

Is a Potential Therapeutic Strategy of Periodontal Intervention on Cardiovascular Disease, Yes or No?

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Abstract

Aims: Cardiovascular disease (CVD) and periodontitis are both chronic inflammatory disorders which are highly prevalent in populations. Bacteria involved in the periodontal disease have been found to be cardiovascular risk markers. Periodontal pathogens may contribute to the atheroma pathogenesis. Severe periodontitis is correlated with the prevalence of bacteraemia, and poor periodontal status is an important risk factor for CVD. However, the association is unclear. If the association is causal, the periodontal therapy will lead to an attenuation of the effects on CVD. The study aimed to study if the periodontal intervention therapy presented therapeutic effects on CVD. **Methods:** English language literature on periodontal intervention therapy on CVD is causal or not. The literature revealed 62 papers associated with this study to investigate the relationship between periodontitis and CVD. **Results:** The literature supported the idea that periodontal infections had been associated with CVD. Certain periodontal therapy is associated with bacteraemia, and the prevalence of bacteraemia may arise from periodontal therapy and poor oral hygiene practices. Periodontal therapy not only presented therapeutic effects by reducing cytokine activity and C-response protein (CRP), but also caused bacteraemia transiently. Effective antibiotic prophylaxis pre- or post-periodontal therapy presented some beneficial effects on bacteraemia or CVD. **Conclusion:** Severe periodontitis causes systemic inflammation and endothelial dysfunction, and goes beyond the oral cavity. Periodontal intervention would contribute to the prevention of atherosclerosis, and antibiotic prophylaxis would be helpful to decrease bacteraemia and reduce the onset of CVD.

Keywords

Periodontal Disease, Cardiovascular Disease, Periodontal Intervention, Antibiotic Prophylaxis, Yes or No

1. Introduction

Periodontitis has been associated with an increased risk of cardiovascular events. Cardiovascular diseases (CVD) are the most prevalent diseases in developed countries. Disorders of blood vessels, hypertension and arteriosclerosis are the chief causes of death in the Western world, and atherosclerosis is the main cause of CVD [1]. Inflammation has emerged as a causative factor in all stages of CVD. Mortality from CVD is expected to increase by 25% in the next two decades [2]. Periodontal disease may contribute to atherogenesis and/or thromboembolic events [3]. The majority of clinical and epidemiological findings confirm the presence of an intimately association between periodontitis and CVD [4], and the prevalence and incidence of CVD are significantly increased in periodontal infection patients [5]. There is increasing evidence that chronic infections, such as periodontal diseases, could play a role in the initiation and development of coronary artery disease [6]. Numerous longitudinal epidemiological and cross-sectional studies have provided powerful evidence that there are significant associations between periodontitis and elevated risk for CVD [7] [8]. Data have shown a consistent relationship between pocket depth and incident myocardial infarction [9]. Periodontal bleeding *per se* is a poor indicator of odontogenic bacteraemia and gingivitis is correlated positively with the prevalence of bacteraemia [10]. Recently, attention has been focused not simply on how systematic diseases influence oral health but on how oral health may have effects that extend beyond the oral cavity. For example, a meta-analysis suggested that individuals suffering from periodontitis may have 1.14 - 2.2 times greater risk of developing coronary heart disease compared with individuals without periodontitis [11]. In addition, experimental evidence has showed that periodontal pathogenic bacteria, mainly *Porphyromonas gingivalis*, play a role in atherogenesis [12]. Several reviews have described the relationship between periodontal periodontal disease and risk of coronary heart disease or other CVD, and have suggested that periodontitis may contribute to CVD in susceptible subjects [13] [14].

