Journal of International Oral Health 2015; 7(7):102-107

Received: 20th January 2015 Accepted: 15th April 2015 Conflicts of Interest: None

Source of Support: Nil

Original Research

Effect of Tetracycline Hydrochloride and Spiramycin Sub Gingival Irrigation with Pulsated Jet Irrigator in Chronic Periodontitis Patients: A Clinical Study

P L Ravishankar[1], K Venugopal[2], Purnima Nadkerny[3]

Contributors:

[1]Professor & Head, Department of Periodontia, SRM Kattankulathur Dental College & Hospital, Kattankulathur, Tamil Nadu, India; [2]Reader, Department of Periodontia, Sri Sai Dental College, Srikakulam, Andhra Pradesh, India; [3]Professor and Head, Department of Periodontia, New Horizon Dental College, Bilaspur, Chhattisgarh, India.

Correspondence:

Dr. Ravishankar PL. Department of Periodontia, SRM Kattankulathur Dental College & Hospital, SRM University, Kattankulathur, Tamil Nadu, India. Phone: +91-9848113248. Email: plrs6@yahoo.com

How to cite the article:

Ravishankar PL, Venugopal K, Nadkerny P. Effect of tetracycline hydrochloride and spiramycin subgingival irrigation with pulsated jet irrigator in chronic periodontitis patient: A clinical study. J Int Oral Health 2015;7(7):102-107.

Abstract:

Background: The present study is designed to evaluate the clinical effects of pulsated subgingival irrigation with tetracycline and spiramycin.

Materials and Methods: Ten patient diagnosed chronic periodontitis were included in the present study. Each patient is assigned to be irrigated with saline (placebo) (Group A), tetracycline HCl at 0.5% concentration (Group B), and 0.5% spiramycin (Group C). Scaling and root planing (SC/RP) was recorded as Group D. Plaque index, gingival index, gingival bleeding index, probing pocket depth were assessed on pre-irrigation (day 0), and at days 7, 14, 21, 28, and 35 day.

Results: The results showed that subgingival irrigation with 0.5% tetracycline and spiramycin produced a significant reduction in clinical parameters compared to the control, while SC/RP was showed better improvement.

Conclusion: The result of this study suggested that subgingival irrigation of tetracycline and spiramycin play a beneficial role in the management of chronic periodontitis patients.

Key Words: Spiramycin, subgingival irrigation, tetracycline hydrochloride

Introduction

Oral and periodontal microbiology occupies an important place in the history of microbiology since the first bacteria to describe by Antoinio Van Leewenhoek in 1683 originated from dental plaque. There is a universal acceptance that the gingival sulcus is under continuous challenge by bacterial plaque and provides a suitable site for harboring various microorganisms. These microorganisms damage the tissues by releasing various toxins, enzymes, and metabolic products, which are considered important in causation of gingivitis and periodontitis.[1,2]

Several studies have reported that supragingival hygiene aids do not totally eliminate bacterial flora. Current periodontal therapy centers around the removal of subgingival plaque in an attempt to reestablish the simpler flora associated with health.[3]

Brushing, flossing, rinsing, and the use of interproximal devices are limited in their ability to clear plaque microbes below the gingival margin.

Since antiseptic mouth rinses cannot penetrate the sulcus beyond 3 mm, there is an increased interest in direct instillation of antimicrobials. Two primary methods are being investigated to improve efficacy: Slow release devices and sub gingival irrigation.[4] Irrigation of periodontal pockets with antimicrobial agents has been found to affect the subgingival microflora and to improve the periodontal conditions to variable degrees. Results of various studies have shown that "flushing action" associated with irrigation disrupts the microbial ecology of periodontal pockets and reestablishment of a disease associated flora is delayed. Oral irrigation has been promoted and used as a dental hygiene aid for over 80 years. Many studies suggested that oral irrigation is effective in altering, both quantitatively and qualitatively, the unattached subgingival plaque. Site specific irrigation devices will deliver medicaments deeper in the pockets, thus ensuring penetration to the base of the pocket.[5]

Different antimicrobials have been used as subgingival irrigants like chlorhexidine, stannous fluoride, metronidazole, tetracycline, hydrogen peroxide, etc.

