PERI-IMPLANTITIS: A REVIEW STUDY

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ABSTRACT:

AIM:
The aim of the review was to evaluate the scientific literature regarding the peri-implantitis.

BACKGROUND:
Peri-implantitis was described as a destructive inflammatory lesion affecting hard and soft tissues of the osseointegrated implant causing bone loss and peri-implant pocketing. Peri-implantitis can be asymptomatic, showing only signs of bleeding on probing, attachment loss, and bone loss. Or peri-implantitis can manifest clinical signs of increasing probing depths, suppuration, draining sinus, and peri-implant mucosal swelling or recession. If peri-implantitis was not detected early and treated, the bony destruction could extend the whole lengthen of the implant, resulting in loss of implant stability. Thus, early peri-implantitis detection and effective treatment is crucial in a practice that focuses on implant rehabilitation of the edentulous patient.

REASON:
The aim of this comprehensive review was to provide a systematically derived overview of systematic reviews pertaining to different aspects of peri-implantitis that will help the clinician understand and manage peri-implantitis in their practice.

KEYWORDS: dental implant**,** peri-implant**,** bone loss**,** peri-implantitis**,** Mucositis

INTRODUCTION:
Dental implants have become widely used in restoring the fully or partially edentulous patient. They have become a predictable alternative to fixed and removable partial dentures and were often the treatment of choice.(1) High implant survival rates of 92.8%–97.1% over a follow-up period of 10 years indicated that dental implants were a valid treatment option for the dental rehabilitation of the partially and fully edentulous patient (2). However, despite its high survival rates, dental implants were prone to biological complications like peri-implantitis (3). Indeed, this shift of composition within biofilms is concomitant with an increase in anaerobic bacterial species such as Porphyromonas gingivalis, Prevotella intermedia, Eikenella corrodens, Actinomyces naeslundi on the surface of the dental implants (4). The prevalence of periimplantitis ranges from 4% to 45% according to the definition used and sample population (5).

Peri-implantitis was described as a destructive inflammatory lesion affecting hard and soft tissues of the osseointegrated implant causing bone loss and peri-implant pocketing (6). Peri-implantitis can be asymptomatic, showing only signs of bleeding on probing, attachment loss, and bone loss. Or peri-implantitis can manifest clinical signs of increasing probing depths, suppuration, draining sinus, and peri-implant mucosal swelling or recession (7). If peri-implantitis was not detected early and treated, the bony destruction could extend the whole lengthen of the implant, resulting in loss of implant stability (8). Thus, early peri-implantitis detection and effective treatment is crucial in a practice that focuses on implant rehabilitation of the edentulous patient.

Some studies indicated that patients, who have lost 1 implant due to peri-implantitis, were more prone to implant failure (9). Patients with periodontal disease seemed to experience more implant loss due to peri-implantitis than periodontally healthy patients (10). Patients who smoke were also at risk for peri-implantitis, but non-smoking patients can develop peri-implantitis, and not all smoking patients develop peri-implantitis (11). Radiographically, patients with periodontitis and smokers have also reported significantly more marginal bone loss around their implants (12). Thus, these factors predisposing peri-implantitis should be closely examined when treatment planning the dental patient for implants. For instance, laser treatments, antiseptics, and antibiotics have been reported as curative alternatives (13). To develop and evaluate potential periimplantitis treatment procedures, several in vitro studies have been and are still conducted.

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Diagnostic findings for peri-implantitis

There were higher levels of proinflammatory cytokines in the peri-implant crevicular fluid of implants with peri-implantitis than in healthy implants (14). The studies included in both systematic reviews were heterogeneous regarding the diagnosis of peri-implantitis. IL-1β release and TNF-α release was significantly higher in peri-implantitis compared to healthy peri-implant mucosa (15). However, the IL-1β levels in peri-implantitis was not statistically significant when compared to peri-implant mucositis

(16). Increased levels of IL-1β and TNF-α in peri-implant crevicular fluid from sites with peri-implantitis have been related to increased gingival index, probing depth, bleeding on probing, and bone loss (17). Other cytokines like IL-4, IL-6, IL-8, IL-10, IL-12, and IL-17 have also been investigated for a link to peri-implantitis. These proinflammatory or anti-inflammatory cytokines associated with peri-implantitis increased with peri-implant establishment and progression (18).

