39	7.34 ± 0.43	7.76 ± 0.74	7.54 ± 0.41	8.03 ± 0.49^{ab}
	28	6.53 ± 0.41	6.34 ± 0.51	7.01 ± 0.56^{b}	6.98 ± 0.56^{b}	7.38 ± 0.49^{ab}
BOP	0	5.90 ± 1.77	6.07 ± 2.49	6.02 ± 2.43	6.07 ± 1.91	5.86 ± 1.51
	14	1.88 ± 1.25	1.81 ± 0.99	4.01 ± 2.59^{ab}	3.75 ± 1.41^{abc}	4.23 ± 3.20^{abd}
	28	1.22 ± 0.71	1.22 ± 1.28	2.40 ± 4.21^{ab}	2.21 ± 4.76^{ab}	2.91 ± 4.79^{abcd}
Microbiological						
SPI	0	18.75 ± 2.38	18.75 ± 2.60	18.75 ± 2.60	16.75 ± 2.31	16.75 ± 2.12
	14	6.88 ± 2.53	6.75 ± 2.60	10.88 ± 2.53^{ab}	9.88 ± 2.36^{ab}	11.00 ± 1.77^{ab}
	28	1.25 ± 1.75	0.88 ± 1.25	6.50 ± 2.20^{ab}	6.50 ± 1.77^{ab}	6.38 ± 1.69^{ab}
GPC	0	17.00 ± 2.56	16.75 ± 2.43	16.63 ± 2.56	23.25 ± 2.60^{abc}	23.25 ± 2.60^{abc}
	14	37.00 ± 1.93	37.00 ± 1.93	31.12 ± 2.17^{ab}	39.38 ± 1.92^{c}	32.88 ± 1.96^{abd}
	28	45.50 ± 3.55	46.25 ± 2.12	37.50 ± 2.27^{ab}	44.50 ± 2.78^{c}	38.12 ± 2.47^{abd}
GPB	0	11.25 ± 2.12	11.25 ± 2.12	11.25 ± 2.12	12.75 ± 1.91	12.75 ± 1.91
	14	26.00 ± 2.00	26.00 ± 2.00	21.37 ± 1.51^{ab}	21.75 ± 1.98^{ab}	20.50 ± 1.31^{ab}
	28	36.25 ± 3.41	37.37 ± 2.50	25.75 ± 2.71^{ab}	25.63 ± 2.88^{ab}	23.13 ± 1.73^{abcd}
GNC	0	34.88 ± 5.03	34.88 ± 5.03	34.75 ± 5.47	31.38 ± 5.29	31.13 ± 5.69
	14	12.25 ± 3.15	12.13 ± 3.14	20.13 ± 5.46^{ab}	14.75 ± 3.88^{c}	21.75 ± 4.33^{abd}
	28	2.88 ± 2.23	2.00 ± 1.51	9.63 ± 4.31^{ab}	6.50 ± 2.62	17.00 ± 4.47^{abcd}
GNB	0	18.63 ± 3.20	18.38 ± 3.66	18.63 ± 2.77	15.88 ± 3.14	16.13 ± 3.64
	14	17.50 ± 2.83	17.88 ± 3.04	15.25 ± 3.01	13.50 ± 3.66	13.63 ± 3.46
	28	13.50 ± 2.39	13.63 ± 3.54	15.13 ± 1.81	13.25 ± 2.25	13.50 ± 1.93

Letters a, b, c and d in superscript represents the treatment group Ia, Ib, IIa and IIb respectively and shows the significance of mean difference between the groups. The treatments representing these letters are significantly different from the respective treatments at level $p<0.05$ (light font) or $p<0.01$ (bold font).

