Original Article

The Effect of Phase I Therapy on the Clinical Parameters, VSC Levels, and RBS Levels in Chronic Periodontitis Patients With Diagnosed Diabetes

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Introduction: The relationship between chronic periodontitis and type 2 diabetes mellitus (DM) is bidirectional. Halitosis or oral malodor has an effect on psychological and social life of persons, and is seen in individuals with diabetes. Aims and Objectives: The aim of this study was to find out the effect of phase I therapy on the clinical parameters, volatile sulfur compound (VSC) levels, and random blood sugar (RBS) levels in chronic periodontitis patients with diagnosed DM. Materials and Methods: Our study included 80 patients with diabetes and chronic periodontitis. We collected subgingival plaque samples at 1 week and 1 month after scaling and root planing. The parameters measured were probing pocket depth and clinical attachment level for all the teeth at four sites per each tooth. RBS levels were recorded for all the patients. Malodor was measured with Tanita Breath Checker (Tanita India Private Limited, Mumbai, Maharashtra, India). Results: We found a statistically significant reduction in clinical parameter levels, VSC levels, and N-benzoyl-DL-arginine-2-naphthylamide (BANA) levels in both the groups from baseline to 4 weeks with highest levels in diabetic chronic generalized periodontitis (CGP) and lowest in nondiabetic CGP at baseline. The mean intergroup comparison of BANA levels was statistically significant at all intervals of time between the two the groups. Conclusion: There is a significant correlation observed between oral malodor levels, RBS, and clinical parameters in the diabetic group.

KEYWORDS: Chronic periodontitis, diabetes mellitus, oral malodor, random blood sugar, volatile sulfur compounds

INTRODUCTION

Periodontal disease is an infection caused due to poor oral hygiene, thereby causing destruction of supporting tissues of teeth. It includes two major entities, inflammation of the gingiva alone (gingivitis) and periodontal ligament (periodontitis), which may cause tooth loss. Several studies have demonstrated correlation between periodontitis and systemic diseases such as diabetes mellitus (DM), cardiovascular disorders, and immunodeficiencies.[1-3]

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Oral malodor is one of the most common cause of patients visiting dentist. It has many local and systemic causes. Local etiology includes calculus and systemic causes include DM, renal disorders, and so on. Bad breath has a considerable impact on patient’s daily social life. Oral malodor has been reported in patients with periodontal disease and a positive association has been established between the severity of periodontitis and volatile sulfur compound (VSC) levels.\(^{[4,5]}\)

VSCs are produced by means of putrefactive action of microorganisms on exogenous and endogenous proteinaceous substrates, such as exfoliated cells, leukocytes, and food debris. Several studies have shown that hydrogen sulfide (H\(_2\)S), methyl mercaptan (CH\(_3\)SH), and to a lesser extent, dimethyl sulfide (CH\(_3\)SCH\(_3\)) constitute about 90% of the total VSC, and they are the chemicals responsible for halitosis.\(^{[6,7]}\)

It has been reported that diabetic patients are more prone to develop gingivitis and periodontal disease than nondiabetic patients. These individuals have features such as increased pocket depth (PD) and mobile teeth. Even in diabetic patients, those with poorly controlled glycemic levels have more attachment loss than well-controlled individuals. Enzymes of Porphyromonas gingivalis, Treponema denticola, and Tannerella forsythia, the causative agents of periodontal diseases, are capable of hydrolyzing the synthetic trypsin substrate, N-benzoyl-dl-arginine-2-naphthylamide (BANA).\(^{[2,3]}\)

We carried out this study to find the effect of phase I therapy on the clinical parameters, VSC levels, and random blood sugar (RBS) levels in chronic periodontitis patients with diagnosed DM.

**Materials and Methods**

**Method of collection of data**

After due authorization from the institutional ethical board and obtaining informed consent from all the patients, a total of 80 patients with chronic periodontitis fulfilling the inclusion criteria were selected from Department of Periodontology and Implantology, Kamineni Institute of Dental Sciences, Narketpally, Nalgonda, Telangana, India.

