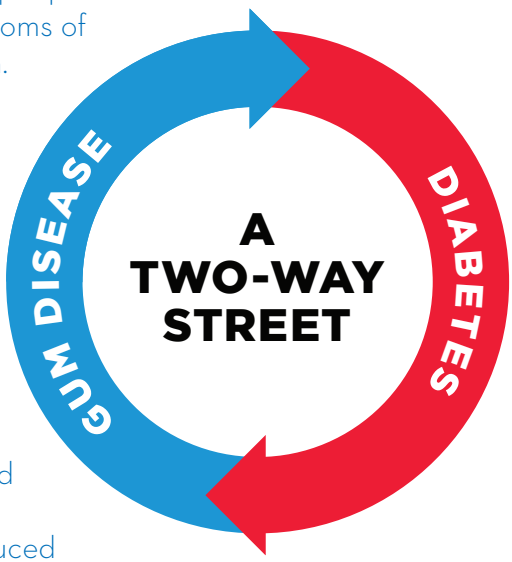
Role of Oral Hygiene in the Management of Gingivitis and Implications for Patients with Diabetes

Microbial Etiology of gingivitis - a plaque induced inflammation of the gingiva. Progressive periodontal diseases are a significant burden to oral health worldwide.[1] In addition to tooth loss, chronic periodontal diseases are increasingly suggested as significant factors in development and/or progression of a variety of systemic conditions including cardiovascular disease, rheumatoid arthritis, Alzheimer's disease and pre-term births.[2-5] Periodontal disease initially presents as gingivitis, a plaque induced inflammation of the marginal and attached gingiva.[6] The clinical symptoms of gingivitis include redness, edema, and bleeding at the gingival margin. Demonstration that periodontal diseases are of microbial origin was proven by landmark experimental gingivitis (EG) studies in the 1960s, which demonstrated that the suspension of oral hygiene resulted in rapid dental plaque formation.[7-9] Left undisturbed, maturation of the dental plaque over time inevitably produced gingival inflammation, albeit with variable onset and progression. The microbial composition of dental plaque during the development of gingivitis was associated with proliferation of Gram negative bacteria when assayed by culturing techniques.[10-12] Pathogens associated with gingivitis display unique metabolic activities (production of hydrogen sulfides and short chain carboxylic acids[13] and express lipopolysaccharides (LPS's) or endotoxins in their cell walls.[14-15] The LPS from Gram negative bacteria, and the lipoteichoic acid produced by some Gram positive pathogens can be considered to be a major factor in the pathogenesis of progressive periodontal diseases.[16]



Gingivitis is a risk factor for a more advanced form of periodontal disease, periodontitis. Gingivitis precedes the development of progressive periodontal disease. The clinical symptoms of gingivitis include redness, edema, and bleeding at the gingival margin. Gingival bleeding, an objective measure of inflammation has been positively correlated to histologic changes in the gingiva, which include a greater percentage of cell-rich collagen-poor connective tissue consistent with an inflammatory infiltrate, as compared to non-bleeding sites.[17] The clinical significance of gingival bleeding should not be underestimated, as chronic inflammation of the gingiva and periodontium has been shown to be a significant risk factor for both periodontal attachment loss and recession. Sites with persistent gingival bleeding over multiple periodic examinations have been shown to have higher odds for progressive attachment loss compared to non-bleeding sites.[18] Over a 26-year observation period in a population of well-maintained, well-educated men who practiced regular oral hygiene, sites that bled consistently throughout the course of the study had approximately 70% more attachment loss than sites that were consistently noninflamed, yielding an odds ratio of 3.22 for inflamed sites (bleeding) converting to attachment loss.[18] These persistent bleeding sites can exist even if patients are considered generally healthy. In addition, the absence of persistent gingival bleeding on probing has also been shown to have a high negative predictive value of 98.1% for disease progression, as measured by ≥2 mm attachment loss, in a periodontal maintenance population over a 2.5-year observation period.[19] The established relationship between persistent gingival bleeding and attachment loss is the mechanistic basis for gingival inflammation as a risk factor for tooth mortality. Importantly, teeth surrounded by persistent inflamed gingival tissue (presence of bleeding) had a 46-fold higher risk of being lost over a 26-year observation period, compared to teeth surrounded by inflammation-free gingival tissues (absence of bleeding).[20]