Figure 2

Table 2. Regression coefficient (β) summary (n=24) w.r.t. time for all parameters and treatments

Parameters	Treatments				
	Ia	Ib	IIa	IIb	III
GS	-1.65**	-1.71**	-1.44**	-1.50**	-1.34**
PD	-1.01**	-1.09**	-0.95**	-1.01**	-0.73**
BOP	-1.67**	-1.73**	-1.29**	-1.38**	-1.05**
SPI	-0.63**	-0.64**	-0.44**	-0.37**	-0.37**
GPC	1.02**	1.05**	0.75**	0.76**	0.53**
GPB	0.89**	0.93**	0.52**	0.46**	0.37**
GNC	-1.14**	-1.17**	-0.90**	-0.89**	-0.50**
GNB	-0.18**	-0.17**	-0.13**	-0.09ns	-0.09ns

ns- not significant ($p>0.05$)
** - significant ($p<0.01$)

Figure 3

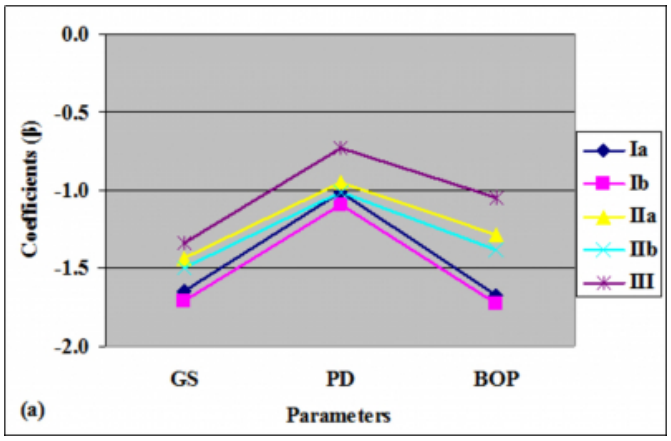
Table 3. Regression coefficient (β) ratio w.r.t. placebo (treatment III) for all parameters and treatments.

Parameters	Treatments			
	Ia	Ib	IIa	IIb
GS	1.2**	1.3**	1.1**	1.1**
PD	1.4**	1.5**	1.3**	1.4**
BOP	1.6**	1.6**	1.2**	1.3**
SPI	1.7**	1.7**	1.2**	1.0**
GPC	1.9**	2.0**	1.4**	1.4**
GPB	2.4**	2.5**	1.4**	1.2**
GNC	2.3**	2.3**	1.8**	1.8**
GNB	2.0**	1.9**	1.4**	1.0 ns

ns- not significant (p>0.05)
** - significant (p<0.01)

Figure 4

Fig 1. Treatment outcomes of clinical parameters (a) and microbiological findings (b) in patient with generalized chronic periodontitis.



DISCUSSION

Successful periodontal treatment is dependent on alterations in the microbial composition of the subgingival microbiota. Therefore the objective of periodontal treatment is to eliminate or reduce the proportion of pathogens to a level manageable by the host. Systemic antimicrobial therapy is based on the premise that antimicrobial agent in the periodontal pocket environment should reach the necessary concentrations to selectively eliminate the pathogens [12] . Lundstrom et al. (1984) [13] , Gordon et al. (1985) [14] and Slots et al. (1979) [15] documented supplementation of mechanical treatment by chemotherapy and investigated for management of periodontitis patients who obviously failed to respond to conventional mechanical therapy. A multiple of reasons responsible for sudden reinfection of specific sites have lead to the use of antibiotics as an adjunctive treatment strategy.

The present data of the clinical findings revealed that SRP alone brought some reduction in gingival score, probing depth, and bleeding on probing but the extent of reduction in all the three clinical parameters were significantly less as compared to MET/ORN+ SRP group. Though insignificant, the ORN alone fared better than MET alone for all the three clinical parameters. Our findings relating to clinical improvement of the drug administration are in accordance with studies indicating a significant improvement of clinical measurements in patients with advanced disease who received SRP and concomitant metronidazole or ornidazole therapy. Saxer and Guggenheim (1983) [16] provided data to support the hypothesis that ORN might be a valuable adjunctive chemotherapeutic agent in the treatment of periodontitis (post- juvenile & rapidly progressive). Loesche et al. (1992) [17] reported that combined metronidazole therapy of pockets 7 mm or greater resulted in a greater mean pocket reduction when compared to root planing. Similarly, Joyston et al. (1986) [18] noted combined therapy was more effective than root planing when patients had severe disease. Mombelli et al. (1986) [19] found a significant decrease in probing depth and bleeding tendency after treating recurrent periodontitis by SRP and ornidazole.