Microbial findings for peri-implantitis

The microbiologic profile of peri-implantitis is different from periodontitis and can be complex and variable (19). It consists of aggressive and resistant microorganisms and may include opportunistic microorganisms, gram-negative anaerobic pathogens, gram-positive nonsaccharolytic anaerobic rods, and Epstein–Barr virus. Although conflicting results have been reported, the following microorganisms were found to be more prevalent in peri-implantitis (20) than in peri-implant health: *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Treponema denticola*, human herpesvirus 4 and 5, Epstein–Barr 1, and human cytomegalovirus 2 (21). In addition, microorganisms such as *Tannerella forsythia*, *Porphyromonas gingivalis*, *Treponema socranskii*, *Staphylococcus aureus*, *Staphylococcus anaerobius*, *Staphylococcus intermedius*, and *Streptococcus mitis* were also found comprising 30% of the total microbiota at peri-implantitis sites (22). Peri-implantitis sites have higher mean colony-forming units in peri-implantitis sites compared with healthy sites (23). The reported active periodontal pathogens are not limited to periodontopathic bacteria, and can include opportunistic bacteria like *Staphylococcus aureus*, *Staphylococcus intermedius*, *Streptococcus mitis*, and *Haemophilus influenza* (24).

Effects of systemic disease on peri-implantitis

Patients with diabetes were at a higher risk of peri-implantitis (25). The gingival index, probing depths, and bone loss were higher in poorly controlled compared to well-controlled diabetic peri-implantitis patients (26). However, conflicting results were reported for type 2 diabetes (27). Patients with cardiovascular disease were also at a higher risk of peri-implantitis (28). In addition, patients with peri-implantitis were found to have a 3 times greater chance of harboring Epstein–Barr virus (29). However, for patients with rheumatoid arthritis, statistical analysis demonstrated no associations (30).

Treatment Modalities:

There are several treatment modalities such as the non-surgical and surgical interventions to treat peri-implantitis. Non-surgical interventions focused on implant surface treatment and detoxification, with or without the use of an anti-microbial agent. The non-surgical interventions included manual debridement, manual debridement with chlorhexidine, ultrasonic debridement, air-abrasive device, local or systemic antibiotics, local antiseptic application, lasers, and host modulation therapy. Non-surgical therapy is most effective at removing only the local irritant from peri-implantitis and is not helpful in osseous defects. Surgical interventions focused on flap elevation, implant surface treatment, and detoxification, with or without the use of an anti-microbial agent, and with or without the use of membranes or grafting materials. The surgical treatments included (1) open-flap debridement with plastic or carbon curettes, ultrasonic scaler, rotating instruments, air powder, or soft laser treatment; (2) resective peri-implant surgery and implantoplasty; and (3) guided bone regeneration techniques with or without different types of membranes (synthetic membranes, resorbable bovine or porcine collagen) in combination with or without bone substitutes (demineralized freeze dried bone alone or in combination with growth factors, autogenous bone, hydroxyapatite, xenografts, and algae-derived calcium carbonate).

Various adjunctive therapies may improve the efficacy of conventional peri-implantitis treatment (31) Debridement together with antibiotics resulted in the greatest probing depth reduction compared to debridement only (32). At a short-term follow-up of 12 months, mechanical debridement and minocycline appeared to improve treatment outcomes of peri-implantitis when compared to debridement and chlorohexidine (33). The use of erbium: yttrium–aluminum–garnet (Er:YAG) laser and carbon dioxide (CO^2) lasers can improve short-term implant clinical parameters up to 6 months (34). Er:YAG laser treatment may also result in greater reduction in bleeding on probing (BOP) scores compared with submucosal debridement with adjunctive submucosal irrigation with chlorhexidine (35,36) Implantoplasty or lasers might provide equivalent effects when compared to other commonly used methods for surface decontamination (37). In addition, the use of submucosal glycine powder air polishing may greatly reduce BOP scores compared to submucosal irrigation with chlorhexidine digluconate and debridement; and produced similar clinical outcomes compared with Er:YAG laser treatment (38) Network meta-analysis of other non-surgical approaches in peri-implantitis treatment showed that single or combined non-surgical interventions also resulted in greater probing depth reduction than debridement alone (27)

