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An oligomeric proanthocyanidin nutritional supplement in the treatment of gingivitis – a pilot study

H. Nilofer Farjana*, Senthamizh Ambika and Angel Mary
Asan Memorial Dental College and Hospital, Chengalpet, Chennai, India
farjanajahangeer@gmail.com

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Abstract

Gingivitis and periodontal disease are the most common oral diseases affecting the supporting structures of teeth. They are found associated with various systemic diseases like cardiac disease, stroke, diabetes, lung disease and premature delivery. Arresting the initial periodontal disease by non-surgical methods is always better than treating progressive periodontal disease that necessitates more interventional methods of treatment. Initial non-surgical therapy when done along with nutritional supplement will result in better outcome. Organic foods are always ideal for the betterment of health. In our study, we have used the dietary polyphenols, oligomeric proanthocyanidin (obtained from plants) in combination with vitamin C as a nutritional supplement along with nonsurgical treatment (oral prophylaxis) in treating gingivitis. It is found that these polyphenols reduce gingival inflammation and plaque adhesion on the tooth surface by controlling the underlying pathophysiology of inflammation resulting in improvement in overall oral health.

Keywords: Oral health, inflammation, proanthocyanidin, plaque adhesion, periodontal disease.

Introduction

Gingiva, cementum, periodontal ligament are the four components of periodontium that supports the tooth. Gingiva is that part of soft tissue covering the root and alveolar process to a point coronal to the cementoenamel junction. Cementum provides attachment to the periodontal ligament collagen fibers, maintains the root surface integrity and supports the tooth[1]. Gingiva acts as a barrier to the penetration of microbes and noxious substances into the deeper tissue. The bacterial plaque (Biofilm) is the common etiological factor for gingival and periodontal disease. It triggers various cascade of inflammatory process in the underlying periodontal tissues. When inflammation and tissue breakdown are limited within the soft tissue without any bone destruction it is called gingivitis. Gingivitis is very commonly found oral disease that leads to redness and swelling of the gingiva. Gingivitis when left untreated lead to chronic inflammatory disease called periodontitis. It causes resorption of the supporting alveolar bone and eventually result in tooth loss. The dental plaque triggers the host mediated immune inflammatory response and release inflammatory mediators cytokines, for example interleukins 1α (IL-1α), interleukins 1β (IL-1β), matrixmetalloproteinases (MMPs) and Tumor necrosis factor (TNF-α)[2].

The gingival inflammation result in vascular changes leading to capillary dilatation and increase in blood flow. This changes are due to the microbial activation of resident leucocytes followed by the stimulation of endothelial cells causing tissue and bone destruction eventually resulting in tooth loss. As therapeutic prevention is necessary to arrest the disease progression, we have plant based foods (Dietary polyphenols) in controlling the inflammation.

Several studies have shown positive correlation between periodontal disease and vascular disease. Microbial dissemination from periodontal lesions cause systemic inflammation assessed by various biomarkers like C-reactive proteins and interleukins associated with periodontal disease[3]. Recent research has proved that optimal oral health is required for preventing and managing chronic inflammatory diseases like cardiovascular diseases and diabetes. Dietary nutrients and selective bioactive compounds like polyphenols has now become a potential component in controlling the onset and rapid destruction of periodontitis. Recently, many studies and nutrigenomics showed that good oral health improves the quality of life in adults.

The proanthocyanidins are large class of polyphenols called flavanols. They are complex polyphenols that has similar polymeric building block like tannins. They are obtained naturally from plant metabolites found in certain fruits, vegetables, seeds and bark of pine trees. They are also found in cranberries, seeds of grapes, cranberries and in tea leaves and hawthorns. The other name for proanthocyanidins are procyanidins. The main precursors are blue-violet and red pigments in plant. The properties of proanthocyanidins have recently investigated as an anti-oxidant, anti-viral, anti-bacterial, anti-carcinogenic, anti-inflammatory, anti-tumor, anti-allergic, DNA repair[4]. They also inhibit lipid peroxidation, platelet aggregation, capillary permeability and fragility which affects

the enzymatic pathways including phospholipase A2, cyclooxygenase and lipo-oxygenase. Proanthocyanidins from cranberry juice cocktail includes repeating epicatechin units with atleast one A-type linkage (O7 C2) as compared to B type linkages found in other tannic-rich foods. This particular structure of cranberries influence their biological activity and considered as prerequisite for anti-adhesive property[5].

