Saudi Dental Journal (2020) **32**, 194–199

King Saud University

Saudi Dental Journal

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Periodontal tray application of chlorine dioxide gel as an adjunct to scaling and root planing in the treatment of chronic periodontitis

Ira Komara *, **Edwin Alfa Winata, Agus Susanto, Ina Hendiani**

Department of Periodontics, Faculty of Dentistry, Universitas Padjadjaran, Indonesia

Received 29 April 2019; revised 21 August 2019; accepted 25 August 2019
Available online 28 August 2019

KEYWORDS

Periodontal tray;
Chlorine dioxide gel;
Chronic periodontitis;
Scaling and root planing

Abstract *Objective:* Clinical improvement after periodontal tray application of chlorine dioxide gel as an adjunct to scaling and root planing (SRP) in the treatment of chronic periodontitis was studied for a period of 30 days.

Materials and methods: The tray fabrication was performed in a dental laboratory using the Soft – Tray Sheets (Ultradent™), whereas scaling and root planing were done using ultrasonic scaler and hand instruments. A total of 36 subjects with chronic periodontitis were divided into 3 treatment groups: group I was treated with SRP procedure combined with the prescription-tray application of chlorine dioxide gel; group II was treated with SRP procedure with the application of chlorine dioxide alone; and group III was treated with SRP procedure alone. Clinical parameters examined were probing pocket depth (PPD) and papillary bleeding index (PBI); measurements were taken at baseline (day0) and 30 days after SRP (day 30). Comparison between treatment groups was tested statistically by Kruskal Wallis test and Analysis of Variance (ANOVA).

Results: There were significant differences in the decrease of the average pocket depth and bleeding index in all the 3 treatment groups ($P = 0.001$). Decreases in the pocket depth of groups I, II, and III were 50.9%, 47.9%, and 27.8%, respectively. Decreases in the papillary bleeding index of groups I, II, and III were 88.2%, 68.9%, and 51.1%, respectively.

Conclusion: The application of chlorine dioxide gel using the custom tray after SRP in the treatment of chronic periodontitis showed better clinical improvement in pocket depth reduction and bleeding index compared to SRP alone.

* Corresponding author at: Department of Periodontics, Faculty of Dentistry, Universitas Padjadjaran, Sekeloa Selatan I, Bandung 40132, Indonesia.
E-mail address: ira.komara@fkg.unpad.ac.id (I. Komara).

Peer review under responsibility of King Saud University.

ELSEVIER Production and hosting by Elsevier

1. Introduction

Chronic periodontitis is an inflammatory condition of the supporting tissues of the teeth induced by microorganisms that stimulate the host immune and inflammatory responses (Pihlstrom et al., 2005; Silva et al., 2015). The cause of this disease is multifactorial, characterized by chronic inflammation,

https://doi.org/10.1016/j.sdentj.2019.08.006
1013-9052

progressive clinical attachment loss, resorption of alveolar bone, and eventually tooth loss (Armitage, 1999; Pihlstrom et al., 2005). Treatment of periodontitis is important to eliminate infections around the dental tissue and also to improve systemic health in general (Teeuw et al., 2014).

Scaling and root planing as periodontal treatment aims to cure inflamed tissues, eliminate pockets, and reduce the number of pathogenic bacteria and products and is usually performed using mechanical instruments. Its effectiveness decreases as the probing pocket depth (PPD) increases, especially as PPD exceeds 5 mm, but generally can improve clinical and reduce disease progression. (Kaldahl et al., 1996). Overall debridement cannot be carried out especially in deep pockets and other areas that are difficult to achieve by mechanical instruments. This condition requires administration of additional chemotherapeutic agents in the form of local and systemic antibiotics to suppress or eliminate specific periodontal pathogenic microorganisms as part of periodontal therapy (Cobb, 1996; Greenstein, 2006).

Topical antiseptics and antibiotics can be used as adjunctive therapy, especially in recurrent periodontitis cases (refractory periodontitis). The antibiotic is used to inhibit or control bacterial infections as bacteria can invest in periodontal tissue, which makes non-surgical mechanical treatment such as scaling and root planing less effective in removing bacteria thus causing periodontal disease (Ciancio and Mariotti, 2012). The use of this antibacterial is an adjunctive therapy to the standard scaling and root planing treatment. Administration of antibacterial locally towards the periodontal pocket has a better potential because it is applied directly, with a higher concentration in the infectious area thus reducing the possibility of the medication's side effects (Ciancio and Mariotti, 2012; Goodson, 1994).