In a study, subgingival irrigation with high concentrations of tetracycline was found to play a beneficial role in the management of patients with chronic periodontitis.[6]

Spiramycin is a macrolide antibiotic, belonging to the same group as erythromycin, created considerable interest in the treatment of periodontal diseases by systemic administration. Studies regarding spiramycin have not been done as an irrigant in the control of subgingival flora. The present study aims at finding out the comparative efficacy of local irrigation of tetracycline and spiramycin in chronic periodontitis using clinical parameters.

Tetracycline hydrochloride

Tetracyclines comprise a group of broad spectrum antimicrobial agents that were introduced in to a clinical practice in the late 1940s. The tetracyclines are primarily bacteriostatic antimicrobials, effective against all Gram-positive bacteria, and many Gram-negative species. Tetracyclines are used extensively in dentistry, particularly as adjuncts to periodontal therapy, an approach base on three perceived advantages: (1) Their effectiveness in suppressing Gram-negative anaerobic periodontopathogenic organisms in the subgingival plaque; (2) Their ability to concentrate in the gingival crevicular fluid at levels, substantially greater than that in serum; and (3) Their ability to bind to the tooth surface and then be slowly released in active form, a property which prolongs therapeutic effectiveness. Tetracyclines have been incorporated into a variety of delivery systems for insertion into periodontal pockets. These include hallow fibers, ethylene vinyl acetate copolymer fibers, ethyl cellulose fibers, acrylic strips.[7]

Nylund and Egelberg (1990)[8] designed a study to evaluate the effects of subgingival irrigation with Tetracycline as a supplement to mechanical plaque control and root debridement on clinical conditions of periodontal furcation areas. They suggested that future investigations on adjunctive antimicrobial furcation therapy need to be performed over longer periods of time and be aimed at evaluating re-occurrence of disease following the initial improvement. Furthermore, the antimicrobial agents may need to be administered in vehicles which provide active subgingival concentrations over prolonged intervals.

Tonetti *et al.* (1990)[9] measured the concentration of Tetracycline in the gingival fluid in the periodontal pocket following placement of controlled drug delivery monolithic fibers and subgingival irrigations. Results showed that zero drug release kinetics can be achieved in the periodontal pocket with a controlled delivery system made of 25 % tetracycline hydrochloride loaded ethylene vinyl acetate fiber.

Spiramycin

Spiramycin, a macrolide antibiotic belonging to the erythromycin group. It has been shown in an *in vitro* study to be active against some periodontopathic bacteria - isolated from subgingival plaque.[10] Successful use of spiramycin in combination with mechanical debridement has been reported, but such studies were without the inclusion of placebo groups or a double blind studies. In experimental animals, spiramycin is reported to be retained in high concentration in alveolar bone, gingival tissue, and salivary glands for long periods and is gradually secreted into surrounding tissues, saliva, and crevicular fluid.[11]

Sznajder *et al.* (1987)[12] conducted a study to evaluate the effect of spiramycin on subgingival microflora in 10 patients. On a double blind basis, patients received placebo or spiramycin 3 g first day and 2 g daily for a fortnight. Results at 2 weeks examination showed a statistically significant reduction in motile rods and spirochetes, as well as pocket depth (PD) decreases. Al-Joburi *et al.* (1989)[13] compared the efficacy of two antibiotics, spiramycin, and tetracycline with a placebo in the treatment of advanced adult chronic periodontitis. They concluded that mechanical debridement with or without adjunctive spiramycin were effective in improving clinical parameters.

Materials and Methods

Total of 10 patients (6 male and 4 female) between the age ranging from 35 to 55 years, exhibiting chronic adult periodontitis were selected to participate in this study.

Selection criteria

Subjects were selected according to the following criteria.

1. Both clinical and radiographic evidence of periodontal disease.
2. No periodontal therapy within the past 6 months.
3. No antibiotic therapy within the past 6 months.
4. Absence of other serious or complicated oral pathosis.
5. No systemic conditions which could influence the course of the disease, (e.g. Diabetes, hematological disorders, osteodystrophies, etc.).
6. Each patient was required to have at least two teeth with PDs of 6 mm or greater and each in a different quadrant.
7. No history of hypersensitivity to antibiotics.
8. Ability to attend the hospital at frequent intervals.

Clinical trial design

Prior to examination, all patients were received information about the design of the study. The duration of the study was comprised for 3 weeks. Furthermore, all clinical parameters were recorded at 28th and 35th day to assess the prolonged action of antimicrobials. Supragingival prophylaxis was performed before commencing the study. Each quadrant from each patient was selected for treatment, and then randomly assigned to the following groups.

