

Effectiveness of Oral supplementation of Resveratrol in Periodontitis Patients

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Abstract

The treatment of periodontitis involves mechanical debridement along with antibiotic therapy. As it is assumed that in patients with periodontal disease, there may be a resistance to antibiotics; resveratrol with a strong anti-microbial and anti-inflammatory properties can play an important role in the treatment process. The aim of the study is to evaluate the effectiveness of resveratrol as an oral supplementation as adjunctive to non-surgical periodontal treatment. A total of 16 patients with gingivitis and periodontitis were enrolled in this study. After scaling and root planning, study group patients were instructed to take 500mg oral resveratrol supplementation daily once for 1 month. After 12

months clinical parameters include GI, PI, BOP, PD, were recorded and compared with the baseline parameters. Study group has showed statistically significant clinical parameters when compared to the control group in 12-month post-operative clinical parameters when compared with the baseline clinical parameters.

Keywords: Resveratrol, oral supplementation, NSPT, Periodontitis, Adjunctive therapy

Introduction

Periodontitis is a chronic inflammatory disease associated with dental biofilm and exaggerated host immune response.^[1] If left untreated leads to the clinical attachment loss, bone loss eventually loss of the tooth

structure. The treatment of periodontitis involves mechanical debridement, however scaling and root planning alone can't eliminate the bacteria and their endotoxins, especially in deeper periodontal pockets, which are not accessible to mechanical debridement. These endotoxins can elicit inflammatory reactions which lead to the release of proinflammatory cytokines, tissue degrading enzymes like elastase, collagenase, proteases etc. [2]

As it is assumed that in patients with periodontal disease, there may be a resistance to antibiotics; resveratrol with a strong anti-microbial and anti-inflammatory properties can play an important role in the treatment process. Resveratrol (3, 5, 4'-trihydroxystilbene) is a polyphenol belonging to the class of stilbenes. [3] It has phytoalexin properties as it is produced by plants in response to stress conditions including bacterial and fungal infections. *Polygonum cuspidatum* (the richest source of resveratrol) is a plant and is known as an herbal medicine. Resveratrol exists in foods such as grapes, peanuts, pistachio, and cranberry. [4,5]

It is known as an anti-microbial, anti-inflammatory, anti-apoptotic, anti-cancer substance, and osteogenic factor. Resveratrol may have an antioxidant effect against oxidative stress in some chronic diseases such as diabetes mellitus and cardiovascular disease. In addition, resveratrol had beneficial effects on the liver disorders and hepatic steatosis by extenuating oxidative stress and reducing hepatic fibrosis.

Despite a higher annual sale of resveratrol supplement in the United States, there are only a few human studies about its beneficial effects Timmers et al., 2013. Based on the results of the limited human and animal studies carried out on diabetic subjects, it was reported that resveratrol can reduce insulin resistance, plasma glucose, hemoglobin A1c, FBS, and inflammatory factors, and

also, it may improve insulin sensitivity. There are many studies carried out to investigate the effects of nonsurgical periodontal treatment (NSPT) on recovery of metabolic status in these patients.

However, there are very few studies investigating the impact of nutrition including the protecting effects of resveratrol on periodontal disease. So, our aim of the study was to evaluate the effectiveness of resveratrol as an oral supplementation as adjunctive to non-surgical periodontal therapy.

Materials and Methodology

A total of 20 patients who were reported to the department of periodontology, Faculty of dentistry, Ramaiah University of applied sciences were selected for this interventional study. Patients were explained the study protocol and Informed consent was taken in the form of written informed consent. This study was approved by institutional ethics committee and was conducted accordance with the Declaration of Helsinki 1975, as revised in 2013

The selection criteria of the study included a detailed history and periodontal examination. Patients with age range of 20-60 years and having gingivitis and periodontitis with probing pocket depth \geq 5mm and clinical attachment level \geq 2mm with at least 20 completely erupted teeth were selected for this study. Patients with atherosclerotic vascular disease (i.e, CVD, stroke, and peripheral artery disease) Immunological disorders, anti-inflammatory and nonsteroidal anti-inflammatory therapy within 3 months prior to periodontal assessment and women who were pregnant or lactating and also patients who had habit of smoking, Patients who received periodontal treatment within last 6 months were excluded from the study.

The statistical analysis was done using the Statistical Package for Social Sciences [SPSS] for Windows

Version 22.0 Released 2013 and Armonk, NY: IBM Corp.

Descriptive Statistics includes expression of study parameters in terms of Mean & SD for each study group. Inferential Statistics using Mann Whitney test to compare the mean values of different study parameters between 2 groups at pre-op and post-op periods. Wilcoxon Signed Rank test was done.

The level of significance was set at $P < 0.05$.

