International Journal of Dental Hygiene

Official Journal of the International Federation of Dental Hygienists

ORIGINAL ARTICLE

HG Yilmaz
H Bayindir

Clinical evaluation of chlorhexidine and essential oils for adjunctive effects in ultrasonic instrumentation of furcation involvements: a randomized controlled clinical trial

Authors' affiliations:
HG Yilmaz, *H Bayindir*, Faculty of Dentistry, Department of Periodontology, Near East University, Mersin, Turkey

Correspondence to:
Dr. Hasan Guney Yilmaz
Faculty of Dentistry
Department of Periodontology
Near East University
Mersin 10
Turkey
Tel.: +90 533 832 8433
Fax: +90 392 680 2025
E-mail: dr.hguneyyilmaz@gmail.com

Abstract: *Background:* The aim of this clinical study was to evaluate and compare the clinical efficacy of subgingival ultrasonic mechanical instrumentation (UMI) irrigated with essential oils (EOs) and chlorhexidine (CHX) at the furcation involvements (FI). *Methods:* Forty-five patients (244 FI) who presented with Class II FI were recruited to the study. Patients were randomly assigned to CHX (UMI irrigated with 0.2% CHX), EO (UMI irrigated with EOs) or control (UMI irrigated with distilled water) groups. All treatments were performed in one session. For all groups, plaque index (PI), gingival index (GI), position of gingival margin (PGM), pocket depth (PD), bleeding on probing (BOP), clinical attachment level (CAL) and horizontal attachment level (HAL) scores were recorded at baseline and 1 and 3 months after therapy. *Results:* In all groups, there were significant reductions in PI, GI, PD and BOP, increase in PGM scores and gain in CAL and HAL scores, at 1 and 3 months compared to baseline. Except in BOP scores, there were no significance differences among the groups at any time point. At 1 and 3 months, there were significant reductions in the BOP scores of the EO group compared with the CHX and control groups. *Conclusion:* Within the limits of this study, the use of EOs as a cooling liquid of UMI may promote slight adjunctive effects at FI compared to CHX and water.

Key words: anti-infective agents; furcation defect; periodontal debridement

Introduction

Periodontitis is an infectious disease characterized by alveolar bone and clinical attachment loss and caused by intraoral biofilm, which contains aerobic and anaerobic bacteria (1). The main goal of periodontal therapy is to disrupt the biofilm, suppress periodontal pathogens in the oral cavity and arrest the disease. Studies have shown that periodontal disease can be successfully treated by mechanical removal of dental biofilm and calculus and oral hygiene instruction (2–5). Ultrasonic mechanical instrumentation (UMI) is an effective method for removing supra- and subgingival bacterial biofilm and dental calculus from tooth surfaces and for reducing probing depths and bleeding on probing scores (6, 7). However, mechanical therapy alone can fail to eliminate pathogenic bacteria because of the existence of intraoral translocation, from one oral site to

Dates:
Accepted 22 November 2011

To cite this article:
Int J Dent Hygiene **10**, 2012; 113–117
DOI: 10.1111/j.1601-5037.2011.00538.x
Yilmaz HG, Bayindir H. Clinical evaluation of chlorhexidine and essential oils for adjunctive effects in ultrasonic instrumentation of furcation involvements: a randomized controlled clinical trial.

another and areas inaccessible to periodontal instruments (8, 9). Furcation involvements (FI), in particular, hinder successful periodontal therapy because of anatomical factors that impede accessibility for individual oral hygiene and professional root debridement in the molar region (10, 11). Therefore, adjunct antibacterial agents to control bacterial colonization on tooth surfaces and soft tissues have been studied extensively (12–14).