OPCs when incubated with human cancer cell showed selective cytotoxic effects on cancerous cells without affecting the normal mucosa. It has been proved that along with selective cytotoxicity[6], OPCs also found to up-regulate certain apoptosis-promoter genes and down-regulate apoptosis inhibitor genes in cancerous cells. One of the in-vitro study using an OPC extract have proved its anti-cancerogenic effect, henceforth OPCs could be used as an adjunct in managing the cytotoxic effects along with other chemotherapeutic agents to normal human cells[7].

Research on nutrition has explored that dietary rich fiber, vitamin C, omega 3-fatty acids and vitamin D is beneficial in treating periodontal disease. In our study we have included vitamin C in combination with proanthocyanidin for treating gingivitis. Vitamin C helps in collagen formation, which helps to maintaining the integrity of the tooth as well as reinforce the immune system. Ascorbic acid (vitamin C) is an intracellular and intracellular aqueous anti-oxidant. It is the first line of anti-oxidant in protecting the body by scavenging the oxygen free radical[8]. It also works synergistically with bioflavonoids and vitamin E by regenerating their oxidised states. Though in-vitro studies[9] have proved the beneficial effects OPCs on periodontal disease, more RCT (randomized controlled trials) are necessary to assess the efficacy of OPCs in the clinical outcome of periodontal disease.

The primary goal of the treatment is to reduce gingival inflammation effectively by scaling (oral prophylaxis) along with nutritional supplement. In our study we have given a supplement containing OPC (oligomeric proanthocyanidin) 100mg along with vitamin C 50mg for treating gingivitis. The objective of our study is to evaluate the amount of tissue response using proanthocyanidin as an adjunt to scaling (oral prophylaxis) in preventing gingivitis.

Materials and methods

Study Design and Population: Inclusion criteria: Mild to moderate generalized chronic gingivitis between the age group of 15-30 years. Periodontal disease (defined as gingival sulcus depth ≤3mm and/or positive bleeding when probing).

Exclusion criteria: Any systemic disease like diabetes, caridiovascular disease, pregnant individuals and patients who were smokers. Patients who have undergone periodontal treatment within a period of 3 months.

An oligomeric proanthocyanidin nutritional supplement were given to the study participants, for a period of 21 days. This is ideal to assess the inflammatory changes of gingiva without any irreversible damage. This is a pilot study that includes 10 subjects fulfilling the criteria to test the hypothesis.

The ethical clearance were obtained from Asan Scientific and Ethical Clearance Committee of Asan Memorial Dental College and Hospital, Chengalpet. The study was explained in detail and then they were asked to give their consent willingly and recorded the duly signed informed consent. A single examiner examined the study participants and recorded the clinical parameters both pre-treatment and post-treatment. Patients eligible for the study were given oligomeric proanthocyanidins nutritional supplement after professional cleaning (oral prophylaxis) of the teeth as seen in Table-1. Patients were asked to take once daily the supplement each night after dinner with water. The supplement was asked to be maintained in the mouth until complete dissolution occurs. They were informed neither to drink nor to eat during 30 minutes after taking the treatment.

Oral hygiene methods were instructed during the period of 21 days (modified bass technique method of tooth brushing using soft tooth brushes), which could minimize the risk of bias in the study. Two re-evaluation visits were performed on the 14th and 21st day during the study for clinical examination and for recording the following clinical parameters: Silness and Löe plaque index and gingival index, gingival bleeding index, John Greene and Jack R. Vermillon oral hygiene index, visual analog scale regarding patient satisfaction over the drug and The brightness of the gingival was assessed with pre-treatment and post-treatment photographs taken by digital single lens visual camera (DSLR).

