Original Article

THE EFFECT OF ADJUNCTIVE USE OF AZITHROMYCIN WITH NON-SURGICAL PERIODONTAL THERAPY

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ABSTRACT

Objective: *The purpose of this study was to investigate the difference of outcome of non-surgical root surface debridement done along with adjective use of systemic antibiotics i.e. Azithromycin 500mg once a day for three days.*

Material and Methods: *A retrospective cohort study of adult patients diagnosed with chronic periodontitis. Twenty-nine patients were selected based on inclusion/ exclusion criteria, who were treated at the hospital and medicated with azithromycin from January 2014 to May 2015. Data was collected from their notes for base-line and after three months (3/12) reassessment. The patients were categorized according to depth of the pockets and behavioral factors like smoking and the differences between the baseline 3/12 reassessment were determined.*

Results: *Good response of treatment was seen in the reassessment for the nonsmokers group (median of 39), whereas the smoker group showed a satisfactory difference between base-line and reassessment showing a median of 24 that may correspond to the less number of subjects in this group. While a good difference was seen in the former smoker group showing a median of 35.*

Conclusions: *Good response was seen in terms of pocket depth reduction, gingival health and patient compliance, with the adjunctive use of azithromycin with non-surgical periodontal therapy in patients treated for moderate to severe periodontitis. To get a statistical results, further studies like root canal treatment needs to be carried out which should overcome the limitations of the current study.*

Key words: *Non-surgical periodontal therapy, Root debridement, Systemic antibiotics*

INTRODUCTION

Periodontal disease is characterized by bacterial destruction of the periodontal attachment apparatus supporting the teeth. The primary etiological factor in both gingivitis and periodontitis is dental plaque[1,2].

Periodontal disease starts as a plaque induced gingivitis represents and may develop into chronic periodontitis in a susceptible individual, causing irreversible loss of periodontal attachment and bone. Chronic periodontitis is a slow progressing form of periodontitis that may undergo period of exacerbation at any stage resulting in additional loss of attachment of bone.

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Supra and subgingival debridement results in mechanical disruption of the plaque biofilm and remain the "Gold Standard" treatment modality for the control of periodontal diseases. For shallow pockets < 3mm, non-surgical therapy results in loss of attachment by 0.5mm, whereas in deep pockets > 4mm there is a marked gain in attachment. The loss of attachment in shallow pockets was due to instrumentation trauma, however in the deeper sites this loss is reversed upon resolution of inflammation[4].

Treatment of these conditions involves the thorough removal of plaque and calculus. The standard treatment of periodontitis remains highly non-specific, consisting on the mechanical debridement of the affected root surface with the objective of reducing the total bacterial load & changing the environmental conditions of their microbial niches. This therapy has proven efficient on long-term basis[4]. However a small

although relevant proportion of sites and patients do not respond to this therapy. Various factors have been proposed to explain this non-responsiveness, mainly being persistence of periodontal pathogens[5].

In patients diagnosed with chronic periodontitis and treated with non-surgical periodontal treatment, deep sites > 7mm were reduced by 2.2mm (mean probing pocket depth)[6]. Factors that may influence the complete removal of dental plaque are extent of disease, anatomic actors, and skill of the operator. In a study it was suggested that more than 90% of cases deposits of plaque and calculus remained in sites of PD > 5mm following RSD[7].

Many types of antibiotics have been used in Periodontology. Because of the microbial aetiology of periodontal diseases there has been great interest in methods of controlling dental plaque chemically. Based on this numerous authors have hypothesized that purely mechanical debridement and removal may not be effective for certain patients in whom additional antimicrobial therapy would be used as an adjunctive with mechanical debridement to improve treatment outcome[8].

Penicillin are active only against bacteria that are undergoing growth and division because of having a beta-lactam ring in their structure they are known as beta-lactam antibiotics. When used for periodontal therapy, penicillin is often combined with Calvulanatee which inhibits β lactamse and predictable blood levels can be attained following oral administration. Metronidazole is a unique antimicrobial agent in that it is effective against anaerobic bacteria and parasites but has little or no effect on facultative and aerobic organism. Tetracycline has a broad spectrum activity and are bacteriostatic. In addition to their antimicrobial effect, tetracyclines are capable of inhibiting collagenases[9].

Azithromycin is a member of macrolides group, which is usually bacteriostatic, but can be bactericidal against highly susceptible organisms or when present in high concentrations. It is usually well tolerated and does not produce the intense nausea seen with erythromycin. It does not effect metabolism of other drugs[10].

Although non-surgical therapy of periodontitis is quite effective, it has certain limitations like complete plaque removal is not possible for teeth that have probing depth > 5mm or furcation involvement.