Group I: Saline irrigation
Group II: Tetracycline hydrochloride irrigation
Group III: Spiramycin irrigation
Group IV: Scaling and root planning (SC/RP) alone

SC/RP was performed at time zero only, using hand curettes. The test quadrants received irrigation subgingivally twice a week for 3 weeks with 0.5% tetracycline hydrochloride, 0.5% spiramycin aqueous solutions and normal saline(0.85% sodium chloride) using subgingival pulsated jet irrigating device (Water Pik, Tylydene Co U.S.A.) under a pre-set pressure (<20 PSI) at dial No. 2.[14]

The irrigating solutions were delivered with the subgingival tip angled at 90° to the long axis of the tooth being irrigated

per the manufacturer's instructions.[15] Each tooth was exposed to 150 ml of the respective irrigation solution.[16] No attempt was made to the time the irrigation process. Excess fluids were removed from the oral cavity by high volume evacuation. Normal oral hygiene instructions were continued throughout the experiment period.

Clinical parameters of each quadrant were taken on 0 day i.e. baseline, 7, 14, 21, 28 and 35 day. Following clinical parameters were used.

1. Plaque index (PI)
2. Gingival index (GI)
3. Gingival bleeding index
4. Probing PD
5. Gingival crevicular fluid volume

Gingival crevicular fluid volume (Quantitative assessment – Mann's Method 1963)

Fluid is collected during a 3 min period from the dried isolated orifice of the pockets using 6 mm × 2 mm strips of Whatman's filter paper No. 1. Three filter-paper strips approximately 2 mm wide and 6 mm long are inserted side by side in the crevice and left in position for 3 min. This procedure ensures that any fluid collected after the drying does not originate in the crevice. The central drying strip is then removed and immediately replaced by a collecting strip 1 mm wide and 6 mm long. The collecting strip does not have any contact with the two lateral drying strips, is left in place for 5 min, and then removed for examination. The two drying strips which have acted as a dam to wall off fluid remainder of the crevice are removed and discarded. The strips were dried and then stained with 0.2% ninhydrin in acetone (Brill). Ninhydrin is specific for a-amino groups and gives a blue or purple color. The area stained was measured with ×10 magnification using a graticule eyepiece (Wilson and Mchugh). Fluid length was measured to the nearest 0.5 mm.

The results so obtained were analyzed statistically by using:

1. Two-way analysis of variance.
2. Scheffe's multiple range test.

Results

Ten patients are attending Division of Periodontics, Rajah Muthiah Dental College and Hospital, Chidambaram, who diagnoses as chronic periodontitis were selected for this study. By split-mouth design, three quadrants received bi-weekly subgingival irrigation of saline (Control Group I), tetracycline (Group II), and spiramycin (Group III) for 3 weeks. Group IV quadrants did not receive any subgingival irrigation, only SC/RP was done at baseline.

Clinical parameters PI, GI, gingival bleeding index, probing PD, and gingival crevicular fluid volume measurement were taken on the baseline, 7, 14, 21, 28, and 35 day. The following results were obtained after a statistical analysis.

Table 1 shows mean and standard deviation values of PI in the four different groups by different days. At the baseline, the mean PI scores for four groups namely saline, tetracycline hydrochloride, spiramycin, and SC/RP were 1.90, 1.71, 1.73, and 1.86, respectively. At the end of the irrigation therapy i.e. on the 21st day the mean PI scores for three groups namely saline, tetracycline, and spiramycin are 0.41, 0.88, and 1.01, respectively. The mean PI score for SC/RP group on 21st day was 0.69 which differed significantly from its baseline value. Overall from baseline to end of the irrigation therapy there was a significant reduction ($P < 0.001$) for all groups. From the 21st day onwards saline, tetracycline hydrochloride, and spiramycin groups showed no significant reduction.

When the mean PI score of experimental period i.e. on days 0, 1, 14, and 21 was compared among four groups by using Scheffe's *post-hoc* test (since significant F value i.e. $P < 0.05$ is obtained), on 7th day the SC/RP group showed statistically significant difference when compared with tetracycline and spiramycin groups. On 14th day, both saline and SC/RP groups showed a significant difference when compared with tetracycline and spiramycin groups. On 21st day, Saline group showed statistically significant difference when compared with tetracycline and spiramycin groups and SC/RP showed statistically difference when compared with spiramycin group.