Chlorine dioxide (ClO2) is a little–known ingredient in oral hygiene yet, it is safe and effective for daily use. Chlorine dioxide, when stabilized in water and used in a low concentration effectively, will neutralize volatile sulfur compounds in the oral cavity (Mani et al., 2012). It has the ability to inhibit *Enterobacter faecalis* bacteria; this makes this material effective as an endodontic irrigant (Eddy et al., 2005). Previous studies have shown the positive effects of chlorine dioxide in the inhibition of volatile sulfur compound formation (Frascella et al., 1998; Frascella et al., 2000; Peruzzo et al., 2007). The effectiveness of chlorine dioxide in periodontal disease was reported by Spindler and Spindler (1998). Chlorine dioxide has an antibacterial effect, is easy to use, and is widely available (Spindler and Spindler, 1998). Various companies have used chlorine dioxide as the main ingredient in oral medicine, especially in the treatment of periodontal disease (Al-bayaty et al., 2010).

The amount of gel concentration in the pocket needs to be maintained; thus, an appliance to deliver the gel into the pocket will be needed to maintain the level in the pocket for a longer period. One appliance that can be used is a horizontal tray, the design of which has to be adjusted to the patient's periodontal conditions. The advantage of using this periodontal tray is that patients can use it daily at home between office visits to deliver chlorine dioxide (and other drugs) to the periodontal pocket has shown effective for supra and subgingival biofilm management (Dunlap et al., 2011). Previous research on the effects of tray applications has been reported by Lazarchik and Van Haywood (2010); Putt and Proskin (2012); the study used peroxide and carbamide peroxide gel. To the best of our knowledge, effect of tray application with chlorine dioxide has never been conducted. This study was performed to determine the effect of scaling and root planing alone or combined with the application of chlorine dioxide gel using customized trays in the treatment of chronic periodontitis.

2. Materials and methods

2.1. Study design

This was a randomized controlled study, and the study subjects were patients who visited the periodontic clinic of Universitas Padjadjaran Dental Hospital. The research design has already been approved by the Health Research Ethics Committee of the Faculty of Medicine Universitas Padjadjaran with the registration number of 178/UN6.KEP/EC/2018.

2.2. Eligibility criteria

The inclusion criteria were patients who were older than 30 years, were diagnosed with chronic periodontitis with a pocket depth ≥ 4 mm, and willingly took part in this study by signing informed consent. Determination of chronic periodontitis other than based on pocket depth and radiograph examination as well. The exclusion criteria were patients with systemic disease, patient who received periodontal treatment in the previous 6 months, patients who were smokers, and patients who used dental prostheses or an orthodontic device. A sample size of minimum of 12 subjects in each group was identified using power test 95% and level of confidence 95%, incorporating means and standard deviations from previous studies (Putt et al., 2014). The patients fulfilling the criteria were allocated a number following recruitment and randomized into three groups: group I was treated with scaling and root planing (SRP) procedure combined with the prescription–tray application of chlorine dioxide gel; group II was treated with SRP procedure with the application of chlorine dioxide; and group III was treated with SRP procedure alone. Chlorine dioxide gel is a material that has been produced and is available on the market (Oxyfresh, USA).

2.3. Fabrication of individual tray

Before fabricating a periodontal tray, a working model was needed on the subjects who had been treated with scaling and root planing a week earlier. The tray shape was similar to the home bleaching tray. Fabrication with the suction method was done using the Sof-Tray Sheets (Ultradent™) with the thickness of 2 to 3 mm. The design of the tray was adjusted to the patient's oral condition, had a seal or closure at the gingival margin. The seal fabrication was intended so the medication application by the tray can be pushed into the pocket. The tray fabrication was performed in a dental laboratory (Fig. 1).

2.4. Clinical periodontal assessments

Clinical assessment is carried out by examiners who were blinded to the treatment. Papillary Bleeding Index (Saxer and Müehlemann) was determined by periodontal probe is

inserted into the gingival sulcus at the base of the papilla on the mesial aspect, and then moved coronally to the papilla tip. This is repeated on the distal aspect of the papilla (Rebelo and De Queiroz., 2011). Observation of bleeding (score) after 30 s. Probing pocket depth (PPD) was measured using the UNC-15 (Osung, Korea) periodontal probe as distance in millimeters from the gingival margin to the attached periodontal tissue. Clinical measurements were taken at six locations (mesiobuccal, buccal, distobuccal, mesiolingual, lingual, and distolingual).

