The effect of grape seed extract supplementation on gingivitis and glycaemic control in diabetic patients

Dr. Kalyan Pokala, Dr. Mulpuri Venkata Ramoji Rao, Dr. Sathish Manthena,
Dr. Penubolu Lakshmi Preethi, Dr. Venkata Naga Sri Harsha Anumolu, Dr. Sai raj Jayana

Department of Periodontics & Implantology, Drs. Sudha & Nageswara Rao Siddhartha Institute of Dental sciences, Chinnaoutpalli, Gannavaram Mandal - 521286

ABSTRACT

AIM: To investigate the effect of grape seed extract oral supplementation as an adjunct to non-surgical periodontal therapy on gingival health and glycaemic control in diabetic patients.

Materials & Methods: A total of 30 participants were randomly assigned to two groups: the intervention group receiving grape seed extract (500mg/day) and the control group receiving a placebo. Randomization was achieved by the clinician using a flip coin method. Clinical periodontal assessments were conducted both before and after the 90 days intervention period, encompassing parameters such as Oral Hygiene Index (OHI), Plaque Index (PI), Gingival Index (GI). Additionally, glycated Hemoglobin (HbA1c) levels were monitored to assess changes in glycaemic control, with measurements taken at baseline and post-intervention.

Results: intra-group comparison of HbA1c levels at different time intervals (baseline and 90th day) for both the test and control groups. It indicates a slight decrease in HbA1c levels on the 90th day compared to baseline for both groups, with high statistical significance observed for the test group ($p<0.002$**) and potential statistical significance for the control group ($p<0.023$*). It shows higher levels of HbA1c in the control group at both time points, although no statistical significance was found between the groups. It demonstrates a decrease in OHI scores from baseline to the 90th day in both groups, with high statistical significance observed for both groups ($p<0.001$*)., there was a statistically significant decrease on the PI values from 2.08±0.4020998 to 0.925±0.2731396 ($p<0.05$). It highlights a decrease in Gingival scores from baseline to the 90th day in both groups, with high statistical significance observed for both ($p<0.001$*). a slight increase in Gingival scores in the control group at both time points, with slightly higher statistical significance between the groups at the 90th day ($p<0.008$**).

Conclusion: Grape seed extract supplementation, when used adjunctively with full mouth disinfection, demonstrates promising outcomes in reducing gingival inflammation associated with chronic periodontitis in type II diabetic patients.

Introduction:

Gingivitis and periodontitis are both inflammatory, infectious disorders of the mouth. A reversible inflammatory response of the marginal gingival to plaque buildup is known as gingivitis, but periodontitis is a damaging, irreversible disorder that causes the loss of the connective tissue that holds teeth to the bone, ultimately resulting in the loss of the afflicted teeth. Gingivitis is mostly caused by dental plaque and the germs that reside in it.[1]

Diabetes mellitus is a group of metabolic disorders that is characterized by elevated levels of glucose in blood (hyperglycaemia) and insufficiency in production or action of insulin produced by the pancreas inside the body. [2,3] Type II diabetes accounts for 90-95% of diabetic patients. Clinical studies have demonstrated a higher prevalence of periodontitis in diabetic patients. Periodontal disease and diabetes seem to be interrelated and in a bidirectional relationship. The risk of periodontitis is increased by approximately three-fold in diabetic individuals as compared to nondiabetic individuals.[4] Periodontal treatment has been associated with improved glycaemic control and reduction in HbA1c levels in type II diabetic individuals.[5,6]

Nonsurgical periodontal therapy, scaling and root planing (SRP) is the major and most important treatment method for periodontitis. Various therapeutic approaches have been explored to manage chronic periodontitis and glycaemic control in diabetic patients. One such avenue is using grape seed extract (GSE), a natural polyphenolic compound known for its antioxidant and anti-inflammatory properties. GSE is derived from the seeds of Vitis vinifera, the common grapevine. It is rich in bioactive polyphenolic compounds such as proanthocyanidins, flavonoids, and resveratrol, which possess potent antioxidant, and anti-inflammatory properties. [8,9] These properties have sparked interest in evaluating the potential of GSE as an adjunctive therapy for chronic periodontitis and its impact on glycaemic control in type II diabetic patients. To the best of our knowledge, there is no randomized controlled trial assessing the effects of oral supplementation of GSE as an adjunct to scaling and root planing on diabetic patients with chronic gingivitis, and because of insufficient information, this study endeavours to investigate the effect of grape seed extract oral supplementation as an adjunct to non-surgical periodontal therapy on gingival health.