The clinical improvements achieved in the present study were associated with the alterations in the microflora because of subgingival debridement in scaled sites and antimicrobial administration. Claffey and Egelberg (1995) [20] reported that SRP alone without antimicrobials resulted in maximum clinical effect within a period of 6 months. Mechanical treatment has proved to be effective and the use of SRP is designed to remove hard and soft deposits below the gingival margin, however, limitations including the inability to adequately instrument deep periodontal pockets as well as removal of micro organisms within the tissues lining the periodontal pocket do exist. Removal of deposits and microorganisms may require surgical intervention and/or the use of antibiotic agents.

The results of the present short term investigation showing a trend towards reduction of the probing depth and bleeding on probing during the monitoring period in both scaled and non scaled sites can thus be considered as a sign of favourable tissue response to the adjunctive effect of antimicrobials. The diminution of probing pocket depth reflects an increase in tissue firmness leading to an increased resistance to penetration by the probe, the formation of an epithelial attachment to the tooth surface and occasionally

also the formation of new connective tissue attachment [212223].

Our results of microbiological findings clearly indicate that both ornidazole and metronidazole drugs have a beneficial role in bringing about the stable condition in gingiva as number of spirochetes, gram negative cocci gradually decrease from baseline onwards to the end of the study period and this is replaced by increase in the population of gram positive cocci and bacilli. Unlike the significant decrease in counts of SPI and GNC in all treatments at day 14 and day 28 from day 0 as well as between day 14 and day 28, GNB showed minimal decrease in count. Our results differ from studies of Heijl et al. (1979) [24] and Mombelli et al. (1989) [19] who showed the reduction of motile rods after ornidazole therapy. Mombelli et al. (1989) [19] reported significant decrease of gram negative anaerobic rods from day 10 onwards to 11 months at sites with PD ≥ 6mm but insignificant at sites with PD ≤ 4mm from 5 months onwards to the end of study. Kamma et al (2000) [25] also showed that one week following SRP significantly reduced the gram negative anaerobic rods while significantly increased the gram positive cocci after ornidazole administration. The favourable results after conventional therapy combined with metronidazole/ornidazole, reported here will be explained as a result of the eradication of tissue resident anaerobic periodontopathogens.

CONCLUSION

Our study pointed the usefulness of systemic ornidazole and metronidazole as an adjunct to mechanical debridement. The present short-term clinical trial found both ornidazole and metronidazole effective, clinically and microbiologically. Though, ornidazole was slightly better than metronidazole and due to its higher plasma half life (14.4 hrs) as compared to metronidazole (7.3 hrs) favours patient compliance because of less frequent intake [26], even though, its superiority over metronidazole was not to be proved, clinically and microbiologically. Study concluded that both the drugs are equally effective but recommend clinicians to prefer ornidazole over metronidazole as adjunct in the treatment of generalized chronic periodontitis because of its better patient compliance, but before that more clinical trial should be warranted to verify the efficacy of ornidazole.

ACKNOWLEDGEMENT

The authors are very grateful to Dr.Bharat Bhushan for his invaluable advice and help for discussion. Authors are also very grateful to Mr. M.P.S. Negi(Statistician CDRI Lucknow) for putting up his hard work in preparation of this manuscript.