Diabetics have a higher risk for developing periodontal diseases (includes both gingivitis and

PERIODONTITIS). Longitudinal human clinical studies support a two-way relationship between diabetes and periodontitis, with more severe periodontal tissue destruction observed in diabetic populations.[21,22] The risk of periodontitis has been reported to be 3-fold higher in diabetic patients compared to healthy controls.[23] A second publication reported that diabetics are 2.3-fold more likely to have moderate periodontitis and 4.8-fold more likely to have severe periodontitis compared to age controlled non-diabetics.[24] More recently, it has been reported that patients with diabetes have an increased risk of the progression of periodontal disease by 86%, with Relative Risk = 1.86, 95% CL 1.3 – 2.8.[25] Importantly, the rate of periodontal destruction in diabetics is directly correlated to lack of glycemic control as measured by HbA1c levels.[26] Poorly controlled diabetics with HbA1c levels higher than 7.0 are at increased risk for periodontal destruction.

THIS RELATIONSHIP IS BI-DIRECTIONAL, WITH THE PRESENCE OF PERIODONTITIS INCREASING THE RISK FOR DIABETES. The outcomes of multiple human clinical studies support this observation. Saito et al, reported in 2004 that periodontitis is associated with an increased risk for diabetes (OR=2.6).[27] Ide et al, reported in 2011 that periodontitis is associated with increased risk for diabetes (HR=1.38).[28] Another clinical study reported similar observations, that periodontitis is associated with increased risk for diabetes (RR=3.45).[29] Additional clinical studies have shown a relationship between periodontal disease and glycemic control and glucose tolerance, which may be the mechanistic link through which periodontitis increases the risk of diabetes. One clinical study, supported that periodontal disease was associated with increased risk for poor glycemic control (Odds Ratio = 6.2).[23] Another clinical study, supports that chronic periodontal infection predicts the progression of HbA1c in non-diabetic populations.[30] Still another clinical study, supports that periodontitis is associated with increased risk for impaired glucose tolerance (Odds Ratio = 2.4).[27]

PERIODONTAL THERAPY IN THE FORM OF SUBGINGIVAL SCALING AND ROOT PLANING IMPROVES GLYCEMIC CONTROL BY LOWERING HBA1C. Scaling and root planing is the preferred dental procedure performed to reduce subgingival periodontal inflammation. HbA1c is a term describing glycated hemoglobin, which is directly correlated to both long term glycemic condition and to the risk of developing diabetes associated complications. Five separate meta-analyses published over the last 15 years consistently support this observation. Janket et al, 2005 found that scaling and root planing reduced HbA1c by 0.66%.[31] Darre et al, 2008 found that scaling and root planing reduced HbA1c by 0.46%.[32] Teeuw et al, 2010 found that scaling and root planing reduced HbA1c by 0.40%.[33] Engebretson et al, 2013 found that scaling and root planing reduced HbA1c by 0.36%.[34] Teshome et al, 2017 found that scaling and root planing reduced HbA1c by 0.53%.[35] Collectively, this body of research proves that effective plaque control has a postive effect on glycemic control in diabetic populations. The research reported by Demmer et al in 2012, supports that chronic periodontal infection predicts the progression of HbA1c in non-diabetic populations, which supports a benefit for plaque control in both healthy and pre-diabetic populations which respect to lowering HbAIc levels.[30]