Patients were randomly allocated in the two groups. Clinical parameters included, gingival index (GI), plaque index (PI), bleeding on probing (BOP) and clinical attachment level (CAL) were calculated at the baseline. Both study and control group patients received non-surgical periodontal therapy including scaling and root planning. After scaling and root planning, study group patients were instructed to take 500mg oral resveratrol supplementation daily once for 1 month, which is commercially available (Health vit), and 30 capsules were placed in amber plastic bottle, given to the patients. Control group people were received placebo that is starch in the form of capsules for 1 month. After 12 months clinical parameters were again recorded for 16 patients, as 4 patients lost during the follow up.

Results

This interventional prospective study of total of 16 patients containing study group and control group showed improved plaque index score when compared to baseline and 12 month post operative clinical parameters. Using Mann Whitney test the mean plaque scores (PI), gingival index (GI), clinical attachment level (CAL) showed statistically significant results when compared to baseline parameters in study group (Table1&2).

The study group mean pocket depth value at baseline is 6.22, post-operative value is 5.11. The mean difference

is 1.11, which is statistically significant. In the control group the mean pocket depth value at baseline is 6.29, post-op is 6.33. The mean clinical attachment level in the study group at base line is 3.54, whereas post-operative value is 2.92, which shows statistically significant result when compared to the control group.

Discussion

In the present study we obtained positive correlation between resveratrol supplementation and reduction in probing pocket depth and clinical attachment level gain in study group compared to the control group. The resveratrol supplementation for 4 weeks had showed improved gingival index scores also. Resveratrol (3,4,5-trihydroxystilbene), a polyphenolic stilbene abundant in wine, the skin of red grapes, peanuts, and berries, has been known to have anti-inflammatory, anticarcinogenic, cardioprotective, and antibacterial properties.^[6] Mouthwash antibiotics are widely used to control periodontal disease: however, excessive use of antibiotics may lead to bacterial resistance against them; therefore, a new treatment strategy is needed.^[7]

Natural ingredients derived from plants such as polyphenols are widely considered for the treatment of periodontal disease. Recently, it has also been reported to be effective in healing and preventing experimental periodontitis in an animal model and has also been shown to have regenerative potential. Its ability to heal inflammation and prevent bone loss due to periodontitis has been reported in several experiments. Jeong-Chae Lee et al., employed an experimental periodontitis model using lipopolysaccharide (LPS) and ligature to investigate the protective effect of resveratrol on periodontal tissue damage, findings support a possibility that resveratrol is to be an attractive bioactive material for the treatment of periodontitis.^[8] This due to Resveratrol inhibits (lipopolysaccharide) LPS-stimulated

expression of inflammation related factors in (human gingival fibroblasts) hGFs, alleviates mitochondrial ROS levels and protein kinase activation in LPS-stimulated hGFs, elevates the induction of (heme oxygenase-1) HO-1 and (nuclear factor-E2 related factor 2) Nrf2 in hGFs, inhibits osteoclast formation.^[9] Nrf2 is an important detector of toxic xenobiotic content and its activation is essential as a cellular redox defense mechanism. Nrf2 interacts with antioxidant defense systems, increases cellular resistance to oxidative stress, and downregulates inflammatory responses via transcriptional activation of its target genes, including the gene encoding HO-1.^[8,10]

In one study carried out by Nafumi et al., the effects of resveratrol were investigated on Wistar male rats with periodontal disease, and it was shown that resveratrol reduced periodontitis and bone loss, increased antioxidant defense, and improved inflammatory factors; therefore, resveratrol supplementation was recommended for improving periodontal status.^[11]

Huyn-joo Park et al conducted study on investigated the effect of resveratrol, a naturally occurring polyphenol, on *P. gingivalis* -9. LPS-accelerated vascular inflammation, a key step in the progression of

periodontitis. Resveratrol significantly inhibited the *P. gingivalis* LPS-induced adhesion of leukocytes to endothelial cells and to the aortic endothelium by down-regulating the cell adhesion molecules, ICAM-1 and VCAM-1.^[12] Moreover, the inhibition of the *P. gingivalis* LPS-induced cell adhesion molecules by resveratrol was mainly mediated by nuclear factor- κ B (NF- κ B).^[13,14]

Nutritional factors (such as anti-inflammatory and antioxidant nutritional compounds) are known to be important factors affecting periodontal disease, so it is expected that improving nutritional habits and diet may be useful in the treatment of periodontal disease. Razie Hormoznejad et al investigate the impact of resveratrol supplementation along with non-surgical periodontal treatment on blood glucose, insulin, insulin resistance, triglyceride (TG), and periodontal markers in patients with type 2 diabetes with periodontal disease. It is recommended that resveratrol supplementation may be beneficial as adjuvant therapy along with non-surgical periodontal treatment in insulin resistance and improving periodontal status among patients with diabetes with periodontal disease.

Table 1: Mean values of clinical parameters during pre-op period in both groups.