By above statistical findings, the plaque scores of single SC/RP was significantly lower than the three irrigation groups throughout the study. When compared tetracycline group with spiramycin group, the former showed a reduction in plaque level, which was not statistically significant.

Table 2 shows mean and standard deviation of GI in the four different groups by different days. At the baseline, the mean GI scores for four groups namely saline, tetracycline hydrochloride, spiramycin, and scaling/root planing are 1.86, 1.88, 1.78, and 1.89, respectively. At the end of the irrigation therapy i.e. on the 21st day, the mean GI scores for saline, tetracycline hydrochloride, and spiramycin groups were 1.16, 0.65, and 1.10, respectively. The mean GI score for SC/RP group on 21st day was 0.65 which showed a statistical significant difference from its baseline value. From baseline to end of the irrigation therapy (21st day) there was a significant reduction ($P < 0.001$) for all groups. From the 21st day onwards all four groups showed no significant reduction.

Mean GI was compared among four groups by using Scheffe's *post-hoc* test, the SC/RP group on 7th day showed statistically significant difference when compared to tetracycline and spiramycin groups. On 14th day, SC/RP group showed statistically significant difference when compared to saline, tetracycline and spiramycin groups. On 21st day, Saline group showed a statistically significant difference, when the mean GI scores on days baseline, 7, 14 when compared to tetracycline and spiramycin groups.

By above statistical findings, the GI scores of single SC/RP was significantly lower than the three irrigation groups. When compared tetracycline group with spiramycin group, the former showed a reduction in GI scores which was not statistically significant.

Table 3 shows mean and standard deviation of gingival bleeding index in the four different groups by different days. At the baseline, the mean gingival bleeding index scores for four groups namely saline, tetracycline hydrochloride, spiramycin and scaling/root planing were 1.73, 1.72, 1.71, and 1.72, respectively. At the end of the irrigation therapy i.e. on the 21st day, the mean gingival bleeding index scores for saline, tetracycline hydrochloride, and spiramycin groups were 1.51, 1.42, and 1.50, respectively. The mean gingival bleeding index score for SC/RP group on 21st day was 1.25, which showed a statistical difference from its baseline value. The mean scores for saline, tetracycline, and spiramycin groups on 21st day showed no statistical difference from their baseline values. On 28th day and 35th day, the mean gingival bleeding index values showed no statistical significance when compared to 21st day values. By applying Scheffe's *post-hoc* test, only SC/RP group on 14th and 21st day showed a statistically significant difference on 14th and 21st days when compared with saline, tetracycline, and spiramycin groups.

By above statistical findings, only SC/RP group showed a statistical reduction from its baseline value. When tetracycline group was compared with Spiramycin group, both groups showed a reduction in values equally.

Table 4 shows mean and standard deviation of probing PD index in the four different groups by different days. At the baseline, the mean probing PD index scores for four groups namely saline, tetracycline hydrochloride, spiramycin, and scaling/root planing were 5.01, 5.07, 4.88, and 4.90, respectively. At the end of the irrigation therapy i.e. on the 21st day, the mean probing PD index scores for saline, tetracycline hydrochloride, and spiramycin groups were 4.64, 4.20, and 4.41, respectively. The mean probing PD index score for SC/RP group on 21st day was 4.02 which showed no statistical difference from its baseline value. All four groups showed no significant reduction on 7th day, only on the 14th day they showed the statistical difference.

When the mean probing PD index scores on days baseline, 7, 14 and 21 were compared among four groups by using Scheffe's *post-hoc* test, only the SC/RP group on 14th day showed statistical difference when compared to saline group.

By above statistical findings, no particular group showed any statistical reduction from their baseline values. When tetracycline group was compared with spiramycin group the former showed a reduction in probing PD index scores which was not statistically significant.

Table 1: Mean and standard deviation of PI for Group I, Group II, Group III and Group IV at baseline, 7, 14, 21, 28, and 35 day.

