



Effect of Melatonin on Periodontal Parameters and Glycemic Control in Periodontitis Patients

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ABSTRACT

Introduction: melatonin is a multifunctional chemical with various biological actions, like antioxidant, immunomodulatory, anti-inflammatory, osteopromotive, bone loss inhibition, oncostatic, and neuroprotective effects. This hormone stimulates the manufacture of type I collagen, which improves osteoblast differentiation and bone growth. The current study aims to determine how melatonin, used in conjunction with nonsurgical periodontal therapy, affects the clinical parameters and HbA1c levels in subjects with stage II-III periodontitis.

Methods: Total 120 subjects known diabetic were allocated into two groups. Control group was given conventional phase 1 treatment alone and the test group along with conventional treatment, 2mg of melatonin was given for 8 weeks. HbA1c and periodontal clinical parameters were taken at baseline and 8 weeks after the treatment.

Results: Paired t test was used to compare before and after within the groups and to assess the statistical difference between groups at various time durations, an independent t test was performed. After treatment was complete, adjunct melatonin administration considerably reduced the mean values of PD and CAL in the test group ($p < 0.001$)

Conclusion: Melatonin as adjunct to non surgical periodontal therapy shows positive results in terms of clinical parameters along with the reduction in HbA1c values.

Keywords: *Periodontal, Patients, Parameters*

INTRODUCTION

An inflammatory condition known as periodontitis affects the tissues that support teeth and is brought on by particular microorganisms or collections of particular microorganisms.[1][2] It causes periodontal pockets to form, gingival recession, or both, and leads to the gradual destruction of the periodontal ligament and bone. It has been demonstrated that changes in the genes involved in the inflammatory response increase the risk of periodontitis.[3]

The most common metabolic disease that is affecting day to day life of the population is diabetes mellitus. It was estimated that 578 million across the world were affected by this metabolic disease.[4] This will give rise to many complications that will affect the systemic health, major complications are neuropathy, delayed wound healing, retinopathy, cardiomyopathy, nephropathy and periodontitis.[5] Most pronounced bidirectional relationship explained in the literature was diabetes and periodontitis as a double edge sword.[6] Uncontrolled diabetes leads to periodontal destruction and poor oral hygiene leads to insulin resistance.[7] The pathophysiology between diabetes and periodontitis was mediated by elevation of inflammatory cytokines such as tumor necrosis factor alpha (TNF), interleukin 1 beta levels in serum that leads to insulin resistance.[8] Other hand, increased glucose levels lead to advanced glycation end products (AGE) elevation in periodontal tissues, leading to periodontal destruction.[7,9] [10]

The pineal gland is principally responsible for producing melatonin, also known as N-acetyl-5-methoxytryptamine, an anti-inflammatory and antioxidant protein which is endogenous in origin. Melatonin is made from tryptophan and released mostly in the night times which is responsible for circadian rhythm modification. It is proved that melatonin is a multifunctional chemical with various biological actions, like antioxidant, immunomodulatory, anti-inflammatory, osteopromotive, bone loss inhibition, oncogenic, and neuroprotective effects. This hormone stimulates the manufacture of type I collagen, which improves osteoblast

differentiation and bone growth. By scavenging free radicals produced during inflammation and reducing bone loss, it has therapeutic effects on a variety of oral cavity lesions. When plasma melatonin is released into the bloodstream, around 70% of it binds to albumin, while the remaining 24% to 33% passively diffuses into the mouth via salivary glands.

Numerous studies have suggested that patients with periodontal disorders have considerably lower salivary melatonin levels, indicating that this biomarker could be used to diagnose and possibly treat periodontitis.[11] Melatonin has a down regulating effect on the expression of inflammatory mediators. To lessen periodontal inflammation, and it downregulates the RANKL/OPG ratios too.[12] In diabetic rats, melatonin therapy has been shown to reduce periodontitis. Furthermore, melatonin as an adjunct in diabetic subjects was associated with a decline in RANKL concentrations and an increase in OPG concentrations, suggesting, melatonin may be able to slow the development of periodontal disease and reduce bone loss while also improving bone quality.[13] Additionally, local melatonin injection in rats resulted in a notable decrease in bone resorption.[14–23] The results cited support the hypothesis that adding topical melatonin administration to traditional periodontal treatments may improve the effectiveness. [13,24]

The current study aims to determine how melatonin, used in conjunction with nonsurgical periodontal therapy, affects the clinical parameters and HbA1c levels in subjects with stage II-III periodontitis.