Comparison of mean values of different study parameters between 2 groups during pre-op period using Mann Whitney Test						
Parameters	Groups	N	Mean	SD	Mean Diff	P-Value
PI	Study	8	0.98	0.75	0.23	0.75
	Control	8	0.75	0.20		
GI	Study	8	0.81	0.55	-0.10	0.67
	Control	8	0.91	0.48		
PD	Study	8	6.22	0.92	-0.07	0.46
	Control	8	6.29	0.89		
CAL	Study	8	3.54	0.92	-0.38	0.46
	Control	8	3.92	1.05		

Table 2: Mean values of clinical parameters during post-op period in both groups

Comparison of mean values of different study parameters b/w pre-op & post-op period in study group using Wilcoxon Signed Rank Test						
Parameters	Time	N	Mean	SD	Mean Diff	P-Value
PI	Pre-op	8	0.98	0.75	0.59	0.01*
	Post-op	8	0.39	0.18		
GI	Pre-op	8	0.81	0.55	0.31	0.03*
	Post-op	8	0.50	0.48		
PD	Pre-op	8	6.22	0.92	1.11	0.01*
	Post-op	8	5.11	0.70		
CAL	Pre-op	8	3.54	0.92	0.63	0.01*
	Post-op	8	2.92	0.84		

Fig 1: Mean values of clinical parameters in both study and control groups.

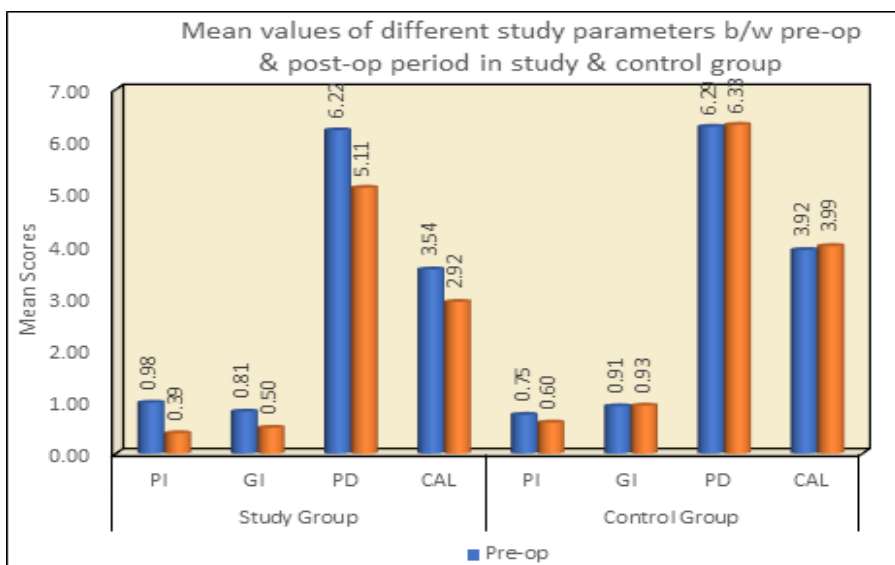


Table 3: summarizing the pre-op & post-op clinical parameters in both the groups.

Comparison of mean values of different study parameters b/w pre-op & post-op period in study group using Wilcoxon Signed Rank Test								
Group	Parameters	Time	N	Mean	SD	Mean Diff	P-Value	
Study Group	PI	Pre-op	8	0.98	0.75	0.59	0.01*	
		Post-op	8	0.39	0.18			
	GI	Pre-op	8	0.81	0.55	0.31	0.03*	
		Post-op	8	0.50	0.48			
	PD	Pre-op	8	6.22	0.92	1.11	0.01*	
		Post-op	8	5.11	0.70			
CAL	Pre-op	8	3.54	0.92	0.63	0.01*		

Control Group		Post-op	8	2.92	0.84		
	PI	Pre-op	8	0.75	0.20	0.15	0.04*
		Post-op	8	0.60	0.21		
	GI	Pre-op	8	0.91	0.48	-0.01	0.71
		Post-op	8	0.93	0.47		
	PD	Pre-op	8	6.29	0.89	-0.04	0.71
		Post-op	8	6.33	0.90		
	CAL	Pre-op	8	3.92	1.05	-0.08	0.28

Conclusion

Resveratrol has anti-inflammatory, antibacterial and antioxidant properties. It is most widely used in medical field in therapeutic modalities of cardiovascular disease, cancer and diabetes etc. In this 12 month follow up study, the study group patients who had taken resveratrol supplementation for 1 month as an adjunct to NSPT when compared to control group had showed statistically significant clinical parameters in means of gingival index (GI), clinical attachment level gain (CAL), pocket depth (PD) compared to the baseline values. It is recommended that resveratrol daily intake for 1 month as an adjunct to NSPT had beneficial effects on periodontal health. Furthermore, long term studies with larger sample size are indicated to validate our current findings. Thus using resveratrol as an nutritional supplement is beneficial for periodontal patients.

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