A lot of studies in literature[11,12] have examine the effect of different periodontal therapies on clinical parameters of periodontal disease, some of which are reviewed by Herrera et al[13] and Haffajee et al[14]. In general these studies have indicated that on average periodontal therapy provides an improvement in clinical parameters soon after therapy and for extended periods after the completion of therapy.

Furthermore it has been shown that Azithromycin is retained in inflamed gingiva for a week and is effective against periodontal disease-related bacteria[15]. As Zithromycin has shown antibacterial activity at sub inhibitory concentration further benefits may be expected in vivo where the half-life is prolonged and tissue distribution high. Azithromycin is likely to be useful in the treatment of periodontal disease cause by P. gingivalis[16].

Azithromycin has certain characteristics that make it an attractive agent for use in the treatment of young patients with chronic periodontitis and with aggressive periodontitis , two important microorganism associated with aggressive periodontitis and chronic periodontitis, A. Anctiomycetemcomitans and P.gingvigvalis are sensitive to Azithromycin in vitro[17].

The purpose of the study was to determine the outcome of non-surgical root surface debridement (RSD) performed along with adjective use of Systemic antibiotics i.e. Azithromycin 500mg OD for three days.

METHODS AND MATERIALS

The retrospective cohort study used adult patients with chronic periodontitis . Adult patients with chronic periodontitis were selected from patents referred to the department of periodontology for periodontal treatment from January 2014 till May 2015.

The inclusion criteria include; age: > 20 years, in good general health, with chronic periodontitis. Subjects were excluded if they had any known allergies to Azithromycin, had received any antibiotic therapy in the past 3 months and had systemic illnesses or medication with periodontal manifestations.

Patient were treated for root surface debridement (RSD) in a 24 hour period with adjunctive use of sys-

temic administration of Azithromycin at the dose of 500mg once daily (OD) for 3 days and that patient had baseline data records plus 3, 6, 9, 12 months (3/12) follow up records.

Forty-seven patients were selected and prescribed azithromycin for periodontal disease. All the notes for the 47 patients were reviewed. Eighteen patients out of 47, did not attend the three-month assessment treatment. Five patients had systemic disease like un-controlled diabetes, which were excluded. So at the end the total number of patient was 24 for which the data was collected at base-line and 3/12 months' re-assessment.

The group of 24 patients, who received RSD plus Azithromycin 500mg OD for 3 days on the completion of the treatment. The records of probing depths at base-line and 3/12 re–assessment of 6 sites (Mesiobuccla, midbuccal, distobuccal, distolingual, midlingual, and mesiolingual) were collected for all the teeth present, excluding 3rd molars.

The pocket depths were divided into 3 categories, shallow, moderate and deep. Shallow pockets were < 3mm moderate pockets were 4-6mm and deep pockets were > 7mm. All the data was entered into an excel spread sheet which included, the age of the patients, number of teeth, number of sites, pocket depth number and percentage at both baseline and reassessment. The different between baselines and 3/12 re-assessment values were computed and average, median and standard deviation and range values were calculated. The statistic were mainly descriptive statistics and not analytical and the difference in the change of pocket depth between baseline 3/12 re-assessment was the main outcome of interest. Thus the primary outcome variable which was evaluated included change in number and percentage of pocket depth at sites with > 3mm at base-line compared with the 3/12 re-assessment.

RESULTS

It can be seen from the data that there were a small number of current smokers whereas the number of subjects in non-smokers and former smoker group was balance. The average age gender, average number of teeth and number of sites for each group have been shown. The number of female patents (15) exceeded the number of male patients (9) and represented a split of approximately 2:1 female to male ration. On average, there was only a few missing teeth in each group and most of the sites were accessible for examination. Detail is given in Table-1.

A baseline data for each patient of the non-smoker group was reviewed. Similar information was recorded for the smoker and former smoker groups. Subject 1 had a lot of mission teeth and subject 16 had quite a few missing teeth. Whereas, the rest of the subjects had, most of their teeth still present.

Subject 5 & 6 had less than 30% of sites involved which would be classified as localized chronic periodontitis; whereas the remaining subjects exhibited generalized chronic periodontitis with more than 30% of sites involved. Detail is given in Table-2.

Comparison of the pocket depth percentages were recorded at baseline and 3/12 re-assessment for all non-smoker subjects is shown in terms for all categories of pocket. The range for all the sites >3mm, and considered to be still in need of treatment, at baseline was 25-70 and at 3/12 re-assessment was 3-23%. At the 3/112 re-assessment only 4 of the subjects had > 15% of sites >3mm, while the remaining 7 subjects were all below 12%. Detail is given in Table-3.