Method

The case control study is double blinded, experimental study was carried out in the outpatient department in chennai population and subjects were divided by flip coin procedure. This study was done on a total of 120 subjects having stage II-III periodontitis. Patients were explained about the study, written and video consent was taken. The current research got approval from Saveetha ethical committee and approval number- IHEC/SDC/PERIO-2005/22/015

Inclusion criteria

1. Systemically healthy individuals
2. Aged between 20 yrs - 60yrs.
3. Untreated Stage II - Stage III periodontitis.

Exclusion criteria

1. Smoker’s and tobacco users.
2. Pregnant ladies and lactating women.
3. Uncontrolled diabetes.
4. Patient who has undergone periodontal therapy before 3 months.
5. Patient on any antibiotic therapy.
6. Patient on mood modulators or sedatives.
7. Patient with history of any drug allergies.

Intervention

In total, 120 participants were divided into two groups, with 60 in the control group and 60 in the other (test group). Diet and physical activity intensity was reported by the patient through questionnaire. Periodontal examination was done using UNC 15 number probes by the same periodontist and by using the same amount of probing force. Recordings were taken at baseline and post treatment 8 weeks of non-surgical periodontal therapy. HbA1c values were taken after 12 hours fasting at baseline and 8 weeks. All the subjects included in the research both test and control group underwent periodontal therapy- ultrasonic scaling and manual root planing in single sitting. Oral hygiene instructions were given. Subjects were strictly advised to not use any kind of mouthwashes or antiseptic solutions to avoid the bias.

In addition to this study group is advised to take 2mg of melatonin tablets daily before bed for 8

weeks. Control group was advised to take placebo tablets for 8 weeks. Oral administration with sufficient quantity of water was prescribed.

Statistics: The mean and standard deviation for each piece of data are displayed. The distribution of the data was examined using the Kolmogorov-Smirnov test. Paired t test was used to compare before and after within the groups and to assess the statistical difference between groups at various time durations, an independent t test was performed.

RESULTS

Distribution of all the study's data was normally distributed. The subjects' average ages in the control and intervention groups were 51.12 ± 3.4 and 52.12 ± 3.7 years, respectively.(Table 1) Melatonin wasn't found to have any negative impacts during the investigation. No differences between the two groups in terms of demographic data, course of diabetes, food components, physical features or medications ($p < 0.05$).

After treatment was complete, adjunct melatonin administration considerably reduced the mean values of PD and CAL in the test group ($p < 0.001$); single SRP treatment alone causes declines in the healthy group, although not to the same extent. At T1, both study groups revealed considerably decreased values for the plaque index and the bleeding index, however the reductions were more pronounced in the melatonin therapy group.(Table 1)

At T1, we observed that glycemic control had improved with scaling and root planing alone as measured by HbA1c values. For the intervention group, which additionally underwent melatonin therapy, the differences were significant.

| S.NO | Control group (60) | | Study group (60) | | P value | |
|-------------------------|--------------------|-----------------|------------------|-----------------|---------|--------|
| | T0 | T1 | T0 | T1 | p0 | p1 |
| PD (mm) (Mean \pm SD) | 5.12 \pm 2.01 | 4.98 \pm 1.02 | 5.21 \pm 2.04 | 3.37 \pm 0.7 | 0.17 | <0.001 |
| p value | 0.12 | | <0.001 | | | |
| CAL(mm) (Mean \pm SD) | 3.12 \pm 0.87 | 2.86 \pm 0.56 | 3.15 \pm 0.65 | 1.34 \pm 0.56 | 0.2 | <0.001 |
| p value | 0.09 | | <0.001 | | | |
| BOP (+) | 100 | 50 | 100 | 30 | 0.9 | 0.09 |

| | | | | | | |
|-----------|---------------|---------------|---------------|---------------|-------|--------|
| p value | <0.05 | | <0.001 | | | |
| PI (+) | 100 | 48 | 100 | 24 | 0.9 | 0.07 |
| p value | <0.05 | | <0.001 | | | |
| HbA1c (%) | 7.5127 ± 0.52 | 7.4623 ± 0.23 | 7.3241 ± 0.54 | 6.1273 ± 0.41 | 0.648 | <0.001 |
| p value | 0.18 | | <0.001 | | | |