Chlorhexidine (CHX) is an antimicrobial agent that has been used to reduce the number of bacteria in the oral cavity (12). It is commonly used as a mouthrinse (0.2%) before surgical procedures but has also been used as a subgingival irrigant at varying concentrations as adjunctive therapy to scaling and root planing (12, 13, 15). Although CHX is one of the most effective agents at plaque control, its long-term use is associated with a number of adverse effects (16–18); therefore, alternative antibacterial agents based on essential oils (EOs) are widely used for chemical disinfection (14). Essential oils have demonstrated antiplaque and antigingivitis effectiveness in different clinical conditions, such as post-surgery periods, implant dentistry, interdental cleaning, halitosis and gingivitis control (14, 19–22).

In previous studies, CHX and EO solutions were applied by home subgingival irrigation devices by the patients themselves, or by professional irrigation with syringes (12–14). However, no studies were found in the literature evaluating the effects of ultrasonic subgingival instrumentation irrigated with EOs or CHX at FI. Therefore, the aim of this randomized controlled clinical study was to evaluate and compare the clinical efficacy of subgingival ultrasonic instrumentation irrigated with EOs and CHX at the furcation sites.

Material and methods

Study population

The present study included 45 patients (28 men and 17 women; mean age, 52.8 ± 10.6 years) with chronic periodontitis. Patient recruitment was performed within the Department of Periodontology, Faculty of Dentistry, Near East University. The inclusion criteria were (i) a diagnosis of moderate to severe chronic periodontitis by the presence of periodontal pockets (≥5 mm) with bleeding of probing (BOP) and (ii) at least one molar with Class II (23) furcation involvement with ≥5 mm probing depth. Patients were excluded if any of the following was present: (i) scaling, root planing or periodontal surgery in the preceding 12 months; (ii) known allergy or other adverse reactions to CHX or EOs; (iii) systemic disease; (iv) smoking or use of medications affecting the periodontal tissues; or (v) pregnancy.

Study design

This was a randomized, single-blind, parallel-arm, controlled clinical study. Following verbal information about the treatment plan, possible discomforts and potential risks, the subjects who signed the informed consent form were included in the study. Study protocol and related consent forms were approved by the Ethics Committee of Near East University. Patients were randomly assigned by a lottery method to CHX (Drogsan, Istanbul, Turkey; ultrasonic subgingival instrumentation (Piezonmaster 700; EMS, Nyon, Switzerland) irrigated with 0.2% CHX), EO (Listerine, Johnson & Johnson, Istanbul, Turkey; ultrasonic subgingival instrumentation irrigated with EOs containing 0.064% thymol, 0.092% eucalyptol, 0.06% methyl salicylate, 0.042% menthol and 21.6% ethanol) or control (ultrasonic subgingival instrumentation irrigated with distilled water) groups. All treatments were performed at one session. The plaque index (PI) (24), gingival index (GI) (25), clinical attachment level (CAL), horizontal attachment level (HAL), probing depth (PD), position of gingival margin (PGM) and BOP were measured at the baseline and 1 and 3 months after treatment by a single calibrated examiner who was not aware of the type of treatment applied. The PI, GI, PD, PGM and BOP were evaluated with a periodontal probe at 6 sites on all teeth. BOP was assessed by percentage of sites bled after probing. The HAL was measured with a curved, scaled periodontal probe (PQ2N7; Hu-Friedy, Chicago, IL, USA) at all furcation sites.

Sample size calculation

A minimum clinically significant difference in CAL of 1.0 mm was determined from available literature. A power analysis was conducted on the basis of this minimum clinically significant difference in CAL, by using alpha at level 0.05, 80% power and a σ of 1 (20). From these data, the required number of subjects for this study was calculated as 11 per group. To compensate for losses during the follow-up, 15 subjects per group were recruited.

Statistical analysis

Mean values of the clinical parameters were calculated for all groups. The normal distribution of all scores was assessed using the Kolmogorov–Smirnov test. To evaluate the changes over time within the groups, one-way repeated ANOVA was used. *Post hoc* comparisons were performed by using the Tukey's test, when significance was detected. A *t*-test was used for comparison among groups at each time point. Values of $P < 0.05$ were accepted as statistically significant.