Recent studies have focused on the systemic effects of periodontal intervention on indicators of CVD. Periodontal therapy has had some success in the modification of many of inflammatory indicators in systemically healthy adults [15]. Thus we must make sure if periodontal intervention could lower the risk of cardiovascular events or even prevent onset and progression of the disease. It's reported that poor oral health, especially poor periodontal status, is an important risk factor for CVD. Certain periodontal procedures are associated with bacteraemia. The prevalence of bacteraemia arise from periodontal therapy and various oral hygiene practices. It has been suggested that oral hygiene practices are responsible for spontaneous bacteraemia. Such bacteraemia is of low grade intensity and of short duration [16]. The studies have shown there is link between dental procedures and infective endocarditis [17]. Penicillin is proved to reduce bacteraemia by 84% - 86% at 5 min and 95% - 97% at 30 min after bacteraemia induction. These findings can be compared with a reduction of 24% - 42% and 49% - 76%, respectively, when no prophylaxis is used. By contrast, antibiotic prophylaxis, such as single doses of 2 g penicillin and 3 g amoxicillin fail to reduce bacteraemia after dental extractions. The evidence that antiseptic mouthwashes such as chlorhexidine and povidone-iodine used prior to dental procedures may reduce the

prevalence of bacteraemia [18]. Incidence of bacteraemia arising after scaling and root planing is 8% - 80%, and that of gingivectomy is 83%, and that of flap procedure is 36% - 88%. Incidence of bacteraemia arising from extraction is 51% - 100% [19].

Whether spontaneous periodontal disease induced bacteraemia or periodontal intervention procedure induced bacteraemia are still unclear. Whether periodontal intervention can be used as a potential therapeutic strategy to CVD is unknown. Therefore, we write this paper to study if periodontal therapy could reduce inflammation to decrease morbidity, and effective antibiotic prophylaxis pre- or post-periodontal therapy to reduce bacteraemia transitorily. This study focuses on the effects of periodontal therapy and antibiotic prophylaxis on CVD.

Periodontal disease is considered a potential risk factor for CVD, and it should be influential in the diagnosis and treatment of CVD patients. Increased inflammatory cytokines and CRP levels may contribute to inflammatory events, including CVD and periodontitis. Periodontal intervention may reduce CVD by inflammatory response regulation of cytokine and CRP levels. But some periodontal procedures may induce bacteraemia temporarily. Periodontal diseases can be treated effectively by periodontal intervention and preventing bacteria from entering the blood stream leading to the distant organ infection, and reducing the inflammatory cytokine (IL-6, TNF- α) and CRP levels in serum, and would likely decrease the incidence of both cardiovascular and periodontal diseases. Some effective antibiotic prophylaxis pre- or post-periodontal therapy could prevent bacteraemia transitorily and prevent the onset of CVD. This paper found that periodontal intervention can reduce the incidence rate and severity of CVD. Antibiotic prophylaxis can improve the therapeutic effects and reduce the incidence of atherosclerosis. Exploration of evidence-based periodontal intervention strategy would help clinicians in planning periodontal therapy to reduce the incidence of atherosclerosis and CVD.

2. Relevant Bacterial Evidence between Periodontal Disease and CVD (Table 1)

Bacteria of periodontal infection are associated with the coronary vascular disease. Oral microorganisms including periodontal bacterial pathogens enter into the blood stream and form transient bacteraemia. Periodontal pathogens are present in atherosclerotic plaques where, like other infectious microorganisms such as *Chlamydia pneumoniae*, they may play a role in the development of CVD. Periodontal pathogen, such as *Aggregatibacter actinomycetemcomitans* (Aa), deteriorates ventricular remodeling after myocardial infarction in Mice [20]. Oral bacteria and bacterial products enter into the blood stream and are thought to be one of the key initiators of biological events linking oral infections to atherosclerotic vascular disease [21]. Increasing risk for systemic disease in subjects suffering from periodontal disease could be an increased prevalence and severity because of bacteraemia associated with oral bacteria [22]. Periodontal bacteria occasionally have been a correlative causative agent for infections at distant organs [23]. Studies have thus evaluated if periodontal bacteria are detectable and culturable from atherothrombotic plaques or vascular biopsies. Bacterial DNA from several periodontal pathogens has been detected in human arterectomy specimens [24]. Experimental studies suggest low concentrations of lipopolysaccharides from *Porphyromonas*

Table 1. Relevant bacterial evidence between periodontal disease and CVD.