**Method**

Patients satisfying the aforementioned criteria were divided into two groups: chronic periodontitis and chronic periodontitis with diabetes. After screening, the diabetic status was evaluated using RBS levels.

**Inclusion criteria**

1. Patients aged 18 years and older
2. PD of minimum 5mm in at least three teeth per quadrant
3. Patients in whom oral prophylaxis was not performed during the last 6 months
4. Patients who did not receive antibiotic therapy 6 months prior to the study
5. Patients complaining of halitosis
6. Patients with diagnosed diabetes

**Exclusion criteria**

1. Pregnant and lactating individuals
2. Patients who are immunodeficient
3. Patients on corticosteroid medications or on cytotoxic drugs

**Study design**

After the selection of the patients, a detailed case history was taken. Patients satisfying the aforementioned criteria were divided into two groups: chronic periodontitis and chronic periodontitis with diabetes. Following clinical parameters were evaluated at baseline, 1 week, and 30 days after phase 1 therapy.

1. Plaque index\(^{[8]}\)
2. Gingival index\(^{[9]}\)
3. Modified sulcular bleeding index\(^{[10]}\)
4. Probing PD using University of North Carolina (UNC)-15 probe
5. Clinical attachment level (CAL) using UNC-15 probe
6. Oral malodor is detected using Tanita Breath Checker (Tanita India Private Limited, Mumbai, Maharashtra, India)
7. Subgingival samples are taken for detection of bacterial toxins using BANA test
8. RBS levels using glucometer

The subgingival plaque sample was collected for microbial analysis from the patients on the day of clinical examination. The sample collection was performed at 1 week and 1 month after scaling and root planing. UNC-15 periodontal probe was used to measure PD and CAL for all the teeth at four sites per each tooth (midbuccal, mesiobuccal, distobuccal, and lingual). Readings were recorded to the nearest millimeter.

**Microbiological examination**

**Method of collection of subgingival plaque sample**

Subgingival plaque sample was taken from tooth with pocket of ≥5mm with a sterile curette at baseline, first week, and fourth week. Area-specific Gracey curettes were introduced through the pocket orifice as far apically as possible and subgingival plaque sample was removed. Sample was transferred to 0.1 mL of working solution.
Enzymatic procedures
BANA (44 mg) and 1 mL dimethyl sulfoxide solution were diluted in 100 mL of buffer to give a working solution of 0.67 mmol/L BANA at pH 7. Of this working solution, 0.1 mL was added to 0.5 mL of the plaque suspension and incubated overnight at 37°C. A drop of 0.1% fast Garnet indicator dye was then added, and the intensity of the chromogenic reaction was read visually and scored as follows: yellow (negative), yellowish orange (weakly positive), orange red (positive), and red (strongly positive) [Figure 1].
A positive result suggested that the plaque contained at least $10^4$–$10^5$ BANA-positive organisms.[8]

Breathe odor measurements
Malodor measurements were made with Tanita Breath Checker. The instrument was kept 1 cm away from the mouth and asked to breathe in as the beep count reaches zero from five. Then the instrument automatically gives the reading depending on the percentage of volatile compounds present in the breathed air. Breath odor levels are given depending on the numerical value that appears on the breath checker. No odor is given as 0, slight odor as 1, moderate odor 2, heavy odor 3, strong odor 4, intense odor 5, and –error E.

Statistical analysis
The intra- and intergroup comparisons of clinical parameters were compared between group I and group II at various study intervals using Mann–Whitney U test and Wilcoxon matched pairs t test.