MATERIALS AND METHODS

A total of 30 participants were recruited from the outpatient department of the Department of Periodontics and Implantology. Inclusion criteria included a diagnosis of type II diabetes (moderate diabetes control HbA1c level – 7% to 8%), age between 30-65 years, should have a simplified oral hygiene index score of 1.3-3.0 (Greene JC 1967)[10] and gingival inflammation with a gingival index score between 1.1-3.0 (Loe & Silness 1967)[11], and mild periodontitis 1-2mm of clinical attachment loss (AAP classification of periodontal disease1999)[12] confirmed by clinical and radiographic assessments. Participants with a history of allergies to grape products, pregnant or lactating women, individuals on antioxidant supplements, and those with severe systemic illnesses were excluded from the study.

Randomization and Blinding

Participants were randomly assigned to two groups: the intervention group receiving grape seed extract (500mg/day) and the control group receiving a placebo. Randomization was achieved by the clinician using a flip coin method. Both participants and researchers involved in data collection and analysis were blinded to the group assignments to minimize bias.

Outcome Measures

The study employed various outcome measures to evaluate the effectiveness of the intervention. Clinical periodontal assessments were conducted both before and after the 90 days intervention period, encompassing parameters such as Oral Hygiene Index (OHI), Plaque Index (PI), Gingival Index (GI). Additionally, glycated Hemoglobin (HbA1c) levels were monitored to assess changes in glycaemic control, with measurements taken at baseline and post-intervention. These comprehensive assessments provided insights into the impact of the intervention on periodontal health, glycaemic control and status.

Results:

Statistical analysis

After calculating the mean oral hygiene index, gingival index, and HbA1cscores of the test and control sides using the above indices. The data is collected and entered into microsoft excel and is subjected to statistical analysis using SPSS version 21.0. The data is checked for normality using Shapiro – Wilk test ($p<0.212$) and it showed the data is normally distributed. Descriptive statistics and inferential statistics such as Independent t test are performed for intergroup comparison and Paired t test is performed for intragroup comparison at baseline and 30^{th} day.

The null hypothesis is set as there is no significance effect of GSE oral supplement as an adjunct on gingival health and HbA1c levels in diabetes patients. Statistical significance level was set at $p<0.05$[1] (95% confidence). Thus, values of $p< 0.05$were regarded as Statistically significant. Therefore, the null hypothesis will be rejected with 95% confidence.

Demographic and baseline clinical parameters were similar across both the study groups [Table-1]. The average age of the test group was 50.05±11 years and of the control group was 57.6±13.63 years. The age difference between the two groups was statistically not significant. At Day 0 (baseline), the scores for OHI, GI were also comparable between the study groups. The differences were not statistically significant ($p>0.05$) [Table-1]. Thus, the similarities in patient selection enabled paired comparisons to be made between the two groups.

Oral hygiene Index (OHI) :

At baseline, in the test group OHI values were 2.46±0.28. After thirty days, there was a statistically highly significant decrease on the OHI values to 0.50 ± 0.11 ($p=0.001$). similarly in the control group at base line the OHI values were 2.52 ± 0.25 and after 90 days there was a significant decrease in OHI values to 0.57 ± 0.08. ($p=0.001$)[Table 2].

Inter group comparison of OHI index scores between the test and control group after 90 days showed no statistically significant difference $p =0.47$[Table3].

Gingival index (GI) :

At baseline, in the test group and control groups mean GI values were 2.60 ±0.31 and 2.67 ± 0.22 respectively. After 90 days, there was a statistically significant decrease in gingival scores in both test and control groups to 0.25 ± 0.12 and 0.49 ± 0.10 respectively with $p = 0.001$in [Table 4].

Inter group comparison of gingival index scores between the test and control group after 90days showed statistically significant difference with p=0.008[Table5].

Glycosylated hemoglobin levels (HbA1c) :

At baseline, in the test group HbA1c values were 7.6 ± 0.73. After 90 days, the values were 7.2 ± 0.58, there was a significant decrease with p=0.002 [Table 6].

Similarly, HbA1c values in the control group at base line and after 90 days were 7.7 ± 0.73 and 7.4 ± 0.62 and there was significant difference with p=0.02[Table 6].

Inter group comparison of HbA1c index scores between the test and control group after 90 days showed no statistically significant difference p =0.07[Table 7].

Tables

Table 1: Inter group comparison for demographic and baseline data using independent t test.