Author(s) year [Ref]	Study design	Outcomes	Conclusions
Hanatani, T., <i>et al.</i> , 2012 [20]	Animal study. 8 male mouse injected Aa, 6 cases injected PBS. Experimental MI induced by permanent ligation of the left anterior descending coronary artery	Plasma level of anti-Aa antibody higher in Aa-infected mice than control mice. 7 days after myocardial ischemia, Aa-positive MI hearts showed larger infarct size and length than control mice. Aa-positive MI hearts showed more MOMA-2 positive myocardial infiltrating cells compared to negative MI.	Periodontal pathogen might deteriorate ventricular remodeling after MI through inflammatory cell infiltration
Iwai, T., 2009 [21]	Mini review. The Medline and Tokyo Medical and Dental University databases were searched to identify the literature currently available on oral bacteria and vascular diseases.	Bacteria from mouth to the bloodstream and then to vein of venous angle near supraclavicular area. Periodontal bacteria, such as Pg, activate platelets and make them mass, including bacteria without phagocytosis. Animal study showed the formation of a small arterial thrombus after continuous intravenous infusion of Pg for 2 - 4 week.	Periodontal bacteria, may play an important role in the development of various vascular diseases, such as atherosclerosis and varicose veins, through bacteremia.
Haraszthy, V.I., <i>et al.</i> , 2000 [22].	Clinical study. 50 specimens obtained, examined Cp, HCMV, and bacterial 16S ribosomal RNA using PCR. 100 ng of chromosomal DNA extracted from specimen. PCR product generated with eubacterial primers transferred and probed with digoxigenin labeled synthetic oligonucleotides for Aa, Bf, Pg, and Pi.	80% of the specimens were positive in 1 or more of PCR assays. 38% were positive for HCMV and 18% positive for Cp. The presence of bacteria in 72% of surgical specimens. 44% of the 50 atheromas were positive for at least one of periodontal pathogens. 30% of surgical specimens were positive for Bf, 26% positive for Pg, 18% positive for Aa, and 14% positive for Pi. 13 (59%) of the 22 periodontal pathogen-positive surgical specimens were positive for 2 or more of the target species	Periodontal pathogens present in atherosclerotic Plaques, such as Cp. They play a key role in the development of atherosclerosis leading to coronary vascular disease.
Kebschull, M., <i>et al.</i> , 2010 [23]	Critical review. (1) Observational studies; (2) interventional studies; (3) Potential mechanisms linking periodontal infections and atherosclerosis. (4) Periodontal pathogens in animal models of atherogenesis. (5) Available mechanistic studies.	Periodontal treatment resulted in favorable effects on subclinical markers of atherosclerosis. In vitro and in vivo studies established plausibility of a link between periodontal infections and atherogenesis. Utilized models are mostly mono-infections of host cells, and may not adequately portray human periodontitis as a polymicrobial, biofilm-mediated disease.	Periodontal therapy results in lower levels of systemic inflammation and favorable effects on subclinical markers of atherosclerosis.
Gaetti-Jardim, E., <i>et al.</i> , 2009 [24]	Clinical study. 44 patients displaying CVD were submitted and endarterectomy of coronary arteries. 60 - 100 mg atherosclerotic tissue removed. Quantitative detection of periodontopathic bacteria using TaqMan probe. Aa, Fn, Pg, Pi, Pn and Tf determined by real-time PCR.	Total bacterial and periodontopathic bacterial DNA found in 94.9% and 92.3% respectively, of atheromatous plaques from periodontitis patients, and in 80.0% and 20.0%, of atherosclerotic tissues from periodontally healthy subjects. DNA represented 47.3% of total bacterial DNA obtained from periodontitis patients. Pg, Aa and Pi detected most often.	Periodontopathic bacteria in coronary lesions are not coincidental and that they may contribute to the development of vascular diseases.
Mattila, K., <i>et al.</i> , 1989 [25]	Clinical study. 100 patients with acute MI and 102 controls selected from community at random. Serum total cholesterol, triglyceride, and high density lipoprotein cholesterol measured on admission and 4 weeks. Lipid values obtained during second visit. Dental scores measured. The index ranged from 0 to 10.	Smoking was more common among acute MI, and had lower concentrations of high density lipoprotein cholesterol and higher serum concentrations of triglycerides and C peptide than the controls. Hypertension was more common among patients than controls. Serum total cholesterol concentration was not associated with MI. Total dental index and the pantomography index highly correlated. Two indexes higher among patients than controls.	Dental health was significantly worse in patients with acute MI than in controls. Periodontal disease and dental caries is more common among patients with acute MI than controls