In short-term follow-ups, surgical interventions reduced probing depth by 30%–50% of the initial probing depth (39). Although regenerative procedures can achieve a mean of 2–2.41 mm radiographic bone fill (25) and can improve clinical parameters of peri-implant tissues, the use of a guided bone regeneration protocol with membrane and bone graft does not seem to be predictable in treatment of peri-implantitis (40) When all surgical and non-surgical approaches were pooled together, surgical approaches showed greater improvements in probing depth and clinical attachment levels. However, when the surgical and non-surgical approaches were analyzed separately, the difference between the approaches were not statistically significant (41).
Successful treatment outcomes of peri-implantitis were described as post-treatment implants with a mean probing depth of less than 5 mm and no progressing bone loss. At 12 months' follow-up, Heitz-Mayfield et al (42) reported successful overall peri-implantitis

treatment outcomes for different combinations of adjunctive treatments for surgical and non-surgical interventions at 76%–100% of patients, and at 75%–93% of implants.

The treatment modalities include mechanical procedures, chemical treatment through the use of antimicrobials and combinations. Ultrasonic devices, manual curettes, air powder abrasion, titanium brush, implantoplasty, cold atmospheric pressure air plasma jet, electrolysis and laser have been assessed (43). Regarding laser systems, diode, carbon dioxide, Er:YAG and GaAlAs lasers with different wavelengths, irradiation times and irradiation modes (pulsed and continuous) were tested (44). Photodynamic therapy (PDT) through the use of laser and LED has been a popular treatment modality and was carried out for the decontamination of dental implant surfaces (15). Studies assessing antimicrobial treatments used different kinds of antiseptics and antimicrobial agents (36). These topical antiseptics used to treat the surfaces of the specimens were chlorhexidine gluconate 0.2%, hydrogen peroxide 3.0%, sodium hypochlorite 1.0%, cetylpyridinium chloride, essential oils or citric acid 40.0% (44). Metronidazole, amoxicillin and the combination of these two antibiotics were used to treat titanium discs covered with bacterial biofilms (36). Additionally, some other molecules or compounds were tested such as grape seed extract, oligosaccharide nanomedicine OligoG and Triethoxysilylpropyl Succinic Anhydride (TESPSA) silane application to determine their antimicrobial properties (37,38).

An effective peri-implantitis treatment requires the following conditions: (1) Removing biofilm from the implant surfaces and (2) Promoting the adhesion of osteoblasts [31]. However, effective debridement of oral biofilms on dental implant surfaces is difficult to achieve due to the rough surface and the design of dental implants in contrast to the surfaces of natural teeth [32]. Therefore, several approaches have been developed to treat peri-implantitis [33, 34]. In some studies, contradictory results have been found. For instance, studies comparing several treatment procedures did not have the same conclusion. The differences between them may be due to the equipment used or sample materials. Mechanical therapy induces significant changes in the composition and microstructure of titanium and implant surfaces as they might be damaged during treatment [11]. To reduce surface damage originated from metal-to-metal contact, a non-metallic instrument could be used [35]. However, these instruments have been shown to inadequately remove microorganisms from rough surfaces, and air-powder abrasive systems might be an interesting option. Implantoplasty also appeared to be a promising treatment because of inducing surface smoothness, surface hydrophily and purity [11]. Special attention should be paid to mechanical therapy because of the difficulty in visualizing the surface and to eliminate microorganisms [36]. Therefore, antibiotics or antiseptic agents have also been proposed to improve peri-implantitis treatment outcomes [15, 19, 23, 37].

REFERENCES:

[1] Tenenbaum H, Bogen O, Séverac F, Elkaim R, Davideau JL, Huck O. Long-term prospective cohort study on dental implants: Clinical and microbiological parameters. Clin Oral Implants Res 2017; 28(1): 86-94.

[2] Doornewaard R, Jacquet W, Cosyn J, De Bruyn H. How do periimplant biologic parameters correspond with implant survival and peri-implantitis? A critical review. Clin Oral Implants Res 2018; 29(Suppl. 18): 100-23. [http://dx.doi.org/10.1111/clr.13264] [PMID: 30306697]

[3] Zitzmann NU, Berglundh T. Definition and prevalence of peri-implant diseases. J Clin Periodontol 2008; 35(8)(Suppl.): 286-91. [http://dx.doi.org/10.1111/j.1600-051X.2008.01274.x] [PMID: 1872 4856]

[4] Kumar PS, Mason MR, Brooker MR, O'Brien K. Pyrosequencing reveals unique microbial signatures associated with healthy and failing dental implants. J Clin Periodontol 2012; 39(5): 425-33. [http://dx.doi.org/10.1111/j.1600-051X.2012.01856.x] [PMID: 2241 7294]