RESULTS
A reduction in the mean plaque score was observed in both the groups at all the visits compared to the baseline, and the reduction was statistically significant within the groups. Mean intragroup comparison of plaque index scores in two groups (I and II) showed reduction in the plaque scores from baseline to 4 weeks: group I = 2.06 ± 0.35 to 0.62 ± 0.21 and group II = 1.76 ± 0.48 to 0.52 ± 0.15. The reduction of these plaque scores was statistically significant in all the groups from baseline to 4 weeks ($P = 0.0001$: [Table 1]).

| Table 1: Comparison of group 1 and group 2 with plaque scores at different time intervals by Mann–Whitney U test |
|---|---|---|---|---|---|---|---|
| Groups | Baseline | 1 Week | 1 Month | Changes from baseline to 1 Week | 1 Month |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Group 1 | 2.06 | 0.35 | 1.37 | 0.40 | 0.62 | 0.21 | 0.68 | 0.39 |
| Group 2 | 1.76 | 0.48 | 1.07 | 0.43 | 0.52 | 0.15 | 0.69 | 0.36 |
| Total | 1.91 | 0.44 | 1.22 | 0.44 | 0.57 | 0.19 | 0.69 | 0.37 |

% of change in group 1

% of change in group 2

Z-value

P-value

* $P < 0.05$ indicates significant at 5% level

#Applied Wilcoxon matched pairs test

Figure 1: BANA test plaque samples: positive (red), weakly positive (reddish orange), weakly negative (yellowish orange), and negative (yellow)
Mean intragroup comparison of gingival index scores in two groups (I and II) showed reduction in the gingival index scores from baseline to 4 weeks: group I = 1.83 ± 0.53 to 0.64 ± 0.36 and group II = 1.90 ± 0.50 to 0.72 ± 0.40. The reduction of gingival index scores was statistically significant in all the groups from baseline to 4 weeks ($P = 0.0001$: [Table 2]).

Mean intragroup comparison of sulcular bleeding scores in two groups (I and II) showed reduction in the sulcular bleeding scores from baseline to 4 weeks: group I = 1.83 ± 0.50 to 0.64 ± 0.36 and group II = 1.90 ± 0.50 to 0.72 ± 0.40, with the reduction of sulcular bleeding was statistically significant in the two groups from baseline to 4 weeks ($P = 0.0001$: [Table 3]).

Mean intragroup comparison of probing PD scores in the two groups (I and II) showed reduction in the PD scores from baseline to 4 weeks: group I = 3.89 ± 0.72 to 3.41±0.84 and group II = 3.78 ± 0.85 to 3.04 ± 0.66. The reduction of probing PD scores was statistically significant in both the groups from baseline to 4 weeks ($P = 0.0001$: [Table 4]).

Mean intragroup comparison of CAL scores in the two groups (I and II) showed reduction from baseline to 4 weeks: group I = 4.23 ± 0.89 to 3.69 ± 0.87 and group II = 3.91 ± 0.63 to 3.50 ± 0.65. The reduction of CAL scores was statistically significant in both the groups from baseline to 4 weeks ($P = 0.00001$: [Table 5]). But the reduction was more significant from baseline to 1 week in group I (0.08 ± 0.20) and group II (0.17 ± 0.19) than to 1 month.

Mean intragroup comparison of malodor levels in both the groups I and II showed decrease from baseline to 4 weeks: group I = 2.85 ± 0.83 to 1.08 ± 0.27 and group II = 3.43 ± 0.81 to 1.24 ± 0.43. The percentage change in group I (62.28%) was observed from baseline to 1 month, which is statistically significant ($P = 0.0001$), and percentage change in group II is 59.12%, observed from baseline to 1 month, which is statistically significant ($P = 0.0001$: [Table 6]).