Before the study, a calibration session was performed to determine intraexaminer consistency at the clinical evaluations. Eight subjects were included in this session, and the measurements were repeated twice at 1-h intervals. Reliability was determined by using Cohen's κ, which was employed to describe the reliability of discrete values for objective evaluation of PI. Based on the duplicate evaluations, the κ value for PI evaluation was 0.88 ± 0.05. The range of mean errors for PD, PGM, CAL and HAL assessments were 0.18–0.22, 0.12–0.18, 0.22–0.26 and 0.20–0.28, respectively, and indicated consistent reliability during the evaluation period.

Results

All 45 patients completed the 3-month study period. A total of 244 furcation involvements were evaluated: 81 in the CHX group, 90 in the EO group and 73 in the control group. The mean and standard deviations of the PI, PD, PGM, CAL, BOP and HAL values are presented in Table 1. The alterations in the distributions of FI in all groups over 3 months can be seen in Table 2. At the baseline evaluation, no significant difference was found in clinical parameters among the groups ($P > 0.05$), (Table 1).

PI, GI and BOP

Plaque index, GI and BOP scores were reduced during the study in all groups. Intragroup comparisons revealed that the difference between baseline scores and those at 1, 3 months after therapy was statistically significant in all groups ($P < 0.05$), (Table 3). When compared with the control and CHX groups, the EO group showed a statistically significant decrease in BOP scores (64.26%, 83.46% and 60.74% decreases were recorded in the CHX, EO and control groups, respectively) at 1 month ($P < 0.05$), (Table 3). In PI and GI scores, there were no differences among the groups throughout the study period ($P > 0.05$), (Table 3).

Clinical parameters: PGM, PD, CAL and HAL

There were no significant differences among the groups in PGM, PD, CAL or HAL at any time point ($P > 0.05$), (Table 4). At 1 and 3 months, significant decreases in PD scores were observed ($P < 0.05$), (Table 4). The mean decrease

Table 1. **Baseline means (±SD) of clinical parameters**

Characteristics	CHX group	EO group	Control group
Patients	15	15	15
Total number of FI	81	90	73
PI	1.33 ± 0.97	1.53 ± 0.99	1.73 ± 1.03
GI	1.60 ± 0.73	1.74 ± 0.70	1.70 ± 0.79
BOP (%)	80 ± 8.2	78 ± 9.8	82 ± 7.4
PD (mm)	6.24 ± 1.36	5.9 ± 1.44	6.36 ± 1.12
PGM (mm)	1.90 ± 1.10	2.10 ± 0.70	1. 90 ± 1.30
CAL (mm)	8. 20 ± 1.20	8.0 ± 1.0	8.10 ± 1.2
HAL (mm)	6.8 ± 2.4	7.2 ± 2.2	7.0 ± 2.2

CAL, clinical attachment level; CHX, chlorhexidine; EO, essential oil; FI, furcation involvements; GI, gingival index; HAL, horizontal attachment level; PD, pocket depth; PGM, position of gingival margin; PI, plaque index.

Table 2. **Alterations in FI in all groups over 12 weeks**

	Baseline	4 weeks	12 weeks
CHX group			
Class I FI	0	28	29
Class II FI	81	50	51
Class III FI	0	3	1
EO group			
Class I FI	0	32	36
Class II FI	90	58	54
Class III FI	0	1	0
Control group			
Class I FI	0	25	23
Class II FI	73	48	50
Class III FI	0	0	0

FI, furcation involvements.