[5] Derks J, Schaller D, Håkansson J, Wennström JL, Tomasi C, Berglundh T. Effectiveness of implant therapy analyzed in a swedish population: Prevalence of peri-implantitis. J Dent Res 2016; 95(1): 43-9. [http://dx.doi.org/10.1177/0022034515608832] [PMID: 26701919]

[6] Renvert S, Polyzois I. Treatment of pathologic peri-implant pockets. Periodontol 2000 2018; 76(1): 180-90. [http://dx.doi.org/10.1111/prd.12149] [PMID: 29239086]

[7] Esposito M, Hirsch J, Lekholm U, Thomsen P. Differential diagnosis and treatment strategies for biologic complications and failing oral implants: A review of the literature. Int J Oral Maxillofac Implants 1999; 14(4): 473-90. [PMID: 10453661]

[8] Caccianiga G, Rey G, Baldoni M, Paiusco A. Clinical, radiographic and microbiological evaluation of high level laser therapy, a new photodynamic therapy protocol, in peri-implantitis treatment: A pilot experience. BioMed Res Int 2016; 2016: 6321906-8. [http://dx.doi.org/10.1155/2016/6321906] [PMID: 27379251]

[9] Sahrmann P, Zehnder M, Mohn D, Meier A, Imfeld T, Thurnheer T. Effect of low direct current on anaerobic multispecies biofilm adhering to a titanium implant surface. Clin Implant Dent Relat Res 2014; 16(4): 552-6. [http://dx.doi.org/10.1111/cid.12018] [PMID: 23167678]

[10] Sahrmann P, Ronay V, Hofer D, Attin T, Jung RE, Schmidlin PR. In vitro cleaning potential of three different implant debridement methods. Clin Oral Implants Res 2015; 26(3): 314-9. [http://dx.doi.org/10.1111/clr.12322] [PMID: 24373056]

[11] Toma S, Lasserre J, Brecx MC, Nyssen-Behets C. In vitro evaluation of peri-implantitis treatment modalities on Saos-2 osteoblasts. Clin Oral Implants Res 2016; 27(9): 1085-92. [http://dx.doi.org/10.1111/clr.12686] [PMID: 26361088]

[12] Yang Y, Guo J, Zhou X, et al. A novel cold atmospheric pressure air plasma jet for peri-implantitis treatment: An in vitro study. Dent Mater J 2018; 37(1): 157-66. [http://dx.doi.org/10.4012/dmj.2017-030] [PMID: 29176301]

[13] Leja C, Geminiani A, Caton J, Romanos GE. Thermodynamic effects of laser irradiation of implants placed in bone: An in vitro study. Lasers Med Sci 2013; 28(6): 1435-40. [http://dx.doi.org/10.1007/s10103-012-1215-z] [PMID: 23053251]

[14] Giannelli M, Landini G, Materassi F, et al. The effects of diode laser on Staphylococcus aureus biofilm and Escherichia coli lipopolysaccharide adherent to titanium oxide surface of dental implants. An in vitro study. Lasers Med Sci 2016; 31(8): 1613-9. [http://dx.doi.org/10.1007/s10103-016-2025-5] [PMID: 27475996]

[15] Valente NA, Mang T, Hatton M, Mikulski L, Andreana S. Effects of two diode lasers with and without photosensitization on contaminated implant surfaces: An Ex vivo study. Photomed Laser Surg 2017; 35(7): 347-56. [http://dx.doi.org/10.1089/pho.2016.4247] [PMID: 28253064]

[16] Ghasemi M, Etemadi A, Nedaei M, Chiniforush N, Pourhajibagher M. Antimicrobial efficacy of photodynamic therapy using two different light sources on the titanium-adherent biofilms of Aggregatibacter actinomycetemcomitans: An in vitro study. Photodiagn Photodyn Ther 2019; 26: 85-9. [http://dx.doi.org/10.1016/j.pdpdt.2019.03.004] [PMID: 30836212]

[17] Huang TC, Chen CJ, Ding SJ, Chen CC. Antimicrobial efficacy of methylene blue-mediated photodynamic therapy on titanium alloy surfaces in vitro. Photodiagn Photodyn Ther 2019; 25: 7-16. [http://dx.doi.org/10.1016/j.pdpdt.2018.11.008] [PMID: 30439531]

[18] Widodo A, Spratt D, Sousa V, Petrie A, Donos N. An in vitro study on disinfection of titanium surfaces. Clin Oral Implants Res 2016; 27(10): 1227-32.