Table 1 showing Glycated hemoglobin levels and periodontal characteristics in control and test group. T0 = evaluation at baseline; T1 = evaluation after 8 weeks; PD = probing depth; CAL = clinical attachment loss; BOP = bleeding on probing index; HbA1c = Glycated hemoglobin; SD = standard deviation; p0 = p Value between groups at baseline; p1 = p Value between groups at 8 weeks; p < 0.05 was considered statistically significant.

DISCUSSION

Periodontal disease is a sixth common complication for diabetes.[5] The bidirectional relationship between diabetes and periodontitis and their pathophysiology makes the classic treatment outcomes for periodontitis worse.[25] Hence the treatment for diabetic patients with periodontitis involves both the glycemic control and periodontal pathogens control. Melatonin is known for its anti-inflammatory, antioxidant, immunomodulatory, osteopromotive, bone loss inhibition, oncostatic, and neuroprotective effects.

The beneficial benefits of melatonin and its physiological and pathological implications in the oral cavity have been demonstrated in numerous research. According to a study using a mouse model of experimental periodontitis, melatonin has positive benefits on inflamed periodontal lesions.[26] Melatonin has been shown to reduce osteoclast activity in diabetes and periodontitis mouse models, hence decreasing bone loss and clinical parameters, but it didn't show any effect on systemically healthy periodontitis models. [27] A 5-year study on 2900 systemically healthy subjects looked at the evolution of HbA1c.[28] The HbA1c values of the participants with severe types of periodontal tissue breakdown were almost five times greater than those of the subjects with healthy periodontal tissues. This was the first research to

demonstrate the connection between periodontal inflammation and changes in HbA1c. Following scaling and root planing, we also noticed a drop in HbA1c in our trial, However, after 8 weeks, only the patient group who also utilized melatonin therapy showed that this difference was statistically significant. Our team has extensive knowledge and research experience that has translate into high quality publications [14–23]

In this study, patients who only received scaling and root planing experienced positive changes in all examined periodontal indicators at 8 weeks from baseline. However, only the plaque index reached statistical significance. Our findings demonstrated the average values of bleeding on probing, probing depth, and clinical attachment level post-intervention considerably decreased after 2 months of melatonin administration. These results are according to the previous study where they have given melatonin locally, decreased plaque and gingival index was seen.[29][11] Similar findings were found in another study where melatonin was given systematically to the patients.[30] In addition they have discussed the mechanism in which melatonin affects diabetes by decreasing oxidative stress.

Therefore, the study lends credence to the hypothesis that melatonin administration may improve clinical indicators of tissue deterioration and periodontal inflammation in diabetic mellitus subjects. The distinction was only noticeable for teeth with mild periodontitis, even though the standard non-surgical therapy on its own displayed the same pattern. We can therefore conclude that melatonin helps diabetic individuals by lessening the severity of their periodontitis and giving them other advantages. Although the presence of DM does not always imply periodontitis, the risk of getting periodontal disease is more in diabetics with poor

glycemic control than in individuals than well-controlled diabetes. On the other side, multiple studies have demonstrated the benefits of non-surgical periodontal treatment.[5,31] In this research, scaling and root planing reduced HbA1c, but the change did not reach a statistically significant level, probably because of the short follow-up period.

CONCLUSION

The goal of this research was to determine the effects of non-surgical periodontal treatment combined with supplementary melatonin therapy on clinical parameters and glycemic control in patients with type 2 diabetes and chronic periodontitis after the course of 8 weeks. It is required to conduct more research to examine the advantages of this treatment over a longer period of duration in blood and saliva, as well as the potential for increased overall and local advantages of other ways to consume melatonin, such as chewing melatonin tablets.

CONFLICT OF INTEREST

Nil

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