Results and discussion

The statistical analysis was done using SPSS software 11 and the results were obtained. The results were found statistically significant between the baseline and during a follow up period of 21 days. Significant reduction in plaque and gingival index with an improvement in the overall oral hygiene status were found $p<0.05$ as shown in Figure-1. Post-treatment photograph Figure-3 showed reduction in the redness (inflammation) of the gingiva when compared to pre-treatment photograph Figure-2. Visual analog scale recordings showed higher patient satisfaction. No noticeable adverse effect of the drug was found except one of the individuals had a complaint of dryness of throat during the first three days of the intake of supplement.

Discussion: Gingivitis occur due to poor oral hygiene that allows plaque (biofilm) to form on the tooth surface, resulting in inflammation of the surrounding soft tissue, gingiva (reversible) and when left untreated it leads to periodontitis (irreversible) resulting in destruction of the teeth and the supporting periodontal tissues which eventually result in tooth loss. Studies have proved that highest salivary interleukins are potential indicator of probing depth in induced gingivitis[10].

Table-1: Preoperative readings.

Patient Name	OHI	PI	GI	GBI	Supplement
Aishwarya	0.5	1	1	1	Given
Angel	1.5	1	1	1	Given
Sedhupathi	1.6	1	1.1	1	Given
Monica	1.6	1.5	1.6	1	Given
Bhagavan dasa	2.9	1.5	2	2	Given
Pavithra	1.5	1	1.6	2	Given
Thasleema	1.6	1	1.1	1	Given
Nivetha	0.3	1.16	1	1	Given
Akila	1.3	1	1	1	Given
Ambiga	2.1	1.1	2	2	Given

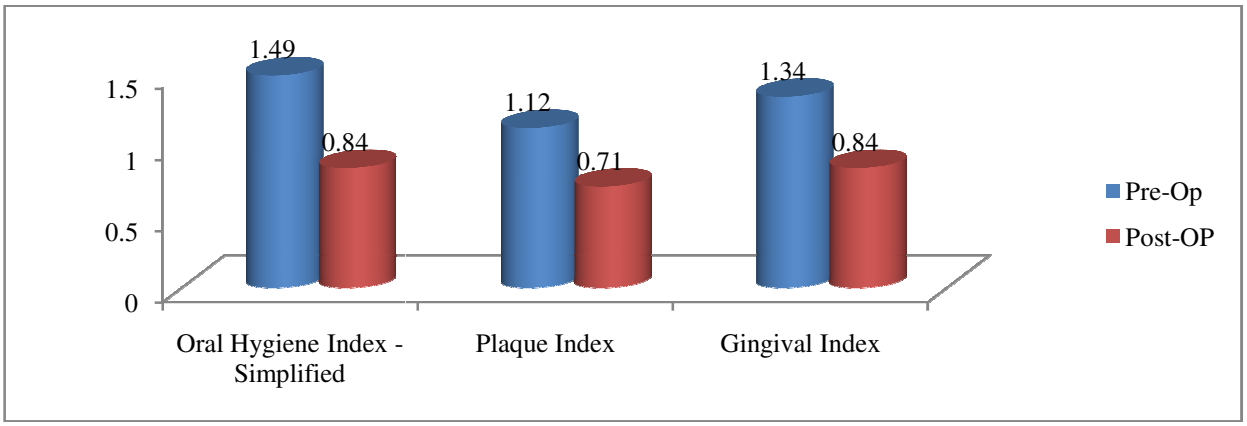

Figure-1: Graph showing pre-treatment and post-treatment findings.

Figure-2: Pre-treatment.

Figure-3: Post-treatment.

The drug given as a supplement is blueberry based nutritional supplement, oligomeric proanthocyanidins[11]. Studies have shown that proanthocyanidins has anti-oxidant, anti-viral anti-bacterial, anti-carcinogenic, anti-inflammatory, anti-allergic properties and vasodilatory actions. Proanthocyandinis have also been shown to inhibit lipid peroxidation, platlet aggregation, capillary permeability and fragility to affect the enzyme systems including phospholipase, A2, cyclooxygenase, and lipo-oxygenase. Proanthocyanidins from cranberry juice cocktail includes repeating epicatechin units with atleast one A-type linkage (O7 C2) as compared to B type linkages found in other tannic-rich foods. This particular structure of cranberries influence their biological activity and considered as prerequisite for anti-adhesive property.