References

1. Winkelhoff AJV, Graf JD. Microbiology in the management of destructive periodontal diseases. J. Clin Periodontol. 1991; 18(6): 406-410.
2. Lindhe J, Liljenberg B, Adielson B. Long-term tetracycline therapy on human periodontal disease. J Clin Periodontol 1983:10:590-601.
3. Gordon J, Walker C, Holviaras C, Socransky S. Efficacy of clindamycin hydrochloride in refractory perioodntitis: 24-months results. J Periodontol 1990:61:686-691.
4. Mills WH, Thompson GW, Beagrie GS. Clinical evaluation of Spiromycin and Erythromycin in control of periodontal disease. J. Clin Periodontol. 1979; 6(5):308-316.
5. Jekins WM, Mac Farlane TW, Gilmour WH, Ramsay I, Mac-Kenzie D. Systemic metronidazole in treatment of periodontitis. J. Clin Periodontol 1989:16:443-450.
6. Liew V, Mack G, Tseng P, Cvejic M, Hayden M, Buchanan N. Single-dose concentrations of tinidazole in gingival crevicular-fluid, serum and gingival tissue in adults with periodontitis. J Dent Res. 1991:70:910-912.
7. Kamma JJ, Nakou M, Mitsis FJ. The clinical and microbiological effects of systemic ornidazole in sites with and without subgingival debridement in early-onset periodontitis. J Periodontol 2000:71:1862-1873.
8. Ramfjord SP. Indices for prevalence and incidence of periodontal disease. J Periodontol 1959;30:51-59.
9. Loe H. The Gingival Index, the Plaque Index and the Retention Index. J Periodontol 1967;38:610-616.
10. Muhlemann HR. Psychological and chemical mediators of gingival health. J Prev Dent. 1977;4:6-16.
11. Roshan PD, Freeman MLH. A modified Fontana technique for staining spirochetes in smears. Am J Syph Gonorrhea Vener Dis. 1952;36(3):244-249.
12. Winkelhoff AJV, Rams TE, Slots J. Systemic antibiotic therapy in periodontics. J Periodontol. 2000; 10 (1): 45-78.
13. Lundstrom A, Johansson LA, Hump SE. Effect of combined systemic antimicrobial therapy and mechanical plaque control in patients with recurrent periodontal disease. J. Clin Periodontol. 1984; 11(5): 321-330.
14. Gordon J, Walker C, Lamster I, West T, Socransky S, Seiger M, Fasciano R. Efficacy of clindamycin in refractory periodontitis. J. Periodontol. 1985; 56(11): 75-80.
15. Slots J, Mashimo P, Levine MJ, Genco RJ. Periodontal therapy in humans: Microbiological and clinical effects of a single course of periodontal scaling and root planning and of adjunctive tetracycline therapy. J. Periodontol. 1979; 50(10): 495-509.
16. Saxer UP, Guggenheim B. Ornidazole (TiberalTM) in periodontal therapy. Acta Parodoniologica in: Schweizerische Monatsschrift fur Zahnheilkunde.1983; 93(10): 991-1001.
17. Loesche WJ, Giordano JR, Hujoel P, Schwartz J, Smith BA. Metronidazole in periodontitis: reduced need for surgery. J. Clin Periodontol. 1992; 19(2): 103-112.
18. Joyston BS, Smales FC, Duckworth R. A follow-up study 3 years after metronidazole therapy for chronic periodontal disease. J. Clin Periodontol. 1986; 13(10): 944-949.
19. Mombelli A, Gusberti FA, Lang NP. Treatment of recurrent periodontal disease by root planning and Ornidazole (Tiberal): Clinical and microbiological findings. J. Clin Periodontol. 1989; 16(1): 38-45.
20. Claffey N, Egelberg J. Clinical indicators of probing

attachment loss following initial periodontal treatment in advanced periodontitis patients. J. Clin Periodontol. 1995; 22(9): 690-696.
21. Mombelli A, Graf H. Depth-force-patterns in periodontal probing. J. Clin Periodontol. 1986; 13(2): 126-130.
22. Caton J, Nyman S, Zanier H. Histometric evaluation of periodontal surgery II. Connective tissue attachment levels after four regenerative procedures. J. Clin Periodontol. 1980; 7(3): 224-231.
23. Fowler C, Garrett S, Crigger M, Egelberg J. Histologic probe position in treated and untreated human periodontal tissues. J. Clin Periodontol. 1982; 9(5): 373-385.
24. Heijl L, Lindhe J. The effect of metronidazole on the development of plaque and gingivitis in the beagle dog. J. Clin Periodontol. 1979; 6(4): 197-209.
25. Joanna JK, Mela N, Fotis JM. The clinical and microbiological effects of systemic ornidazole in sites with and without subgingival debridement in early-onset-periodontitis patients J. Periodontol. 2000; 71(12): 1862-1873.
26. Golsterin EJC, Sutter VL, Finegold SM. Comparative susceptibilities of anaerobic bacteria to metronidazole, ornidazole and SC-28538. Antimicrob Agents Chemotherapy.1978; 14(4):609-613.

Author Information

Karam Jeet Jaswal
Postgraduate (MDS), Deptt. of Periodontics, Faculty of Dental sciences CSM Medical University Lucknow (U.P)

Jaya Dixit, BDS, MDS
Prof & Head, Deptt. of Periodontics, Faculty of Dental sciences CSM Medical University. Lucknow (U.P)

Amita Jain, MD
Professor, Deptt. of Microbiology, CSM Medical University Lucknow (U.P)