2.4.1. Papillary bleeding index

Papillary Bleeding Index by Saxer and Müehlemann was as follows (Wolf and Hassell, 2011): Score 0 – no bleeding;

Score 1 – bleeding forms a point;
Score 2 – bleeding forms a line;
Score 3 –bleeding forms a triangle;
Score 4 – bleeding spreads

2.5. Treatment procedures

All research subjects received initial scaling and root planing (SRP) treatment using ultrasonic and hand instruments (Al Hulami et al., 2011; Pietrzak and Brzezińska, 2012). Clinical parameters measured before treatment were the papillary bleeding index (PBI) and pocket depth (PPD) measurements. Group I and II received the application of chlorine dioxide gel which was inserted into the pocket using a syringe after the SRP. In Group I, the casting with alginate material was carried out on day 7 to avoid distortion due to gingival enlargement in chronic periodontitis patients. The working stage of an individual tray was performed in the laboratory using a vacuum. The use of tray on the research subjects was carried out on day 10 after SRP.

The researcher provided instructions on the usage the periodontal tray. Chlorine dioxide was applied to the tray with a blunt–tip syringe every day. The tray was fitted to the correct jaw arch. Installation of the tray was done after the patient completed brushing. The tray usage was carried out twice a day in the morning and night after brushing. Tray is used for ten minutes using the stop watch timer. The use of the gel was precisely measured for 1 ml in the tray so that as much as 40 ml was needed (1 ml × 2 times daily (morning and night) × 20 days) during the period of 20 days the use of the gel was a method of monitoring for the home usage. Patients were instructed to bring the tubes on recall visits which were every 10 days to check for compliance. On day 30 after SRP, as well as on the first visit, the operator measured the PPD and PBI in the teeth studied in the entire group.

Fig. 1 Individual periodontal soft tray.

2.6. Statistical analysis

Statistical analysis was performed using SPSS 20.0 (New York, USA), with a Shapiro–Wilk test used to test data normality. All data were presented in the form of averages ± SD; the percentage of decreases (%), differences in PPD, PBI, and percentage (%) between all the treatment groups were analyzed statistically using the Kruskal–Wallis test and Analysis of Variance (ANOVA), with the significant difference (P-value) < 0.05.

3. Results

The study consisted of 36 subject, 22 men and 14 women, aged between 31 and 72 years (Table 1). The average decreases in the pocket depth before and after SRP in group I, II, and III were 50.9%, 47.9%, and 27.8%, respectively. There was a significant difference ($P = 0.001$), where the decrease in the pocket depth was found to be higher in group I which used a tray with chlorine dioxide (Table 2). The decreases in the gum bleeding index in group I, II, and III were 88.2%, 68.9%, and 51.1%, respectively, and was statistically significant ($P = 0.001$; Table 3).

4. Discussion

Primary goal of periodontal therapy are reduction/elimination of bacteria communities (biofilm) on tooth surface and in periodontal pockets and management of inflammatory responses associated with these localized biofilm infection (Hung and Douglas, 2002). Periodontitis can be treated with non-surgical treatments such by way of scaling, root planing, and the use of chemotherapeutic agents, in combination with instructions to patients to maintain their oral hygiene. In our study, each subject received scaling and root planing treatment as the initial therapy; in group I, a periodontal tray was used with the application of chlorine dioxide gel, while in group II, chlorine dioxide was applied without the periodontal tray. The results showed that use of a periodontal tray with the application of chlorine dioxide gel was proven to be more effective in decreasing the pocket depth and bleeding index compared with SRP or chlorine dioxide application alone. The result of our study was consistent with previous studies using the custom tray with peroxide gel. The study conducted by Putt and Proskin (2012) showed that the use of peroxide gel with tray in combination with SRP was statistically significantly more effective than the traditional SRP therapy alone in reducing pocket depth and gum bleeding 10 weeks after

Table 1 Research Subject Characteristics.

Characteristics	Group			P-value*
	I (n = 12)	II (n = 12)	III (n = 12)	
Gender:				
Men	8	6	8	0.627
Women	4	6	4	
Age (y):				
Mean (SD)	42.2 (11.9)	40.2 (8.3)	39.9 (8.0)	0.958
Range	31–72	31–61	31–59	

Notes:
Group I = SRP + Chlorine Dioxide Gel + Periodontal Tray.
Group II = SRP + Chlorine Dioxide Gel.
Group III = SRP.
* gender was tested with Chi-Square; age was tested with Mann –Whitney.