Mean intragroup comparison of RBS levels in both the groups (I and II) showed decrease from baseline to 4 weeks: group I = 122.00 ± 11.81 to 114.75 ± 9.05 and group II = 169.55 ± 23.52 to 153.33 ± 16.76. The percentage change in group I is observed to be 5.94% from baseline

### Table 2: Comparison of group 1 and group 2 with gingival index scores at different time intervals by Mann–Whitney U test

| Groups | Baseline | 1 Week | 1 Month | Changes from baseline to 1 Week | 1 Month |
|--------|----------|--------|---------|---------------------------------|--------|
|        | Mean     | SD     | Mean    | SD     | Mean    | SD    | Mean    | SD    |
| Group 1| 1.83     | 0.50   | 1.11    | 0.63   | 0.64    | 0.36  | 0.72    | 0.30  |
| Group 2| 1.90     | 0.50   | 1.36    | 0.62   | 0.72    | 0.40  | 0.54    | 0.31  |
| Total  | 1.86     | 0.50   | 1.23    | 0.63   | 0.68    | 0.38  | 0.63    | 0.32  |
| % of change in group 1 | 39.57%# | $P = 0.0001^*$ | 64.88%# | $P = 0.0001^*$ |
| % of change in group 2 | 28.47%# | $P = 0.0001^*$ | 62.01%# | $P = 0.0001^*$ |
| Z-value | −0.8756 | −1.8283 | −0.8564 | −2.6654 | −0.6207 | 0.0077* | 0.5348 |
| P-value | 0.3812 | 0.0675 | 0.3918 | 0.0077* | 0.5348 |

* $P < 0.05$ indicates significant at 5% level

#Applied Wilcoxon matched pairs test

### Table 3: Comparison of group 1 and group 2 with MSBI scores at different time intervals by Mann–Whitney U test

| Groups | Baseline | 1 Week | 1 Month | Changes from baseline to 1 Week | 1 Month |
|--------|----------|--------|---------|---------------------------------|--------|
|        | Mean     | SD     | Mean    | SD     | Mean    | SD    | Mean    | SD    |
| Group 1| 1.75     | 0.40   | 1.06    | 0.48   | 0.56    | 0.23  | 0.70    | 0.35  |
| Group 2| 1.77     | 0.38   | 1.24    | 0.41   | 0.75    | 0.69  | 0.53    | 0.27  |
| Total  | 1.76     | 0.39   | 1.15    | 0.45   | 0.66    | 0.52  | 0.61    | 0.32  |
| % of change in group 1 | 39.63%# | $P = 0.0001^*$ | 68.13%# | $P = 0.0001^*$ |
| % of change in group 2 | 30.12%# | $P = 0.0001^*$ | 57.52%# | $P = 0.0001^*$ |
| Z-value | −0.2406 | −1.8908 | −1.2798 | −2.4008 | −0.7073 | 0.0164* | 0.4794 |
| P-value | 0.8099 | 0.0587 | 0.2006 | 0.0164* | 0.4794 |

* $P < 0.05$ indicates significant at 5% level

#Applied Wilcoxon matched pairs test
to 1 month, which is statistically significant \((P = 0.0002)\), and group II is 9.57\%, observed from baseline to 1 month, which is statistically significant \((P = 0.0001)\): [Table 7]. The mean intergroup comparison of RBS levels is statistically significant at all intervals of time between the two the groups, that is, \(P\) value of 0.00001.

Mean intragroup comparison of BANA levels in both the groups (I and II) showed decrease from baseline to 4 weeks, positive to negative in both the groups. The mean intergroup comparison of BANA levels is statistically significant at all intervals of time between the two groups [Table 8].

| Table 4: Comparison of group 1 and group 2 with PPD scores at different time intervals by Mann–Whitney U test |
| Groups | Baseline | 1 Week | 1 Month | Changes from baseline to |
| Group 1 | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Group 2 | Mean | SD | Mean | SD | Mean | SD |
| Total | Mean | SD | Mean | SD | Mean | SD |
| % of change in group 1 | 3.20\%# | 12.20\%# | \(P = 0.0010\)* | \(P = 0.0001\)* |
| % of change in group 2 | 7.66\%# | 19.50\%# | \(P = 0.0011\)* | \(P = 0.0001\)* |
| Z-value | \(-1.1258\) | \(-1.9293\) | \(-2.0207\) | \(-3.1273\) | \(-0.1203\) |
| \(P\)-value | 0.2602 | 0.0537 | 0.0433* | 0.0018* | 0.9043 |