[19] Rismanchian M, Nosouhian S, Shahabouee M, Davoudi A, Nourbakhshian F. Effect of conventional and contemporary disinfectant techniques on three peri-implantitis associated microbiotas. Am J Dent 2017; 30(1): 23-6. [PMID: 29178710]

[20] Giannelli M, Landini G, Materassi F, et al. Effects of photodynamic laser and violet-blue led irradiation on Staphylococcus aureus biofilm and Escherichia coli lipopolysaccharide attached to moderately rough titanium surface: In vitro study. Lasers Med Sci 2017; 32(4): 857-64. [http://dx.doi.org/10.1007/s10103-017-2185-y] [PMID: 28283813]

[21] Rogers S, Honma K, Mang TS. Confocal fluorescence imaging to evaluate the effect of antimicrobial photodynamic therapy depth on P. gingivalis and T. denticola biofilms. Photodiagn Photodyn Ther 2018; 23: 18-24. [http://dx.doi.org/10.1016/j.pdpdt.2018.04.015] [PMID: 29753881]

[22] Monzavi A, Fekrazad R, Chinipardaz Z, Shahabi S, Behruzi R, Chiniforush N. Effect of various laser wavelengths on temperature changes during periimplantitis treatment: An in vitro Study. Implant Dent 2018; 27(3): 311-6. [http://dx.doi.org/10.1097/ID.0000000000000751] [PMID: 29489549]

[23] Bürgers R, Witecy C, Hahnel S, Gosau M. The effect of various topical peri-implantitis antiseptics on Staphylococcus epidermidis, Candida albicans, and Streptococcus sanguinis. Arch Oral Biol 2012; 57(7): 940-7. [http://dx.doi.org/10.1016/j.archoralbio.2012.01.015] [PMID: 2236 5324]

[24] Astasov-Frauenhoffer M, Braissant O, Hauser-Gerspach I, et al. Microcalorimetric determination of the effects of amoxicillin, metronidazole, and their combination on in vitro biofilm. J Periodontol 2014; 85(2): 349-57. [http://dx.doi.org/10.1902/jop.2013.120733] [PMID: 23594193]

[25] Shrestha B, Theerathavaj MLS, Thaweboon S, Thaweboon B. In vitro antimicrobial effects of grape seed extract on peri-implantitis microflora in craniofacial implants. Asian Pac J Trop Biomed 2012; 2(10): 822-5. [http://dx.doi.org/10.1016/S2221-1691(12)60236-6] [PMID: 23569 854]

[26] Roberts JL, Khan S, Emanuel C, et al. An in vitro study of alginate oligomer therapies on oral biofilms. J Dent 2013; 41(10): 892-9. [http://dx.doi.org/10.1016/j.jdent.2013.07.011] [PMID: 23907083]

[27] Vilarrasa J, Delgado LM, Galofré M, et al. In vitro evaluation of a multispecies oral biofilm over antibacterial coated titanium surfaces. J Mater Sci Mater Med 2018; 29(11): 164. [http://dx.doi.org/10.1007/s10856-018-6168-8] [PMID: 30392142]

[28] Walter C, Kulik EM, Weiger R, Zitzmann NU, Waltimo T. Additive or synergistic antimicrobial effects of amoxicillin and metronidazole on whole plaque samples: A preliminary report. J Int Acad Periodontol 2011; 13(1): 11-6. [PMID: 21387982]

[29] Stübinger S, Henke J, Donath K, Deppe H. Bone regeneration after peri-implant care with the CO2 laser: A fluorescence microscopy study. Int J Oral Maxillofac Implants 2005; 20(2): 203-10. [PMID: 15839113]

[30] Kuo HN, Mei HI, Liu TK, Liu TY, Lo LJ, Lin CL. In vitro laser treatment platform construction with dental implant thread surface on bacterial adhesion for peri-implantitis. BioMed Res Int 2017; 2017: 4732302-7. [http://dx.doi.org/10.1155/2017/4732302] [PMID: 28791302]