Table 3. **Mean (±SD) of PI, GI and BOP in all groups over 12 weeks**

	Baseline	4 weeks	12 weeks
PI			
CHX group	1.33 ± 0.97	1.10 ± 0.72	1.24 ± 0.88
EO group	1.53 ± 0.99	1.14 ± 0.68	1.18 ± 0.74
Control group	1.73 ± 1.03	1.20 ± 0.82	1.20 ± 0.88
GI			
CHX group	1.60 ± 0.73	1.32 ± 0.80	1.30 ± 0.77
EO group	1.74 ± 0.70	1.38 ± 0.68	1.29 ± 0.54
Control group	1.70 ± 0.79	1.21 ± 0.56	1.24 ± 0.65
BOP			
CHX group	80 ± 8.2	42 ± 14.8*	34 ± 12.4*
EO group	78 ± 9.8	28 ± 16.8*,†	24 ± 12.6*,†
Control group	82 ± 7.4	44 ± 14.4*	36 ± 14.8*

BOP, bleeding on probing; CHX, chlorhexidine; EO, essential oils; GI, gingival index; PI, plaque index.
*Post-treatment BOP scores were lower than baseline BOP scores in all groups ($P < 0.05$).
†The differences at 4 and 12 weeks after treatment were statistically significant between EOs and CHX and between EOs and control group ($P < 0.05$).

Table 4. **Mean (±SD) of PD, PGM, CAL and HAL in all groups over 3 months**

	Baseline	4 weeks	12 weeks
PD			
CHX group	6.24 ± 1.36	3.20 ± 1.54*	2.9 ± 1.61*
EO group	5.9 ± 1.44	3.1 ± 1.26*	2.7 ± 1.56*
Control group	6.36 ± 1.12	3.4 ± 1.38*	3.1 ± 1.46*
CHX group	1.90 ±1.10	3.0 ± 0.80*	3.4 ± 1.2*
PGM			
EO group	2.10 ± 0.70	3.2 ± 1.1*	3.4 ± 1.3*
Control group	1.90 ± 1.30	2.9 ± 1.30*	3.2 ± 1.2*
CHX group	8.20 ± 1.20	6.2 ± 1.3*	6.3 ± 1.2*
CAL			
EO group	8.0 ± 1.0	6.3 ± 1.2*	6.1 ± 1.4*
Control group	8.10 ± 1.2	6.4 ± 1.4*	6.3 ± 1.4*
CHX group	7.8 ± 2.4	6.4 ± 1.8*	6.0 ± 1.4*
HAL			
EO group	7.6 ± 2.2	6.0 ± 1.4*	5.7 ± 1.6*
Control group	8.2 ± 2.4	6.4 ± 2.1*	6.2 ± 1.2*

CAL, clinical attachment level; CHX, chlorhexidine; EO, essential oil; HAL, horizontal attachment level; PD, pocket depth; PGM, position of gingival margin.
*Post-treatment PD, PGM, CAL and HAL scores were statistically significant compared to the baseline scores in all groups ($P < 0.05$).

in PD at 3 months compared to baseline was 3.34, 3.2 and 3.26 mm in the CHX, EO and control groups, respectively. The mean gain in CAL and HAL compared to baseline values was 1.9 and 1.8, 1.9 and 1.9, and 1.8 and 2 mm in the CHX, EO and control groups, at 3 months, respectively. Position of gingival margin scores increased throughout the study period, and significant differences were found at 1 and 3 months compared to baseline scores for all groups ($P < 0.05$), (Table 4). There were no significant differences in intergroup comparisons at any time point for gingival recession ($P > 0.05$). The mean increase in gingival recession was 1.5, 1.3 and 1.3 mm in the CHX, EO and control groups, respectively, at 3 months (Table 4).

Discussion

The mechanical removal of subgingival microbial biofilms is essential for controlling inflammatory periodontal diseases because local bacteria are the primary aetiologic factors in the development of the disease (1). Ultrasonic mechanical instrumentation is as effective as manual debridement regarding clinical attachment gain, PD reduction and BOP reduction (5, 6, 26). Further, UMI appears to be effective in disrupting the biofilm and removing bacterial deposits from the root surface with only minimal loss of tooth substance (6, 7, 27). With special slim and probe-shaped tips, anatomically difficult areas can be treated more effectively than with hand curettes (12).