*\(P < 0.05\) indicates significant at 5\% level
#Applied Wilcoxon matched pairs test

| Table 5: Comparison of group 1 and group 2 with CAL scores at different time intervals by Mann–Whitney U test |
| Groups | Baseline | 1 Week | 1 Month | Changes from baseline to |
| Group 1 | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Group 2 | Mean | SD | Mean | SD | Mean | SD |
| Total | Mean | SD | Mean | SD | Mean | SD |
| % of change in group 1 | 1.95\%# | 12.59\%# | \(P = 0.0001\)* | \(P = 0.0001\)* |
| % of change in group 2 | 4.34\%# | 10.45\%# | \(P = 0.0001\)* | \(P = 0.0001\)* |
| Z-value | \(-2.1170\) | \(-2.1939\) | \(-0.6255\) | \(-4.8286\) | \(-1.1739\) |
| \(P\)-value | 0.0343* | 0.0282* | 0.5317 | 0.0130* | 0.2404 |

*\(P < 0.05\) indicates significant at 5\% level
#Applied Wilcoxon matched pairs test

| Table 6: Comparison of group 1 and group 2 with HALIT scores at different time intervals by unpaired t test |
| Groups | Baseline | 1 Week | 1 Month | Changes from baseline to |
| Group 1 | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Group 2 | Mean | SD | Mean | SD | Mean | SD |
| Total | Mean | SD | Mean | SD | Mean | SD |
| % of change in group 1 | 43.86\%# | 62.28\%# | \(P = 0.0001\)* | \(P = 0.0001\)* |
| % of change in group 2 | 35.77\%# | 59.12\%# | \(P = 0.0001\)* | \(P = 0.0001\)* |
| Z-value | \(-3.1232\) | \(-4.4785\) | \(-3.6490\) | 0.1592 | \(-1.4260\) |
| \(P\)-value | 0.0025* | 0.00001* | 0.0005* | 0.8739 | 0.1579 |

*\(P < 0.05\) indicates significant at 5\% level
#Applied paired t test
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Correlation between RBS level and oral malodor levels in both the groups

Mean intragroup comparison of malodor levels with RBS in both the groups I and II showed decrease from baseline to 4 weeks: group I = 2.85 ± 0.83 to 1.08 ± 0.27 and group II = 3.43 ± 0.81 to 1.24 ± 0.43. The percentage change in group I is 62.28%, observed from baseline to 1 month, which is statistically significant (P = 0.0001), and group II is 59.12%, observed from baseline to 1 month, which is statistically significant (P = 0.0001).

The mean intergroup comparison of malodor levels is statistically significant at all intervals of time between the two the groups, that is, P values 0.0025, 0.00001, and 0.0005.

Mean intragroup comparison of RBS levels in both the groups (I and II) showed decrease from baseline to 4 weeks: group I = 122.00 ± 11.81 to 114.75 ± 9.05 and group II = 169.55 ± 23.52 to 153.33 ± 16.76. The percentage change in group I is observed to be 5.94% from baseline to 1 month, which is statistically significant (P = 0.0002), and group II is 9.57%, observed from baseline to 1 month, which is statistically significant (P = 0.0001).

The mean intergroup comparison of RBS levels is statistically significant at all intervals of time between the two the groups, that is, P value 0.00001. Hence, the results show a significant positive correlation between RBS levels and oral malodor levels at various intervals of time. Assessment of correlation between the clinical parameters (plaque index [PI], gingival index [GI], modified sulcus bleeding index [MSBI], probing pocket depth [PPD]) and VSC levels (Tanita score) in nondiabetic and diabetic patients revealed a significant correlation between oral malodor levels, RBS, and clinical parameters in the diabetic group. A higher clinical parameters, VSC, and RBS levels were observed in the diabetic patients.