[31] Claffey N, Clarke E, Polyzois I, Renvert S. Surgical treatment of periimplantitis. J Clin Periodontol 2008; 35(8)(Suppl.): 316-32. [http://dx.doi.org/10.1111/j.1600-051X.2008.01277.x] [PMID: 1872 4859]

[32] Renvert S, Roos-Jansåker AM, Claffey N. Non-surgical treatment of peri-implant mucositis and peri-implantitis: A literature review. J Clin Periodontol 2008; 35(8)(Suppl.): 305-15. [http://dx.doi.org/10.1111/j.1600-051X.2008.01276.x] [PMID: 18724 858]

[33] Heitz-Mayfield LJA, Salvi GE, Mombelli A, et al. Supportive periimplant therapy following anti-infective surgical peri-implantitis treatment: 5-year survival and success. Clin Oral Implants Res 2018; 29(1): 1-6. [http://dx.doi.org/10.1111/clr.12910] [PMID: 27335316]

[34] Smeets R, Henningsen A, Jung O, Heiland M, Hammächer C, Stein JM. Definition, etiology, prevention and treatment of peri-implantitis: A review. Head Face Med 2014; 10: 34. [http://dx.doi.org/10.1186/1746-160X-10-34] [PMID: 25185675]

[35] Gantes BG, Nilvéus R. The effects of different hygiene instruments on titanium surfaces: SEM observations. Int J Periodontics Restorative Dent 1991; 11(3): 225-39. [PMID: 1666395]

[36] Chan Y, Lai C-H. Bactericidal effects of different laser wavelengths on periodontopathic germs in photodynamic therapy. Lasers Med Sci 2003; 18(1): 51-5. [http://dx.doi.org/10.1007/s10103-002-0243-5] [PMID: 12627274]

[37] Schwarz F, Bieling K, Bonsmann M, Latz T, Becker J. Nonsurgical treatment of moderate and advanced periimplantitis lesions: A controlled clinical study. Clin Oral Investig 2006; 10(4): 279-88. [http://dx.doi.org/10.1007/s00784-006-0070-3] [PMID: 16969659]

[38] Zablotsky MH, Diedrich DL, Meffert RM. Detoxification of endotoxin-contaminated titanium and hydroxyapatite-coated surfaces utilizing various chemotherapeutic and mechanical modalities. Implant Dent 1992; 1(2): 154-8. [http://dx.doi.org/10.1097/00008505-199205000-00009] [PMID: 1288 809]

[39] Quirynen M, Teughels W, De Soete M, van Steenberghe D. Topical antiseptics and antibiotics in the initial therapy of chronic adult periodontitis: Microbiological aspects. Periodontol 2000 2002; 28: 72-90. [http://dx.doi.org/10.1034/j.1600-0757.2002.280104.x] [PMID: 1201 3349]

[40] Mouhyi J, Sennerby L, Pireaux JJ, Dourov N, Nammour S, Van Reck J. An XPS and SEM evaluation of six chemical and physical techniques for cleaning of contaminated titanium implants. Clin Oral Implants Res 1998; 9(3): 185-94. [http://dx.doi.org/10.1034/j.1600-0501.1998.090306.x] [PMID: 1053 0133]

[41] Meffert RM. Treatment of failing dental implants. Curr Opin Dent 1992; 2: 109-14. [PMID: 1520919]

[42] Cortelli SC, Cortelli JR, Holzhausen M, et al. Essential oils in onestage full-mouth disinfection: Double-blind, randomized clinical trial of long-term clinical, microbial and salivary effects. J Clin Periodontol 2009; 36(4): 333-42. [http://dx.doi.org/10.1111/j.1600-051X.2009.01376.x] [PMID: 1942 6180]

[43] Arweiler NB, Henning G, Reich E, Netuschil L. Effect of an aminefluoride-triclosan mouthrinse on plaque regrowth and biofilm vitality. J Clin Periodontol 2002; 29(4): 358-63. [http://dx.doi.org/10.1034/j.1600-051X.2002.290412.x] [PMID: 1196 6934]

[44] Monteiro JSC, de Oliveira SCPS, Pires Santos GM, Pires Sampaio FJ, Pinheiro Soares LG, Pinheiro AL. Effectiveness of antimicrobial photodynamic therapy (AmPDT) on Staphylococcus aureus using phenothiazine compound with red laser. Lasers Med Sci 2017; 32(1): 29-34. [http://dx.doi.org/10.1007/s10103-016-2079-4] [PMID: 27677473]