SNF2 IS AN EFFECTIVE ANTIMICROBIAL IN PLAQUE AND GINGIVITIS CONTROL. The management of gingivitis can be attained through repeated mechanical removal of microbial dental plaque from the teeth and/or suppression of bacterial plaque biofilm growth and metabolism. The mechanical control of plaque is accomplished with daily oral hygiene including thorough tooth brushing and flossing. The suppression of plaque growth and metabolism can be achieved through the application of topical antimicrobials added to toothpastes or mouthrinses. Antimicrobials with proven efficacy for the control of plaque associated gingivitis include chlorhexidine, cetypyridinium chloride, mixtures of essential oils, triclosan and stannous fluoride, among others.[36,37] The use of stannous fluoride for the treatment and prevention of plaque and gingivitis began in the 1980's with the application of topical gels, however today its use includes multiple commercial dentifrices sold and distributed around the world.[38-40] Clinical studies have demonstrated significant efficacy of stannous fluoride for the reductions in the amount of supragingival plaque and plaque associated gingivitis – these having been the subject of systematic reviews of randomized clinical studies.[41-43] A recent meta-analysis revealed that during Crest Pro Health (CPH) stannous fluoride dentifrice use 3 out of 4 participants using CPH transitioned to gingival health[44] as defined by guidelines for the 2017 World Workshop of Periodontology.[45] The results of this meta-analyses representing 18 studies in 2,890 patients support that stannous fluoride dentifrices reduce gingival bleeding sites by 51% relative to sodium fluoride control dentifrices in studies of up

to 3 months duration.[44]

Stannous fluoride has both, bactericidal and bacteriostatic effect on plaque bacteria. Recently, it has been demonstrated that dentifrice SnF2 can penetrate into subgingival crevicular fluid during brushing and stannous is retained in subgingival plaque.[46] This SnF2 has been shown to decrease biofilm virulence via attaching to lipopolysaccharide (LPS) and lipoteicoic acid (LTA) molecular patterns on bacterial surfaces interfering with pathogen stimulation of toll receptors[47,48] the latter of which are associated with the initialization of the inflammatory processes involved in periodontal disease.[49-54] Samples of plaque from subgingival areas in subjects brushing with stannous fluoride dentifrice have been shown to exhibit decreased virulence ex vivo.[55,56] In addition, stannous fluoride formulations have been shown to reduce bacterial metabolic products including short chain fatty acids propionic and butyric acid which are derived from bacterial metabolism in deeper parts of plaque biofilms in anaerobic environments.[57] Collectively, research demonstrates significant efficacy for stannous fluoride for the treatment and prevention of gingivitis and has established plaque control including quantity and toxicity as mechanisms for clinical efficacy.

Role of SnF2 in plaque and gingivitis control in patients with diabetes. There are numerous studies showing that the prevalence, progression, severity, and extent of chronic oral diseases are significantly increased in diabetic patients. The main oral complications associated with diabetes, including infection of the gums, periodontal disease, tooth decay, dry mouth, bacterial infections and fungus, halitosis, and prolonged healing of wounds from dental treatments. Diabetes often worsens oral health, particularly that of the gum tissues and bone, which, in turn, deteriorates blood sugar control as described earlier. Due to the risk of diabetic patients to progressive periodontal diseases, it is more important for these patients to develop and maintain good oral hygiene. The patient and dental professional must work together to stop this vicious cycle before it begins by being attentive to daily oral hygiene: brushing and flossing, getting regular oral health checkups, and properly treating periodontal disease early on. Oral hygiene in diabetic patients can be improved by increased education on the requirements for elevated oral hygiene and also by the selection and application of selective oral products applied to their personal hygiene. The causative factors for gingivitis in diabetic patients, toxic plaque can likely be ameliorated by improved hygiene including the selection and use of antimicrobial products with proven efficacy in the prevention of plaque and gingivitis. The use of stannous fluoride dentifrice as part of oral hygiene may represent a useful tool for diabetic patients in maintaining their oral health.

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