	Test group	Control group	p-value unpaired t-test
Age in years	50.05 ± 11.00	57.6 ± 13.63	0.08 (NS)
OHI	2.46 ± 0.28	2.52 ±0.25	0.11(NS)
GI	2.60 ± 0.31	2.67 ±0.22	0.26(NS)
HbA1c	7.6 ± 0.73	7.7 ± 0.53	0.12 (NS)

Table 2: Intra group comparison of control and test groups for oral hygiene index at different time intervals – Paired t test

Group	Time	N	Mean	Std. Error Mean	95% Confidence Interval		p Value
					Lower	Upper	
Test group	0 DAY	15	2.46±0.19	0.05	1.83	34.39	p<0.001***
	AFTER 90 DAYS	15	0.50±0.24	0.06			
Control group	0 DAY	15	2.56±0.16	0.04	1.87	34.15	p<0.001***
	AFTER 90 DAYS	15	0.56±0.21	0.05			

Table 3: Inter Group Comparison of Control and Test Group for Oral Hygiene Index at different time intervals Using unpaired t test.

Time	Group	N	Mean	Std. Error Mean	95% Confidence Interval		p Value
					Lower	Upper	
0 DAY	Test group	15	2.46±0.19	0.05	-0.24	0.028	p<0.116
	Control group	15	2.56±0.16	0.04			
AFTER 90 DAYS	Test group	15	0.50±0.24	0.06	-0.23	0.111	p<0.478
	Control group	15	0.56±0.21	0.05			

Table 4: Intra group comparison of control and test groups for gingival index at different time intervals – Paired t test

Group	Time	N	Mean	Std. Error Mean	95% Confidence Interval		p Value
					Lower	Upper	
Test group	0 DAY	15	2.60±0.16	0.04	2.198	2.49	p<0.001***
	AFTER 90 DAYS	15	0.26±0.18	0.05			
Control group	0 DAY	15	2.67±0.15	0.03	2.02	2.35	p<0.001***
	AFTER 90 DAYS	15	0.48±0.23	0.06			

Table 5: Inter group comparison of control and test groups for gingival index at different time intervals – unpaired t test

Time	Group	N	Mean	Std. Error Mean	95% Confidence Interval		p Value
					Lower	Upper	
0 DAY	Test group	15	2.60±0.16	0.04	-0.186	0.05	p<0.264
	Control group	15	2.67±0.15	0.03			
AFTER 90 DAYS	Test group	15	0.26±0.18	0.05	-0.37	-0.06	p<0.008**
	Control group	15	0.48±0.23	0.06			

Table 6: Intra Group Comparison of Control and Test Group for Hba1C at different time intervals

Group	Time	N	Mean	Std. Error Mean	95% Confidence Interval		*P* Value
					Lower	Upper	
Test group	0 DAY	15	7.60±0.25	0.07	0.159	0.551	p<0.002**
	90th DAY	15	7.25±0.25	0.66			
Control group	0 DAY	15	7.74±0.23	0.06	0.048	0.552	p<0.023*
	90th DAY	15	7.44±0.31	0.08			

Paired t–test, statistical significance set as *P*<0.05*

Table 7: Inter Group Comparison of Control and Test Group for Hba1C at different time intervals.

Time	Group	N	Mean	Std. Error Mean	95% Confidence Interval		*P* Value
					Lower	Upper	
0 DAY	Test group	15	7.60±0.25	0.07	-0.323	0.043	p<0.12
	Control group	15	7.74±0.23	0.06			
90th DAY	Test group	15	7.25±0.25	0.66	-0.408	0.021	p<0.07
	Control group	15	7.44±0.31	0.08			

Independent t –test, statistical significance set as *P*<0.05*

Discussion:

The phrase "periodontal disease" is used to refer to a wide range of illnesses and ailments affecting the periodontal tissues. Gingivitis and periodontitis are the two main diseases brought on by an accumulation of tooth plaque biofilm. Gingivitis is an inflammatory lesion that is restricted to the gingiva. Periodontitis, a more severe and destructive form of gingivitis, can develop in susceptible individuals from gingivitis.

In general, there are two types of gingival disease: Gingivitis brought on by dental plaque biofilm and gingival illnesses brought on by non-dental plaque. Presence of both local risk factors (predisposing factors) and systemic risk factors (modifying factors) will influence the threshold of plaque accumulation required to cause gingival inflammation and impact upon its rate of progression at specific sites or at a whole mouth level between individuals. Systemic risk factors are personal traits that can have an adverse impact on an individual's immune-

inflammatory response to a certain dental plaque biofilm burden, leading to increased or "hyper" inflammation.