The lower success rate in the treatment of FI may result from the incomplete removal of subgingival plaque and calculus in the interradicular area owing to the peculiar anatomy of the furcation space (10, 11). Furthermore, the microbial shift after periodontal debridement may be transient, and bacterial recolonization of the root surface by pathogenic bacteria, which frequently occurs after treatment, may lead to disease recurrence (8, 9). Therefore, subgingival irrigations with antimicrobials may help therapists treat refractory sites with tortuous pockets or furcations where solutions can penetrate into areas inaccessible to instrumentation. In this concept, topical applications of subgingival antibiotics are used as an adjunct therapy for the treatment of furcation involvements (12, 13, 28, 29). Recently, Dannewitz *et al.* (29) investigated the adjunctive effect of subgingival application of doxycycline gel on scaling and root planing (SRP) for the treatment of FI. The authors reported that the use of subgingival doxycycline had a moderate short-term effect on FI. However, multiple applications were required to achieve this effect, and repeated use of antibiotics presents the risk of hypersensitivity reactions, systemic toxicity and development of bacterial resistance (30).

Ultrasonic or sonic debridement routinely uses water as a coolant, but it is possible to utilize a chemotherapeutic agent as an irrigant. Povidone-iodine (PVP-I) is an effective antiseptic and is also used as adjunct therapy to SRP in FI (31, 32). Del Peleso Ribeiro *et al.* (32) evaluated the effect of 10% PVP-I, used as the cooling liquid of an ultrasonic instrumentation in conjunction with subgingival root debridement of FI. They stated that topical application of PVP-I provided limited additional benefits to ultrasonic debridement. However, the topical use of PVP-I presents the risk of hypersensitivity reactions and staining of the tooth surface and mucosa; further, its prolonged use has been associated with thyroid dysfunction (33–35).

The most commonly studied antiseptic is CHX, and it is considered as the most effective antimicrobial for supragingival plaque control (12). It has also been used as an irrigant in ultrasonic scaling devices at varying concentrations. Some studies have indicated a slight adjunctive effect with CHX (36), while others have not (37). Recently, Guarnelli *et al.* (38) investigated the adjunctive effect of CHX with UMI in aggressive periodontitis patients. They reported that the professional use of CHX with UMI showed no additional benefits over UMI alone in aggressive periodontitis patients. Consistent with this report, in the current study, the CHX group did not show statistically significant CAL and PD reductions when compared with the other groups.

One important indicator of the success of subgingival debridement is the effective reduction in periodontal inflammatory symptoms, like BOP. In the present study, the EO group showed significant reduction in BOP scores compared to the CHX and control groups at 1 month. This may be explained by the lack of interaction with blood and fluid proteins in the case of EOs; however, there are no data to support this. In addition, EOs did not foam when used as an irrigation solution with UMI; therefore, subgingival instrumentation could be performed more efficiently than with the CHX group. Recently, Feng *et al.* (20) compared the clinical efficacy of UMI irrigated with EOs (test group) and water (control group) at the residual pockets. They stated that the test group showed additional CAL gain and PD reduction when compared to those of the control group.

In conclusion, within the limits of the present study, the use of EOs as a cooling agent for ultrasonic instrumentation promote slight adjunctive effect compared to CHX and water at the FI. Long-term, controlled clinical trials with large populations are required to verify the potential effects of the use of antimicrobials as cooling agents at the furcation sites.

Acknowledgements

The authors report no conflicts of interest related to this study.

References

1 Van Dyke TE. The management of inflammation in periodontal disease. *J Periodontol* 2008; **79:** 1601–1608.

2 Claffey N, Loos B, Gantes B, Martin M, Heins P, Egelberg J. The relative effects of therapy and periodontal disease on loss of probing attachment after root debridement. *J Clin Periodontol* 1988; **15:** 163–169.

3 Huynh-Ba G, Kuonen P, Hofer D, Schmid J, Lang NP, Salvi GE. The effect of periodontal therapy on the survival rate and incidence of complications of multirooted teeth with furcation involvement after an observation period of at least 5 years: a systematic review. *J Clin Periodontol* 2009; **36:** 164–176.