Time in days	Saline	Tetracycline	Spiramycin	Scaling/root planing	Significance
0	1.90±0.31	1.71±0.44	1.73±0.29	1.86±0.30	NS
7	1.21±0.20	1.25±0.15	1.30±0.20	0.98±0.17	*P*<0.001
14	0.71±0.06	1.08±0.20	1.19±0.20	0.83±0.23	*P*<0.001
21	0.41±0.10	0.88±0.22	1.01±0.18	0.69±0.23	*P*<0.001
28	0.38±0.09	0.85±0.23	0.98±0.18	0.56±0.13	
35	0.36±0.09	0.79±0.23	0.92±0.16	0.27±0.08	

PI: Plaque index

Table 2: Mean and standard deviation of GI for Group I, Group II, Group III and Group IV at baseline, 7, 14, 21, 28, and 35 day.

Time in days	Saline	Tetracycline	Spiramycin	Scaling/root planing	Significance
0	1.82±0.25	1.88±0.25	1.78±0.22	1.89±0.26	NS
7	1.46±0.28	1.70±0.25	1.55±0.22	0.11±0.32	*P*<0.001
14	1.19±0.16	1.55±0.24	1.43±0.22	0.87±0.25	*P*<0.001
21	1.16±0.19	1.10±0.23	1.10±0.20	0.65±0.25	*P*<0.001
28	1.12±0.20	0.92±0.30	0.96±0.20	0.48±0.18	
35	1.08±0.19	0.81±0.23	0.91±0.18	0.40±0.17	

GI: Gingival index

Table 3: Mean and standard deviation of gingival bleeding index for Group I, Group II, Group III, and Group IV at baseline, 7, 14, 21, 28, and 35 day.

Time in days	Saline	Tetracycline	Spiramycin	Scaling/root planing	Significance
0	1.73±0.29	1.72±0.28	1.71±0.23	1.72±0.22	NS
7	1.69±0.28	1.58±0.25	1.68±0.20	1.49±0.21	NS
14	1.60±0.28	1.54±0.26	1.58±0.20	1.32±0.17	*P*<0.01
21	1.51±0.24	1.42±0.25	1.50±0.20	1.25±0.20	*P*<0.02
28	1.44±0.23	1.31±0.25	1.45±0.19	1.19±0.20	
35	1.40±0.23	1.25±0.25	1.40±0.19	1.15±0.18	

Table 5 shows mean and standard deviation of gingival crevicular fluid volume measurement in the four different groups by different days. For gingival crevicular fluid volume measurement between 1st and 21st days all four groups showed a reduction, which was not statistically significant, when compared SC/RP group with saline, tetracycline hydrochloride, and spiramycin groups on different days, SC/RP group showed no significant difference. When Tetracycline group was compared with spiramycin group, the former showed a reduction on in gingival crevicular fluid volume measurement which was not statistically significant.

Discussion

Periodontal therapy centers around the removal and control of plaque and the restoration of a normal bacterial flora in the gingival sulcus. This can be accomplished by therapeutic procedures that may kill the invading bacteria *in situ*.[17] For example, subgingival irrigation with a chemotherapeutic agent in sufficiently high concentration when delivered with a syringe may be a beneficial adjunctive modality of treatment to enhance periodontal health by reducing pathogenic flora and thereby improving the clinical parameters. The present study has been undertaken to evaluate the efficacy of saline, tetracycline, and spiramycin as subgingival irrigants and also compare these results with those obtained after SC/RP in patients suffering from chronic periodontitis. Previous investigations have demonstrated that Tetracycline plus SC/RP, using either systemic or local delivery methods, is no more effective than SC/RP alone.[6] Listgarten *et al*.[18] reported that systemic Tetracycline alone had a significant effect while the drug was administered, but that effect was short lived. These studies are in general agreement that the antibiotic without SC/RP is not an effective means of producing a clinical or microbial result of any significant duration.

In the present study, the PI, GI, gingival bleeding index, probing PD, and estimation of gingival crevicular fluid volume were monitored in patients receiving bi-weekly subgingival irrigation with TCL HCL, spiramycin, and saline for 3 weeks in three group of patients. Similar findings were also monitored patients who had undergone single SC/RP.

Silverstein (1988)[6] showed that mean plaque scores were reduced in seven patients suffering from adult periodontitis by using Tetracycline hydrochloride as a subgingival irrigant for 8 weeks from 0.71 to 0.61. Subgingival irrigation with saline also reduced plaque scores to some extent. In contrast to the above finding, the present study revealed SC/RP better beneficial reduction in plaque scores, when compared to TCL HCL and spiramycin group.