Abbreviations: Aa, *Aggregatibacter actinomycetemcomitans*; Pg, *Porphyromonas gingivalis*; Cp, *Chlamydia pneumoniae*; Bf, *Bacteroides forsythus*; Pi, *Prevotella intermedia*; Fn, *Fusobacterium nucleatum*; Pn, *Prevotella nigrescens*; Tf, *Tannerella forsythia*; HCMV, human cytomegalovirus; MI, myocardial infarction; MOMA-2, Monocyte/Macrophage marker; PCR, polymerase chain reaction; CVD, cardiovascular disease.

gingivalis and *Prevotella intermedia* profoundly stimulate the secretion of interleukins by human macrophages. Periodontal pathogens may increase the risk of CVD through mechanisms such as platelet activation and aggregation [25].

3. Effects of Periodontal Intervention on Inflammatory Cytokines

Inflammatory cytokines include pro-inflammatory mediators, such as tumour necrosis factor (TNF)- α , interleukin (IL)-1 β , IL-6 and IL-12, chemokines (e.g. IL-8), and anti-inflammatory mediators (e.g. IL-10, IL-1 antagonist and IL-4), play distinct biological effects [26]. The chemokine mainly attracts and activates neutrophils, and is considered important mediators for granulocyte accumulation. IL-6 secreted by various cell types, such as fibroblast cells, monocyte macrophage cells, and epithelium cells, and its level is increased by bacterial lipopolysaccharide stimulated. IL-6 can promote coagulation and result in the development of atherosclerosis. The enhancement of IL-6 levels has been associated with both cardiovascular-risk and periodontal disease [27]. TNF- α stimulates the production of chemokines and cytokines, collagenase, prostaglandin E2 [28], cellular adhesion molecules and bone resorption-related factors. Based on the biological properties of pro-inflammatory cytokines, high levels of TNF- α and IL-6 in plasma have been associated with an increased morbidity and mortality of cardiovascular events [29]. Peripheral blood mononuclear cells from periodontitis subjects released higher levels of TNF- α and IL-6 than those from healthy subjects. In contrast, mononuclear cells obtained from healthy subjects presented higher amounts of IL-8 than those from periodontitis individuals [30]. In a prospective study of apparently healthy men, the IL-6 levels of those who subsequently had a myocardial infarction were higher than matched control without myocardial infarction during a 6-year follow-up [31]. IL-6 levels may be a predictor of risk of future myocardial infarction in apparently healthy men. Severe periodontitis can result in systemic inflammation characterized by elevated serum IL-6 [32]. A recent study reported that subjects with both coronary artery disease and periodontitis had significantly higher serum IL-6 concentrations compared with subjects with coronary artery disease who had no periodontitis [33]. TNF- α is involved in the initiation and development of coronary artery disease [34], and its levels increased in patients with periodontitis [35]. Conversely, IL-10 suppresses the inflammation reaction and minimizes tissue destruction [36].