DISCUSSION

Chronic periodontitis was initially thought to be a local inflammatory condition, but research showed that this condition has a systemic impact. Recent studies have shown systemic effects of this condition and its role in the etiology of type 2 DM.[7,9]

The mechanisms by which DM affects the periodontium and causes gingivitis and periodontitis have been extensively studied and confirmed. The inflammatory response is thought to be mainly due to the chronic effects of hyperglycemia and the formation of biologically active glycated proteins and lipids that promotes inflammatory responses. Many studies revealed the influence of periodontal disease and its treatment on glycemic control.[10] These studies hypothesize that successful treatment of periodontitis in patients with DM leads to better control of glucose metabolism.[11]

There is an increasing support regarding the fact that the gram-negative microorganisms in periodontal infection
adversely affect glycemic control. The mechanism that elucidate the classic micro- and macro-vascular complications of DM, such as increase of advanced glycation end products, and their effects on increased tissue oxidant stress, altered endothelial cell function, and elevated activity of matrix metalloproteinases, are also seen in the periodontium. The role of DM in the progression of periodontal disease entails numerous factors, such as poor metabolic control and presence of local irritants on teeth. There is an increased persistence of bacteria in periodontal pockets of individuals with DM. This is thought to be due to impaired neutrophil adherence, chemotaxis, and phagocytosis, thereby increasing periodontal destruction. It has been also shown that in patients with DM, there is an increased rate of apoptosis. The monocyte macrophage cell line may be hyperresponsive to bacterial antigens in diabetic patients, resulting in increased pro-inflammatory cytokines and mediators. Therefore treating periodontitis in patients with DM may result in reduction of the soluble mediators responsible for periodontal tissue destruction and hence lessen the insulin resistance of the tissues.[11,12]

Immunological studies have shown an increase of TNF-α and IL-1β in patients with periodontal disease. The increase in TNF-α concentration is thought to be as a result of stimulation of monocytes. Thus, elevated TNF-α affects insulin sensitivity via direct and indirect mechanisms, thereby worsening the diabetic status leading to further periodontal breakdown. Thus, TNF-α has a vital role in the vicious cycle linking periodontal disease and DM. Treating periodontal inflammation might restore insulin sensitivity, resulting in improved metabolic control.[13,14]

Socransky et al.[15] described the presence of the red complex of three species, P. gingivalis, T. forsythia, and T. denticola. This complex is strongly related to PD and bleeding on probing. These gram-negative anaerobes have an enzyme that can hydrolyze the synthetic trypsin substrate, BANA.[15,16] Loesche et al.[8] described a microbiological test (BANA test) that uses a chromophore added to a synthetic peptidase as a substrate (benzoyl-DL-arginine-naphthylamide). This test is fairly valuable for detecting red complex organisms and hence useful in the initial diagnosis of chronic periodontitis.

If plaque at any tooth site shows BANA positive, it indicates the presence of 5 × 10^6 or more anaerobic bacteria. Whereas if plaque is BANA negative, it means less than 1 × 10^6 of the anaerobic bacteria are present. It has been suggested that BANA hydrolysis by subgingival plaque may be used as a simple and objective test for identifying the sites in individuals who may need treatment to lessen their pathogenic microflora.[16]

This study revealed no difference in mean plaque score, gingival score, and percentage bleeding score between the nondiabetic and the diabetic patients, which is similar to the observation made by a few authors.[3,4] But we observed a highly strong association between the periodontal disease and BANA test results. Thus results of this study suggest that the BANA test is a simple, adjunct assay together with VSC determination in order to provide additional quantitative data, which contribute to the overall association with odor-judge estimation.

**CONCLUSION**

This study provides evidence that a significant correlation is observed between oral malodor levels, RBS, and clinical parameters in the diabetic group.

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**Conflicts of interest**
There are no conflicts of interest.

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