Miyata (1987),[19] Ciancio (1989)[20] experimented the effect of tetracycline hydrochloride and saline as subgingival irrigants and showed a reduction in plaque scores. The present study was in accordance with above findings.

The gingival score in present investigation demonstrated significant reduction after subgingival irrigation with saline and TCL HCL. SC/RP showed better reduction than TCL HCL and saline. These findings are in accordance with several studies conducted by Jacob Shiloh (1994),[21] Silverstein (1987),[6] Wennstrom (1987).[22] SC/RP has been proven to be an effective treatment modality for the majority of patients and majority of sites with periodontitis. However, a significant number of sites may continue to loose periodontal attachment.[23] This may be due to the limited effects that SC/RP exert on microorganisms in deep pockets and in furcation areas.[24] Therefore, irrigation has been reported to be of value in improving the penetration of chemotherapeutic agents into the gingival sulcus, deep periodontal pockets and furcation areas. This demonstrates that subgingival irrigation with the antimicrobial agent can provide an incremental benefit when used as an adjunct in the treatment of periodontitis.[25,26]

Table 4: Mean and standard deviation of probing PD index for Group I, Group II, Group III, and Group IV at baseline, 7, 14, 21, 28, and 35 day.

Time in days	Saline	Tetracycline	Spiramycin	Scaling/root planing	Significance
0	5.01±0.48	5.07±0.45	4.88±0.39	4.90±0.38	NS
7	4.84±0.45	4.64±0.43	4.71±0.40	4.40±0.39	NS
14	4.72±0.47	4.32±0.41	4.57±0.38	4.01±0.43	*P*<0.001
21	4.64±0.46	4.20±0.38	4.41±0.37	4.02±0.70	NS
28	4.48±0.47	4.11±0.40	4.25±0.43	3.82±0.38	
35	4.45±0.48	4.10±0.38	4.17±0.38	3.80±0.37	

PD: Pocket depth

Table 5: Mean and standard deviation of gingival crevicular fluid volume measurement for Group I, Group II, Group III, and Group IV at baseline, 7, 14, 21, 28, and 35 day.

Time in days	Saline	Tetracycline	Spiramycin	Scaling/root planing	Significance
0	3.45±1.26	3.42±1.20	3.40±1.21	3.40±1.22	NS
7	3.43±1.27	3.36±1.24	3.37±1.15	3.28±1.16	NS
14	3.36±1.22	3.32±1.20	3.34±1.17	3.20±1.14	NS
21	3.30±1.21	3.20±1.21	3.30±1.19	3.17±1.15	MS
28	3.27±1.20	3.22±1.18	3.28±1.16	3.17±1.01	
35	3.27±1.21	3.22±1.18	3.28±1.88	3.20±1.01	

Conclusion

This study demonstrated that subgingival jet irrigation with tetracycline and spiramycin in its specially designed formulation can be well tolerated by patients and effective in reducing the inflammatory clinical signs of periodontits along with SC/RP as evident from this study. It can be deduced that 0.5% tetracycline hydrochloride and 0.5%spiramycin are more or less equally effective, it may be concluded that spiramycin can be used as subgingival irrigant. However, when the efficacy of root planing was compared with subgingival irrigation, root planing provided the more benefit. Further investigations are needed to document the effect of subgingival irrigation in periodontal condition with large number of patients, higher concentrations of antimicrobials, and a longer period of time.