Table 2 Results of Pocket Depth (PPD) Measurement on Day 0 and Day 30.

Periodontal Pocket Depth (mm)	Group			P-value
	I (n = 12)	II (n = 12)	III (n = 12)	
Day 0 (Baseline):				
Mean (SD)	4.37 (0.517)	4.51 (0.621)	4.47 (0.442)	0.637*
Range	3.83–5.58	3.83–6.33	3.75–5.29	
Day 30:				
Mean (SD)	2.14 (0.31)	2.33 (0.25)	3.23 (0.39)	< 0.001**
Range	1.67–2.83	2.00–2.83	2.75–4.04	
% Decrease (Average)	50.9%	47.9%	27.8%	< 0.001**

Notes:
* Kruskal–Wallis Test.
** F-test (Variance Analysis).

Table 3 Results of Bleeding on Probing (BOP) Index Measurement on Day 0 and Day 30.

Bleeding on Probing	Group			P-value*
	I (n = 12)	II (n = 12)	III (n = 12)	
Day 0 (Baseline):				
Mean (SD)	3.10 (0.39)	3.04 (0.68)	3.17 (0.58)	0.863
Range	2.5–4.0	1.75–4.00	2.0–4.0	
Day 30:				
Mean (SD)	0.37 (0.25)	0.94 (0.50)	1.56 (0.48)	< 0.001
Range	0.0–0.75	0.0–2.0	1.0–2.5	
% Decrease (Average)	88.2%	68.9%	51.1%	< 0.001

Notes:
* F-test (Variance Analysis).

SRP. In our study, the use of chlorine dioxide gel application was followed with the evaluation time of 30 days after SRP, while in the studies by Putt and Proskin, the use of peroxide gel application was followed with a longer evaluation time of 10 weeks.

Application of intra-sulcular chlorine dioxide after SRP could reduce the periodontal pocket depth (PPD) greater than the SRP group alone. The research conducted by Splinder in 1998 stated that the use of chlorine dioxide in periodontal treatment was able to reduce the periodontal pocket depth.

The use of chlorine dioxide was able to reduce the periodontal pocket depth by more than 4 mm to ≤ 3 mm. Intra-sulcular administration of chlorine dioxide gel can degrade the Volatile Sulfur Compounds (VSCs) that cause bad breath and periodontal disease (Mani et al., 2012). Increasing oxygen concentration in periodontal pockets is not beneficial for anaerobic pathogenic bacteria; thus, reduction in the number of anaerobic pathogenic bacteria in the periodontal pocket allows better periodontal tissue repair. Another study on the effect of chlorine dioxide conducted by Al-Bayaty et al. (2010) concluded that chlorine dioxide gel had a strong antibacterial effect against dental biofilms, and can be proposed as a good alternative compound for the development of professional gel to control and inhibit various types of dental biofilms and microorganisms (Al-Bayaty et al., 2010).

Intra-sulcular addition of chlorine dioxide gel helps the wound healing process from the initial stages so that the daily use of periodontal tray with an application of chlorine dioxide gel becomes less meaningful. The ability of ClO2 to inhibit the growth of both aerobic and anaerobic pathogenic bacteria in forming dental biofilms helps the wound healing process. Research conducted by Kandwal and Ghani (2014) regarding mouthwash and toothpaste that contained chlorine dioxide showed its effects on decreasing the plaque biofilm formation. The bactericidal effect of chlorine dioxide was able to prevent the formation of dental biofilm (Kandwal and Ghani, 2014). The reduction in the PPD showed the remodelling phase that occurred in the healing process of periodontal tissue. In this phase, there are proliferation and migration of fibroblasts which then stimulate the collagen synthesis as an extracellular matrix. Fibroblasts and collagen formed in periodontal tissues cause an increase in the tissue pressure which increases the tissue resistance towards the probing pressure which clinically causes a pocket depth reduction (Polimeni et al., 2006).