Periodontal therapy can reduce the levels of pro-inflammatory cytokines at three months post-therapy, and thus may lower the CVD incidence. In addition, the current study concluded that periodontal therapy had minimal impact on levels of TNF- α and IL-1 β [37]. The effects of periodontal intervention on serum IL-6 are not consistent. Some studies showed that periodontal therapy results in a decrease in IL-6 levels [38], although others found no significant differences post-therapy [39]. In a recent study on coronary artery disease patients with periodontitis, periodontal therapy reduced serum concentrations of IL-6 at 6 months post-therapy [33]. Similar findings can be obtained in which periodontitis patients with coronary heart disease received mechanical periodontal therapy and control patients did not receive periodontal therapy. The serum IL-6 levels in periodontal therapeutic group decreased significantly than those in the control group at 3 months after periodontal therapy. The effect of periodontal therapy

on circulating TNF- α levels is not consistent. An investigation showed that the TNF- α levels decreased significantly after periodontal therapy [40]. And others reported that no effect could be seen following periodontal intervention [41].

4. Effect of Periodontal Intervention on C-Reactive Protein

CRP, an acute phase reactant protein, is responsible for the increase in the vascular inflammation. Its main function is thought to result in the activation of the complement system. In humans, the levels of CRP in plasma rise rapidly (as much as 1000 folds or more) after an acute inflammatory stimulus. This increase is mainly due to increased synthesis of this protein by hepatocytes that are stimulated by various cytokines, particularly IL-6 [42]. CRP level measurement can provide a more sensitive means of detecting signs of inflammation and trauma. CRP concentration in serum is significantly increased in patients with coronary heart disease and myocardial infarction. Elevated plasma levels of CRP have been documented as a major risk factor for CVD, and may be used as an important indication of coronary artery disease and acute myocardial infarction [43]. In a cohort study, it was noted that increasing levels of serum high-sensitivity CRP were associated with the risk of cardiovascular events, and that CRP was the strongest univariate predictor of the risk of such events [44]. CRP can increase low density lipoprotein uptake into macrophages and inhibit endothelial nitric-oxide synthase expression in aortic endothelial cells. CRP can also induce adhesion molecule expression in human endothelial cells in serum and may contribute to the hypercoagulative state in coronary disease patients [45]. Recently, accumulated evidence has demonstrated the association between periodontitis and CRP. The serum CRP is increased in systemically healthy subjects with periodontitis [46]. It was reported that subjects with periodontitis had 1.65 mg/L higher serum CRP compared with individuals without periodontitis [47]. Studies have showed that periodontitis patients with CVD or hypertension had significantly higher serum sensitivity CRP concentrations than patients without periodontitis [48]. Periodontal diseases are associated with changes in serum components that are consistent with the increased circulation of IL-6 and elevated levels of high sensitivity CRP [49]. Recently, clinical trials have shown a significant reduction of CPR levels and other inflammatory markers in serum after periodontal therapy [50]. Furthermore, a multi-centered randomized control study showed that periodontal therapy can reduce the CRP levels from high to moderate in non-obese periodontal disease patients [51]. Similar results confirmed by a randomized controlled trial that the levels of CRP reduced after periodontal therapy [52]. Periodontal intervention and periodontal maintenance may contribute to the systemic inflammation and thereby decrease the incidence and morbidity of CVD [53]. But other studies have found that periodontal intervention, especially one that involves periodontal surgery and dental extraction, will increase the levels of inflammatory mediators immediately [54]. Therefore, full-mouth disinfection agent has been introduced as a short-term method to suppress periodontal pathogens within 24 h [55].

5. Effects of Periodontal Procedures on CVD and Antibiotic Prophylaxis (Table 2)

Gingival inflammation is correlated positively with the prevalence of bacteraemia [11].

Table 2. Effects of periodontal procedures on CVD and antibiotic prophylaxis.