There is growing evidence that there is a two-way link between diabetes and periodontal disease. The degree of hyperglycaemia and the severity of periodontitis are clearly correlated. With diabetes increasing the risk for periodontitis and periodontal inflammation negatively influencing glycaemic management. Periodontitis was occasionally referred to as the "sixth complication of diabetes" in the early 1990s and the ADA in 2003 recognised that periodontal disease is frequently observed in patients with diabetes.[13] Inflammation is a central feature of the pathogenesis of diabetes and periodontitis.

Elevated serum levels of IL-6 and TNF-α have been demonstrated in diabetes.[14] Nesto R reported that increase in levels of CRP is associated with insulin resistance in type 2 diabetes mellitus.[15] Serum levels of IL-6 and CRP are also raised in patients with periodontitis, with IL-6 levels correlating with the extent of disease.[16] Periodontal treatment has been shown to reduce serum levels of inflammatory mediators, including IL-6, TNF-α, CRP and MMPs, in patients with and without diabetes.[17] According to the adage "We are what we eat," eating contributes to overall health in humans, including dental health. Dietary recommendations for Americans (2010) state that fruits and vegetables should make up half of your plate. Fruits are frequently referred to as "health foods" because of their abundance in dietary fiber, antioxidants, minerals, and vitamins. Natural products, especially medicinal plant-derived secondary metabolites, represent an important source of new chemical entities that can be used in pharmacological research, especially for inflammatory and infectious diseases. Grapes are one unique fruit that are implicated worldwide in the health research literature for the presence of several phytonutrients, especially in their skin and seeds.

Grapes and grape seeds are rich in polyphenolic compounds like monomeric catechin and oligomeric proanthocyanidins. They belong to the family of natural compounds called flavonoids. In this randomized control trial, we attempted to investigate whether oral supplementation of grape seed extract after scaling has any positive effect on gingival health and glycaemic control in type II diabetes individuals with gingivitis. In our study we observed that individuals in both the groups i.e., those individuals that received GSE oral supplements and the ones that received only scaling and root planing showed significant improvement in oral hygiene index and gingival index 90 days after oral prophylaxis (scaling). These results were in accordance with results obtained in a study by Das M et al in 2001, where 36 patients received subgingival application of 4% GSE gel after scaling and root planing.[18] Individuals who received GSE extract showed significant reduction in gingival inflammation than the group that received scaling and root planing alone even 90 days after scaling and root planing. The findings thus demonstrated that GSE supplementation improved host resilience and inhibited the biological and mechanical irritants implicated in the start of gingivitis and the development of periodontal disease. Studies on rat models showed that GSE supplementation significantly reduced HbA1c levels.[19]

In our study both the groups there was only statistically significant improvement in HbA1c levels with less magnitude of change at clinical level. In all the patients belonging to both the

groups HbA1c levels were still ≥ 7.0%. In 2010, a meta-analysis of five studies involving 371 patients also reported a significant weighted mean reduction in HbA1c of 0.40% over a follow up period of 3–9 months after periodontal therapy. Although the exact processes are not yet known, they most likely have to do with decreased systemic inflammation (e.g., decreased blood levels of mediators like TNF- and IL-6) after periodontal disease has been treated and resolved.[20] The results of our study are in accordance with the study by B. P. Gargari et al 2011.[21] They did not observe any significant difference of HbA1c level in type II diabetic participants 30 who received 200mg of GSE supplementation for 2 months.

In contrast a study on 160 Chinese men and women with prediabetes or early untreated diabetes the group that received purified anthocyanin supplementation showed significant reduction in HbA1c levels.[22] In our study we did not detect significant improvement in HbA1c levels in both the groups, possibly due to the study being underpowered to find significant difference for HbA1C levels. The reasons why our results differ from those of previous studies include, variations in the supplementation dosage, length of study, and flavonoid content of grape seed extracts. Flavonoid content variations have been linked to the sample's origin, variety, level of ripeness, cooling method, and protein, fat, and carbohydrate content.

Conclusion:

Grape seed extract supplementation, when used adjunctively with full mouth disinfection, demonstrates promising outcomes in reducing inflammation associated with chronic periodontitis in type II diabetic patients. In our study both the groups there was only statistically significant improvement in HbA1c levels with less magnitude of change at clinical level. Further studies are warranted to elucidate its long-term effects and potential as a therapeutic agent in managing periodontal complications in diabetic individuals.

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