The results obtained after treatment, showing the differences in the percentages of sites in each category are shown in Table 4. There was a increase of 32% in the shallow pockets, with a range of -6 to -58. The average improvement for the moderate and deep category sites was 21% and 11 % respectively, with the range of 1 to 43% for the moderate category and -2 to 29% for the deep category. Subject number 2,10, 14, 15, 16 and 18 had shown a very good response compared to the

Table-1: Demographic data of the patients

	Non Smokers	Smokers	Former Smokers
Number	11	2	11
Average age	47	44	42
Male	4	0	5
Female	7	2	6
Average No of teeth	26	27	25
Average No. of Sites	155	165	149

Table-2: Example of baseline data Entry for non-smoker subjects with chronic periodontitis

Subject No.	No. of Teeth	No. of Sites	Shallow		Moderate		Deep		No. > 3mm	% > 3mm
			n	%	n	%	n	%		
1	18	108	75	69	21	19	12	11	33	31
2	28	168	93	55	48	29	27	16	75	45
3	27	162	108	67	52	32	2	1	54	33
5	28	168	122	73	16	10	30	18	46	27
6	27	162	122	75	37	23	3	2	40	25
8	28	168	106	63	52	31	10	6	62	37
10	27	162	69	43	73	45	20	12	93	57
14	26	156	47	30	64	41	45	31	109	70
15	27	162	74	46	85	52	3	2	88	54
16	22	132	71	54	34	26	27	20	61	46
18	26	156	60	38	70	45	26	17	96	62

Table-3: Comparison of baseline and 3/12 Re-assessment data in non-smokers with chronic periodontitis

Subject No.	Baseline %				Re-assessment %			
	Shallow	Moderate	Deep	> 3mm	Shallow	Moderate	Deep	> 3mm
1	69	19	11	31	77	19	5	23
2	55	29	16	45	97	3	0	3
3	67	32	1	33	85	12	4	15
5	73	10	18	27	92	8	0	8
6	75	23	2	25	81	17	2	19
8	63	31	6	37	85	13	2	15
10	43	45	12	57	81	19	0	19
14	30	41	29	70	88	12	0	12
15	46	52	2	54	91	9	0	9
16	54	26	20	46	94	6	1	6
18	38	45	17	62	93	6	1	7

Table-5: Summary of statistics for smokers and non-Smokers groups

	No. of Teeth	No. of sites	Baseline %			No. of Teeth	Re-assessment %		
			Shallow	Mod	Deep		Shallow	Mod	Deep
Non-Smokers									
Median	27	162	55	31	12	27	88	12	1
Max	28	168	75	52	29	28	97	19	4
Min	18	108	30	10	1	18	77	3	0
Smokers									
Median	28	165	55	29	16	28	79	18	3
Max	28	168	73	40	23	28	86	25	3
Min	27	162	36	18	8	27	72	11	2
Former Smoker									
Median	25	150	48	30	13	25	88	11	0
Max	28	168	88	59	45	28	100	25	3
Min	18	108	19	10	1	18	73	0	0

other with the range of 39 to 58% of sites improving to a shallower category.

Table 5 shows the summary statistics for smoker and non-smokers group at the baseline and re-assessment divided according to category of pocket. All teeth were present at re-assessment except five extractions done in non-smokers group because of poor prognosis of these teeth. The effect of RSD and adjunctive Azithromycin was almost the same on smokers and non-smokers. Non-smokers at re-assessment for moderate and deep pockets were 12% and 1 % respectively. Whereas for smokers it was 18% and 3% and for former smokers, the moderate and deep sites, were 11 and 0% respectively.

Table 6 summarize the statistical description of the data at baseline, 3/12 Re-assessment and the differences between them. There was a very good response at re-assessment for the non-smoker and the former smokers group, with a improvement of 39% of sites in the smokers and a median of 35% of sits in the formers smokers. In contrast, the smoker group shows a difference of 24% of sites.

Table-4: Difference between baseline and 3/12 Re-assessment

Subject No.	% Shallow	% Moderate	% Deep	% >3mm
1	-7	1	6	7
2	-42	26	16	42
3	-18	20	-2	18
5	-19	1	18	19
6	-6	6	0	6
8	-22	18	4	22
10	-39	26	12	39
14	-58	29	29	58
15	-45	43	2	45
16	-40	20	20	40
18	-54	38	16	54

Table-6: Summary of difference between smokers & non-smokers at baseline & 3/12 Re-assessment

	No. of Teeth	No. of Sites	Baseline % >3	Re-assessment % > 3	Difference
Non-smokers					
Median	27	162	45	12	39
Max	28	168	70	23	58
Min	18	108	25	3	6
Smokers					
Median	27.5	165	45	21	24
Max	28	168	63	28	35
Min	27	162	27	14	13
Former smokers					
Median	25	150	52	12	35
Max	28	168	81	27	69
Min	18	108	12	0	9

DISCUSSION

The aim of the present retrospective study was to assess the effective of adjunctive use of azithromycin with nonsurgical treatment of chronic periodontitis patients.