4 Van der Weijden GA, Timmerman MF. A systematic review on the clinical efficacy of subgingival debridement in the treatment of chronic periodontitis. *J Clin Periodontol* 2002; **29 (Suppl. 3):** 55–71.

5 Tomasi C, Leyland AH, Wennström JL. Factors influencing the outcome of non-surgical periodontal treatment: a multilevel approach. *J Clin Periodontol* 2007; **34:** 682–690.

6 Ioannou I, Dimitriadis N, Papadimitriou K, Sakellari D, Vouros I, Konstantinidis A. Hand instrumentation versus ultrasonic debridement in the treatment of chronic periodontitis: a randomized clinical and microbiological trial. *J Clin Periodontol* 2009; **36:** 132–141.

7 Del Peloso Ribeiro E, Bittencourt S, Nociti FH Jr, Sallum EA, Sallum AW, Casati MZ. Comparative study of ultrasonic instrumentation for the non-surgical treatment of interproximal and non-interproximal furcation involvements. *J Periodontol* 2007; **78:** 224–230.

8 Quirynen M, Papaioannou W, van Steenberghe D. Intraoral transmission and the colonization of oral hard surfaces. *J Periodontol* 1996; **67:** 986–993.

9 Quirynen M, De Soete M, Dierickx K, van Steenberghe D. The intra-oral translocation of periodontopathogens jeopardizes the outcome of periodontal therapy. A review of the literature. *J Clin Periodontol* 2001; **28:** 499–507.

10 Svärdström G, Wennström JL. Furcation topography of the maxillary and mandibular first molars. *J Clin Periodontol* 1988; **15:** 271–275.

11 Nordland P, Garrett S, Kiger R, Vanooteghem R, Hutchens LH, Egelberg J. The effect of plaque control and root debridement in molar teeth. *J Clin Periodontol* 1987; **14:** 231–236.

12 Greenstein G; Research, Science and Therapy Committee of the American Academy of Periodontology. Position paper: the role of supra- and subgingival irrigation in the treatment of periodontal diseases. *J Periodontol* 2005; **76:** 2015–2027.

13 Krayer JW, Leite RS, Kirkwood KL. Non-surgical chemotherapeutic treatment strategies for the management of periodontal diseases. *Dent Clin North Am* 2010; **54:** 13–33.

14 Pistorius A, Willershausen B, Steinmeier EM, Kreislert M. Efficacy of subgingival irrigation using herbal extracts on gingival inflammation. *J Periodontol* 2003; **74:** 616–622.

15 Gunsolley JC. Clinical efficacy of antimicrobial mouthrinses. *J Dent* 2010; **38 (Suppl. 1):** S6–S10.

16 Gürgan CA, Zaim E, Bakirsoy I, Soykan E. Short-term side effects of 0.2% alcohol-free chlorhexidine mouthrinse used as an adjunct to non-surgical periodontal treatment: a double-blind clinical study. *J Periodontol* 2006; **77:** 370–384.

17 McCoy LC, Wehler CJ, Rich SE, Garcia RI, Miller DR, Jones JA. Adverse events associated with chlorhexidine use: Results from the Department of Veterans Affairs Dental Diabetes Study. *J Am Dent Assoc* 2008; **139:** 178–183.

18 Carlin V, Matsumoto MA, Saraiva PP, Artioli A, Oshima CT, Ribeiro DA. Cytogenetic damage induced by mouthrinses formulations in vivo and in vitro. *Clin Oral Investig* 2011, doi: 10.1007/s00784-011-0559-2.

19 Cavalca Cortel li S, Cavallini F, Regueira Alves MF, Alves Bezerra A Jr, Queiroz CS, Cortelli JR. Clinical and microbiological effects of an essential-oil-containing mouth rinse applied in the ''one-stage full-mouth disinfection'' protocol – a randomized doubled-blinded preliminary study. *Clin Oral Investig* 2009; **13:** 189–194.