Author(s) year [Ref]	Study design	Outcomes	Conclusions
Bahekar, A.A., <i>et al.</i> , 2007 [11]	Systematic review. Literature revealed 5 prospective cohort studies, 5 case control studies, 5 cross-sectional studies. Individual studies were adjusted for confounding factors such as age, sex, diabetes mellitus, and smoking.	Prospective cohort studies indicated that individual with PD had a 1.14 times higher risk of developing CHD than controls. Case control studies showed great risk of developing CHD. Prevalence of CHD in cross-sectional studies significantly greater among individual with PD than in those without PD. Cohort studies showed 1.24 times increase risk of development of CHD in patients with <10 teeth.	Both the prevalence and incidence of CHD were significantly increased in PD. The PD must be a risk factor for CHD. Prospective studies required to prove the risk reduction with the treatment of PD.
Ioannidou, E., <i>et al.</i> , 2006 [15]	Review. English literature of periodontal treatment on CRP levels assessed, at least 2 months after periodontal treatment. The search conducted in MEDLINE between 1966 and July 2005 and Cochrane Central Register of Controlled Trials.	Literature yielded 814 citations of which 10 met the inclusion criteria. Meta-analysis of RCT included that the difference in serum CRP levels is not significantly different between the two arms. The single-cohort studies suggested that the difference on serum CRP levels was not significantly different before and after treatment.	Evidence indicated that systemic inflammation presented in patients with periodontal disease. RCT and single cohort studies do not support that periodontal treatment can reduce CRP levels.
Seymour, R.A., <i>et al.</i> , 2003 [19]	Review. The paper reviewed the effect of cardiovascular drugs on the periodontium and management of patients with periodontal diseases. The risk of infective endocarditis arising from periodontal procedures, and the inter-relationship between periodontal disease and CAD.	Stopping anticoagulant therapy prior to periodontal procedures is putting patients at a greater risk of thromboembolic disorders compared to the risk of prolonged bleeding. Spontaneous bacteraemia arising from a patient's oral hygiene practices is more likely to be the cause of endocarditis than one-off periodontal procedures. The risk of death from penicillin appears to be greater than the risk of death arising from infective endocarditis.	CAD can interact with the periodontium. Further investigation must Manage anticoagulant therapy and the risk from infective endocarditis.
Hokamura, K., <i>et al.</i> , 2010 [56]	Minireview. Clarify the involvement of Pg on the mechanisms of development of aortic intimal hyperplasia. Intravenous administration of Pg induced intimal hyperplasia in the mouse model with photochemical impairment of the femoral artery.	No changes identified in the mice without aortic impairment, even with Pg infection. S100A9 and the SMemb were significantly over expressed on surfaces of smooth muscle cells present in injured blood vessels. Increased expressions of S100A9 and SMemb proteins observed in aneurismal specimens obtained from Pg infected patients. Bacteremia induced by Pg leads to intimal hyperplasia associated with over expressions of S100A9 and SMemb.	Pg is a causative event in the development of aortic hyperplasia in periodontitis. Upregulation of the S100A9 by Pg is important event in development of intimal hyperplasia in aorta.
Hall, G., <i>et al.</i> , 1993 [57]	Clinical study. 60 healthy patients randomized to receive placebo, penicillin-V (2 g), or amoxicillin 1 hour before dental extraction was performed. Blood samples for microbiological investigation collected before, during, and 10 minutes post surgery and processed by lysis filtration	The overall incidence of bacteremia after dental extraction was 95%, 90%, and 85%, respectively, for the 3 groups. For >90% of 126 strains of viridans streptococci tested, the MIC of penicillin-V and ampicillin were ≤ 0.125 mg/L	The protective effect of prophylactically administered penicillins must be due to interference with the steps in the development of endocarditis, other than the transient bacteremia that occurs initially.
Maharaj, B., <i>et al.</i> , 2012 [59]	Clinical study. 160 patients for antimicrobial prophylaxis before dental extraction. Group A served as control, group B rinsed with chlorhexidine, group C took 3 g amoxicillin orally, group D took 600 mg clindamycin.	The proportion of patients who had post-extraction bacteraemia in groups A, B, C and D was 35%, 40%, 7.5% and 20%, respectively. The differences between the control and amoxicillin groups and between the chlorhexidine and amoxicillin groups were statistically significant.	None of the treatments prevented post-extraction bacteraemia and confirmed earlier reports that bacteraemia is not completely eliminated by antibiotics.