References

1. Addy M, Langeroudi M. Comparison of the immediate effects on the sub-gingival microflora of acrylic strips containing 40% chlorhexidine, metronidazole or tetracycline. J Clin Periodontol 1984;11(6):379-86.
2. Adriaens PA, De Boever JA, Loesche WJ. Bacterial invasion in root cementum and radicular dentin of periodontally diseased teeth in humans. A reservoir of periodontopathic bacteria. J Periodontol 1988;59(4):222-30.
3. Abdulpur MS. Periodontal microbiology. J Indian Soc of Periodontol 1995;19(1):54-9.
4. Itic J, Serfaty R. Clinical effectiveness of subgingival irrigation with a pulsated jet irrigator versus syringe. J Periodontol 1992;63(3):174-81.
5. Rethman J. Current concepts in irrigation therapy. Pract Periodontics Aesthet Dent 1991;3(6):13-8.
6. Silverstein L, Bissada N, Manouchehr-Pour M, Greenwell H. Clinical and microbiologic effects of local tetracycline irrigation on periodontitis. J Periodontol 1988;59(5):301-5.
7. Seymour RA, Heasman PA. Tetracyclines in the management of periodontal diseases. A review. J Clin Periodontol 1995;22(1):22-35.
8. Nylund K, Egelberg J. Antimicrobial irrigation of periodontal furcation lesions to supplement oral hygiene instruction and root debridement. J Clin Periodontol 1990;17(2):90-5.
9. Tonetti M, Cugini MA, Goodson JM. Zero-order delivery with periodontal placement of tetracycline-loaded ethylene vinyl acetate fibers. J Periodontal Res 1990;25(4):243-9.
10. Quee TC, Roussou T, Chan EC. *In vitro* activity of rodogyl against putative periodontopathic bacteria. Antimicrob Agents Chemother 1983;24(3):445-7.
11. Leung FC, Gardner JM, Paor WS, Yankell SL. Spiramycin excretion in animals. II. Repeated oral doses in rats. J Dent Res 1972;51(3):712-5.
12. Sznajder N, Piovano S, Bernat MI, Flores L, Macchi R, Carraro JJ. Effect of spiramycin therapy on human periodontal disease. J Periodontal Res 1987;22(4):255-8.
13. Al-Joburi W, Quee TC, Lautar C, Iugovaz I, Bourgouin J, Delorme F, *et al.* Effects of adjunctive treatment of periodontitis with tetracycline and spiramycin. J Periodontol 1989;60(10):533-9.
14. Fine JB, Harper DS, Gordon JM, Hovliaras CA, Charles CH. Short-term microbiological and clinical effects of subgingival irrigation with an antimicrobial mouthrinse. J Periodontol 1994;65(1):30-6.
15. Badersten A, Nilvéus R, Egelberg J. Effect of nonsurgical periodontal therapy. I. Moderately advanced periodontitis. J Clin Periodontol 1981;8:57-72.
16. Stabholz A, Kettering J, Aprecio R, Zimmerman G, Baker PJ, Wikesjö UM. Retention of antimicrobial activity by human root surfaces after in situ subgingival irrigation with tetracycline HCl or chlorhexidine. J Periodontol 1993;64(2):137-41.
17. Mehta A. Risk factors associated with periodontal diseases and their clinical considerations. Int J Contemp Dent Med Rev. 2015;2015:Article ID: 040115. doi: 10.15713/ins.ijcdmr.31.
18. Listgarten MA, Lindhe J, Hellden L. Effect of tetracycline and/or scaling on human periodontal disease. Clinical, microbiological, and histological observations. J Clin Periodontol 1978;5(4):246-71.
19. Miyata H, Kamoi K. [Article in Japanese] Effects of irrigation of pockets on clinical symptoms and oral bacterial flora in patients with periodontal disease – with scaling and root planing. Nihon Shishubyo Gakkai Kaishi 1987;29:76-90.
20. Ciancio SG, Mather ML, Zambon JJ, Reynolds HS. Effect of a chemotherapeutic agent delivered by an oral irrigation device on plaque, gingivitis, and subgingival microflora. J Periodontol 1989;60:310-5.
21. Shiloah J, Patters MR. DNA probe analyses of the survival of selected periodontal pathogens following scaling, root planing, and intra-pocket irrigation. J Periodontol 1994;65(6):568-75.
22. Wennstrom JL, Jeijl L, Dahlen G. Periodic subginggival antimicrobial irrigation of periodontal pockets. 1. Clinical observation. J Clin Periodontol 1987;14(9):541-50.
23. Kaldahl WB, Kalbwary KL, Patila KD. Incidence of breakdown sites during periodontal maintenance care. J Periodontol 1992;63:1008.
24. Loos B, Claffey N, Egelberg J. Clinical and microbiological effects of root debridement in periodontal furcation pockets. J Clin Periodontol 1988;15(7):453-63.
25. Eakle WS, Ford C, Boyd RL. Depth of penetration in periodontal pockets with oral irrigation. J Clin Periodontol 1986;13(1):39-44.
26. Macaulay WJ, Newman HN. The effect on the composition of subgingival plaque of a simplified oral hygiene system including pulsating jet subgingival irrigation. J Periodontal Res 1986;21(4):375-85.