20 Feng HS, Bernardo CC, Sonoda LL *et al.* Subgingival ultrasonic instrumentation of residual pockets irrigated with essential oils: a randomized controlled trial. *J Clin Periodontol* 2011; **38:** 637–643.

21 Fine DH, Markowitz K, Furgang D *et al.* Effect of an essential oil-containing antimicrobial mouthrinse on specific plaque bacteria in vivo. *J Clin Periodontol* 2007; **34:** 652–657.

22 Stoeken JE, Paraskevas S, van der Weijden GA. The long-term effect of a mouthrinse containing essential oils on dental plaque and gingivitis: a systematic review. *J Periodontol* 2007; **78:** 1218–1228.

23 Hamp SE, Nyman S, Lindhe J. Periodontal treatment of multirooted teeth. Results after 5 years. *J Clin Periodontol* 1975; **2:** 126–135.

24 Silness J, Loe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontol Scand* 1964; **22:** 121–135.

25 Loe H, Silness J. Periodontal disease in pregnancy I. prevalence and severity. *Acta Odontol Scand* 1963; **21:** 533–551.

26 Hallmon WW, Rees TD. Local anti-infective therapy: mechanical and physical approaches. A systematic review. *Ann Periodontol* 2003; **8:** 99–114.

27 Wennström JL, Tomasi C, Bertelle A, Dellasega E. Full-mouth ultrasonic debridement versus quadrant scaling and root planing as an initial approach in the treatment of chronic periodontitis. *J Clin Periodontol* 2005; **32:** 851–859.

28 Tomasi C, Wennström JL. Locally delivered doxycycline as an adjunct to mechanical debridement at retreatment of periodontal pockets: outcome at furcation sites. *J Periodontol* 2011; **82:** 210–218.

29 Dannewitz B, Lippert K, Lang NP, Tonetti MS, Eickholz P. Supportive periodontal therapy of furcation sites: non-surgical instrumentation with or without topical doxycycline. *J Clin Periodontol* 2009; **36:** 514–522.

30 Sloan B, Scheinfeld N. The use and safety of doxycycline hyclate and other second-generation tetracyclines. *Expert Opin Drug Saf* 2008; **7:** 571–577.

31 Rosling B, Hellström MK, Ramberg P, Socransky SS, Lindhe J. The use of PVP-iodine as an adjunct to non-surgical treatment of chronic periodontitis. *J Clin Periodontol* 2001; **28:** 1023–1031.

32 Del Peloso Ribeiro E, Bittencourt S, Ambrosano GM *et al.* Povidone-iodine used as an adjunct to non-surgical treatment of furcation involvements. *J Periodontol* 2006; **77:** 211–227.

33 Niedner R. Cytotoxicity and sensitization of povidone-iodine and other frequently used anti-infective agents. *Dermatology* 1997; **195:** 89–92.

34 Nobukuni K, Hayakawa N, Namba R *et al.* The influence of long-term treatment with povidone-iodine on thyroid function. *Dermatology* 1997; **195:** 69–72.

35 Clark WB, Magnusson I, Walker CB, Marks RG. Efficacy of Perimed antibacterial system on established gingivitis(I). Clinical results. *J Clin Periodontol* 1989; **16:** 630–635.

36 Reynolds MA, Lavigne CK, Minah GE, Suzuki JB. Clinical effects of simultaneous ultrasonic scaling and subgingival irrigation with chlorhexidine. Mediating influence of periodontal probing depth. *J Clin Periodontol* 1992; **19:** 595–600.

37 Allison C, Simor AE, Mock D, Tenenbaum HC. Prosol-chlorhexidine irrigation reduces the incidence of bacteremia during ultrasonic scaling with the Cavi-Med: a pilot investigation. *J Can Dent Assoc* 1993; **59:** 676–682.

38 Guarnelli ME, Franceschetti G, Manfrini R, Trombelli L. Adjunctive effect of chlorhexidine in ultrasonic instrumentation of aggressive periodontitis patients: a pilot study. *J Clin Periodontol* 2008; **35:** 333–341.