Application of chlorine dioxide gel by the addition of periodontal tray after scaling and root planing can reduce the gingival bleeding index of chronic periodontitis patients. Gingival bleeding and increase in the gingival fluid are early signs of inflammation. Gingival bleeding varies depending on the severity and can be clinically detected easily. Changes in the morphology and gingival function will occur along with the plaques formation and attachment to the teeth. Plaque is a soft layer consisting of a group of microorganisms that multiply and attach to the surface of uncleaned teeth. Microorganisms formed in dental plaque are the main cause of gingivitis because these microorganisms produce toxins that can enter the tissues and cause gingival damage (Marriotti, 1999).

With a gingival fluid increase, the gel concentration in the gingival pocket will decrease. Addition of periodontal tray is used to maintain the amount of gel in the periodontal pocket so that bacterial colonization in the pocket and the teeth surface will be controlled. The use of periodontal tray can overcome the problem of increasing gingival fluid because of the benefits of the tray as a chlorine dioxide gel reservoir that serve as a tool to channel the gel back into the pocket with mechanical procedures that can be performed by patients at home (Putt et al., 2014).

Scaling and root planing is an initial stage of periodontal treatment, while the addition of chlorine dioxide gel afterwards is an additional therapy to support the success of SRP. The gel has a positive effect on wound healing and bacterial growth control. The disadvantage of chlorine dioxide gel is the presence of gingival fluid which can reduce the ability of chlorine dioxide to inhibit the pathogenic bacteria growth. The use of local delivery antimicrobial agents (LDAs) by placing them into periodontal pockets was aimed at reducing the subgingival bacterial flora and the clinical signs of periodontitis. Local delivery agent that provide antimicrobial or chemotherapeutic activity as adjuncts to SRP for deeper pocket (≥5 mm) of chronic periodontitis patient's (Puri and Puri, 2013). The limitation of this study is the short evaluation period of 30 days. An evaluation over a longer period is required to provide a clearer picture of the role of the custom tray use and chlorine dioxide in non-surgical SRP treatment. The reduction in pocket depth in this study was investigated in a relatively shallow pockets, therefore it cannot be extrapolated in patients with deep pockets. Further evaluation and study are needed to clarify such this results.

5. Conclusion

Under the limitation of this study, the application of chlorine dioxide gel using the custom tray as an adjunct to chronic periodontitis treatment showed better clinical improvements in pocket depth reduction and bleeding index compared to SRP alone.

Ethical approval

The article ethical approved by the Health Research Ethics Committee of the Faculty of Medicine Universitas Padjadjaran with the registration number of 178/UN6.KEP/EC/2018.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not for profit sector.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Al-Bayaty, F., Taiyeb-Ali, T., Abdulla, M.A., Hashim, F., 2010. Antibacterial effect of chlorine dioxide and hyaluronate on dental biofilm. Afr. J. Microbiol Res. 4 (14), 1525–1531.

Al Hulami, H., Babay, N., Awartani, F., Anil, S., 2011. The effect of locally delivered doxycycline as an adjunctive therapy to scaling and root planing in smokers. Saudi Dent. J. 3 (3), 143–148.

Armitage, G.C., 1999. Development of a classification system for periodontal diseases and conditions. Ann. Periodontol. 4 (1), 1–6.

Ciancio, S., Mariotti, A., 2012. Antiinfective therapy. In: Newman, M. G., Takei, H.H., Klokkevold, P.R., Carranza, F.A. (Eds.), Carranza's clinical periodontology. 11th ed. St. Louis: Elsevier, pp. 482–491.

Cobb, C.M., 1996. Non-surgical pocket therapy: mechanical. Ann. Periodontol. 1 (1), 443–490.

Dunlap, T., Keller, D.C., Marshall, M.V., William Costerton, J., Schaudinn, C., Sindelar, B., Cotton, J.R., 2011. Subgingival delivery of oral debriding agents: a proof of concept. J. Clin. Dent. 22 (5), 149–158.

Eddy, R.S., Joyce, A.P., Roberts, S., Buxton, T.B., Liewehr, F., 2005. An in vitro evaluation of the antibacterial efficacy of chlorine dioxide on E. faecalis in bovine incisors. J. Endod. 31 (9), 672–675.

Frascella, J., Gilbert, R., Fernandez, P., 1998. Odor reduction potential of a chlorine dioxide mouthrinse. J. Clin. Dent. 9 (2), 39–42.

Frascella, J., Gilbert, R.D., Fernandez, P., Hendler, J., 2000. Efficacy of a chlorine dioxide-containing mouthrinse in oral malodor. Compend. Contin. Educ. Dent. (Jamesburg, NJ: 1995) 21 (3), 241–244.