Oligomeric proanthocyanidins (OPCs) have been shown to have antiviral and immune stimulatory effects. Although its antiviral effect and their mechanisms were not precisely defined. Studies

suggest that OPCs increased sensitivity to IFN I might find its application in many viral infections and known to have a novel, robust antiviral property[12].

OPCs are found to be effective in preventing and treating atherosclerosis. Oxidation of low-density lipoproteins is essential in controlling the pathogenesis of atherosclerosis. Mohana et al identified OPCs as a new therapeutic agent in reducing atheromatic changes by preventing monocyte to macrophage conversion in an in-vivo study[13].

Wang et al studied the antioxidant property of OPCs[14]. In his in-vivo study, he investigated the effects of OPCs against carbon tetrachloride (CCl_4) induced liver steatosis and injury. It is found that there is reduction in the levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), total triglyceride (TG), total cholesterol (TC), low-density cholesterol (LDL-c) and liver malondialdehyde (MDA) with an increase in the levels of serum high-density lipoprotein (HDL-c) and liver superoxide dismutase (SOD). Thereby proving that OPCs can cause improvement in reducing oxidative stress and resulting liver injury.

In recent years, many studies tries to find out edible and biocompatible substance that could interfere with the formation of bacterial plaque (biofilm). Further cranberries were found to reduce dental caries and formation of biofilm by Streptococcus mutans and Streptococcus sobrinus. Yamanaka et al evaluated the effect of cranberry juice on Streptococcus adhesion to tooth surface. It is found that bacterial adhesion to the hydroxyapatite pellets decreased significantly[15].

Proanthocyanidins from grape seed, found to have an inhibitory effect on HIV infection in vitro. The expression of chemokine receptors 3 and 5 on Th-2 lymphocytes are the prerequisite for HIV infection of the central nervous system[16]. An OPC extract incubated with immunocompetent peripheral blood mononuclear cells suppress the gene expression of HIV-1. This inhibition prevent binding of the HIV virus to receptor sites on normal white blood cells, henceforth prevent the infection[17].

Study by Howell et al determined that oligomeric proanthocyanidins isolated from cranberries inhibited in vitro adhesion of E. coli to uroepithelial cells and thereby having a preventive effect on urinary tract infections[18]. Anti-inflammatory effect and antimicrobial effect of OPCs were reported by various studies[12,19-24]. Numerous studies have shown positive effect of OPCs on periodontal disease. We have found at the end of our study, that oligomeric proanthocyanidin (OPC) have a positive beneficial effect on periodontal tissues, which was well seen by the reduction of scores of the Silness and Löe plaque index and gingival bleeding index. With an additional finding of decrease in the redness (inflammation) of the gingiva.

The antibacterial activity of proanthocyanidins is not only limited to Gram-negative species like Porphyromonas gingivalis but also found effective against Gram-positive bacteria. Kylli et al have recently found proanthocyanidins from lingonberry (Vaccinium vitisidaea) and European cranberry (Vaccinium microcarpon)[25]. Mayer et al, have found that grape seed extract, which is economic and easily available in various flavonoids, oligo and polymeric proanthocyanidins. It is also found that OPC are active against 10 different pathogens like various strains of Staphylococcus and Pseudomonas and Escherichia coli. But the extent of antibacterial activity of proanthoycanidins and proanthocyanidin containing preparations still needs to be explored[26].

Conclusion

Oligomeric proanthocyanidin in combination with vitamin C reduces gingival inflammation and provides an overall positive effect in periodontal tissues assessed by comparing pre-treatment and post-treatment scores of Silness and Löe plaque index and gingival bleeding index. Also the supplement reduces plaque accumulation on the tooth surface, though studies by Diaz Sanchez et al on oligomeric proanthocyanidin nutritional supplement have concluded that there was no effect in the plaque accumulation. Further research with more of randomized controlled trial are necessary to study the effect of proanthocyanidin on plaque accumulation.

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