Abbreviations: CHD, coronary heart disease; PD, periodontal pocket depth; CRP, C-reactive protein; RCT, randomized controlled trials; CAD, coronary artery disease; Pg, *Porphyromonas gingivalis*; S100A9, S100 calcium-binding protein A9; SMemb, embryonic isoform of myosin heavy chain; MIC, minimal inhibitory concentration.

Periodontal bleeding *per se* is a poor indicator of odontogenic bacteraemia. The certain periodontal procedures are associated with bacteraemia. The prevalence of bacteraemia arise from periodontal therapy and various oral hygiene practices. In many instances the prevalence of bacteraemia after such innocuous events is comparable with that occurring after periodontal procedures. It has been suggested that oral hygiene practices are responsible for spontaneous cases of bacteraemia. Such bacteraemias either from periodontal procedures or oral hygiene practices are of low-grade intensity (10 - 200 CFU/ml of blood) and of short duration [15]. Bacteremia induced by *Porphyromonas gingivalis* (Pg) leads to intimal hyperplasia associated with overexpressions of embryonic isoform of myosin heavy chain and oral hematogenous spreading of Pg is a causative event in the development of aortic hyperplasia in periodontitis patients [56]. Penicillin has been shown to reduce bacteraemia by 84% - 86% at 5 min and 95% - 97% at 30 min after bacteraemia induction. These results can be compared with a reduction of 24% - 42% and 49% - 76%, respectively, when no prophylaxis used [19]. By contrast, other workers have shown that single doses of 2 g penicillin and 3 g amoxicillin fail to reduce bacteraemia after dental extractions [57]. Although most attention has been focused on antibiotic prophylaxis, there is evidence that antiseptic mouthwashes such as chlorhexidine and povidone-iodine used prior to certain periodontal procedures may reduce the prevalence of bacteraemia [58]. Maharaj B [59] found that there were none of the significant treatments prevented post-extraction bacteraemia and confirmed earlier reports that bacteraemia was not completely eliminated by antibiotics. Recently, studies have showed that there is no obvious increase in the incidence of infective endocarditis cases or deaths in the two years after the guideline was introduced about the cessation prescribing antibiotic prophylaxis. The findings support the cessation of prescribing antibiotic prophylaxis [60]. Therefore further clinical trials should determine if periodontal intervention combined with drug therapy would reduce the incidence of CVD.

6. Conclusion

Periodontal inflammatory response could exacerbate vascular inflammation via secreted cytokines that ultimately modulate atherosclerosis and CVD. The inflammatory cytokine IL-6 and TNF- α , and CRP levels in serum increased are association with CVD and periodontal diseases. Periodontal intervention had a positive impact on the established risk factors for CVD to reduce inflammatory responses. Periodontal intervention studies have strengthened the evidence for an association between the periodontal disease and CVD, and have also indicated a causal link. As some periodontal procedures may increase bacteraemia temporarily, effective antibiotic prophylaxis is necessary to the prevention bacteraemia and the onset of CVD [61]. However, detailed mechanism of spontaneous periodontal disease induces bacteraemia and the influence of periodontal intervention procedures inducing bacteraemia leading to CVD is unknown. Because of these different research results, carefully designed randomized trials based on this concept with longer follow-up and clinical observation are required to prove if periodontal intervention combined with drug therapy would reduce the incidence of CVD.

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Conflict of Interest Statement

The authors confirm no conflict of interest.

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