Goodson, J.M., 1994. Antimicrobial strategies for treatment of periodontal diseases. Periodontol 2000 (5), 142–168.

Greenstein, G., 2006. Local drug delivery in the treatment of periodontal disease: assessing the clinical significance of the results. J. Periodontol. 77 (4), 565–578.

Hung, H.C., Douglas, C.W., 2002. Meta-analysis of the effect of scaling and root planning, surgical treatment and antibiotic therapies on periodontal probing depth and attachment loss. J. Clin. Periodontol. 29, 975–986.

Kaldahl, W.B., Kalkwarf, K.L., Patil, K.D., Molvar, M.P., Dyer, J.K., 1996. Long-term evaluation of periodontal therapy: I. Response to 4 therapeutic modalities. J. Periodontol. 67 (2), 93–102.

Kandwal, A., Ghani, B., 2014. A comprative evaluation of effect of chlorine dioxide mouthrinse on plaque induced gingivitis and oral malodor: a clinical study. Int. J. Dent. Health Sci. 1 (1), 24–33.

Lazarchik, D.A., Van Haywood, B., 2010. Use of tray-applied 10 percent carbamide peroxide gels for improving oral health in patients with special-care needs. J. Am. Dent. Assoc. 141 (6), 639–646.

Mariotti, A., 1999. Dental plaque-induced gingival diseases. Ann. Periodontol. 4 (1), 7–19.

Mani, S., Mani, A., Saini, R., 2012. Chlorine dioxide: a potential mouthrinse for oral health. Int. J. Exp. Dent. Sci. 1, 118–189.

Peruzzo, D.C., Jandiroba, P.F., Nogueira Filho, G.D., 2007. Use of 0.1% chlorine dioxide to inhibit the formation of morning volatile sulphur compounds (VSC). Braz. Oral Res. 21 (1), 70–74.

Pietrzak, A., Brzezińska-Błaszczyk, E., 2012. Effect of scaling and root planing on interleukin-1β, interleukin-8 and MMP-8 levels in gingival crevicular fluid from chronic periodontitis patients. J. Periodontal Res. 47 (6), 681–688.

Pihlstrom, B.L., Michalowicz, B.S., Johnson, N.W., 2005. Periodontal diseases. Lancet 366 (9499), 1809–1820.

Polimeni, G., Xiropaidis, A.V., Wikesjö, U.M., 2006. Biology and principles of periodontal wound healing/regeneration. Periodontol 2000 41 (1), 30–47.

Putt, M.S., Proskin, H.M., 2012. Custom tray application of peroxide gel as an adjunct to scaling and root planing in the treatment of periodontitis: a randomized, controlled three-month clinical trial. J. Clin. Dent. 23 (2), 48–56.

Putt, M.S., Mallatt, M.E., Messmann, L.L., Proskin, H.M., 2014. A 6-month clinical investigation of custom tray application of peroxide gel with or without doxycycline as adjuncts to scaling and root planing for treatment of periodontitis. Am. J. Dent. 27 (5), 273–284.

Puri, K., Puri, N., 2013. Local drug delivery agents as adjuncts to endodontic and periodontal therapy. J. Med. Life. 6 (4), 414–419.

Rebelo, M.A.B., De Queiroz, A.C., 2011. Gingival indices: state of art. In *Gingival diseases-their aetiology, prevention and treatment*. IntechOpen.

Silva, N., Abusleme, L., Bravo, D., Dutzan, N., Garcia-Sesnich, J., Vernal, R., Hernandez, M., Gamonal, J., 2015. Host response mechanisms in periodontal diseases. J. Appl. Oral Sci. 23 (3), 329–355.

Spindler, S.J. and Spindler, G.A., 1998. Evaluation of a stabilized chlorine dioxide paste-rinse combination regimen vs. a phenol-related rinse regimen.

Teeuw, W.J., Slot, D.E., Susanto, H., Gerdes, V.E., Abbas, F., D'aiuto, F., Kastelein, J.J., Loos, B.G., 2014. Treatment of periodontitis improves the atherosclerotic profile: a systematic review and meta-analysis. J. Clin. Periodontol. 41 (1), 70–79.

Wolf, H.F., Hassell, T.M., 2011. Color atlas of dental hygiene: Periodontology. Thieme, New York, pp. 69–70.