In the present study the baseline data was compared with the 3/12 re-assessment because the greatest change in pocket depth reduction and gain in clinical attachment occurs in 1-3 months post RSD, although healing and maturation of the periodontium may occur over the following 9-12 month[18,19] RSD combined with 3 day regimen of azithromycin once daily for 3 days resulted in significant better clinical outcomes.

In this study the improvement in the clinical outcome was determined by measuring the probing pocket depth (PPD), where as other parameters were not taken into account because of the personal preferences of the operators. Thus measures such as attachment loss and bleeding on probing were not taken into account because it was a retrospective study and often these variables were not recorded at both the baseline and 3/12 re-assessment[20].

The number of subject within the study was limited because this is a new approach to treatment. Out of the 47 subjects who had been prescribed Azithromycin for periodontal disease over the period of the examination, the major reasons for non inclusion were: not having had the 3 month assessment yet, antibiotics taken in the last 3 month, systemic disease & not meeting other criteria such as having periodontal diseases other than chronic periodontitis. As a consequence, the sample size for the study had to be reduced.

From the results it can be seen that there was a very good response in the non-smokers group and in the former smoker group. Limited data was available for the smokers group which showed un-satisfactory

results as compared to the other groups. Because of the small sample size of the smoker group (n=2), valid results could not be obtained as compared to the other two groups.

From Table 1 it can be seen that the smokers could be merged with the former smokers due to small number of subjects in this category, but this was not done because of the high variation in the time of cessation of smoking ranged from 3 months to 20 years. The statistics used in this study were descriptive rather than analylitical and therefore they were kept separate despite the small number of current smokers.

The main risk factors for periodontal disease are plaque, smoking, genetics, systemic diseases such as uncontrolled diabetes. Some people would take the view that to treat periodontal disease it is important to control factors like, plaque and smoking, before doing any non-surgical therapy with systemic antibiotics as a first line of treatment[21], whilst Azithromycin was given in selective patients such as non-smoker patients who had severe disease and pus discharge.

From Table 2 it can be seen that subject 5 & 6 had < 30% of sites diagnosed with pockets >3mm and would therefore be classified as localized chronic periodontitis as, according to the new classification, generalized chronic periodontitis is classified as having more then 30% of sites involved[22].

The range for the sites >3mm that are in need of treatment on re-assessment was 3 – 23. Subject 1 showed poor response at 3/12 re-assessment as there are 23% of sites left having >3 mm which needs further treatment. Some of the sites which did not show improvement and account for the increased number of sites left at 3/12 re-assessment, might be due to the deep sites improving and converting into moderate sites rather than into shallow sites, which results in an increased number of moderate sites. This is not reflected in the basic analysis we have undertaken here.

There was an average increase of 32% of the shallow group with the range of -6 to -58 while the average improvement for moderate and deep was 21 and 11% respectively. Also it can be seen that the only negative value in all subject was seen in subject number 3 which had 2% of deep sites which showed deterioration at 3/12 re-assessment. Other than that, improvement could be seen in all of the subjects, throughout all the pocket categories.

There was a very good response in the non-smoker group with the adjunctive use of Azithromycin with RSD. The difference between base-line and re-assessment, around 39% and the range was 6 to 58% for the non-smoker group. While the former smoker group showed good improvement at re-assessment of the treatment, but it was not as good as the non-smoker group, having a median difference of 35%, with the range of 9 to 69%.

The smoker group showed a satisfactory difference between the base-line and re-assessment, showing a median of 24% with the range of 13 to 35%, but this result was not as good as the other two groups. The reason for the less satisfactory results for the smoker group may be due to the limited number of patients in this group, which makes extrapolation of the data impossible. Nevertheless, the results obtained from these patients did show similarities to the trend observed in other studies that smoking has a impact on the outcome of treatment.

CONCLUSIONS AND RECOMMENDATIONS

Good response was seen in terms of pocket depth reduction, gingival health and patient compliance with the adjunctive use of azithromycin with non-surgical periodontal therapy in patients treated for moderate to severe periodontitis. To get a statistical result, further studies like large sample prospective RCT needs to be carried out which should overcome the limitations of the current study.

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