Clinical and Experimental Health Sciences

Effect of Non-surgical Periodontal Therapy on Salivary Melatonin Levels

Kubra Kundak[1], Aysen Yarat[2], Basak Dogan[3], Leyla Kuru[3]

[1] Marmara University, Institute of Health Sciences, Department of Periodontology, Istanbul, Türkiye.
[2] Marmara University, Faculty of Dentistry, Department of Basic Health Sciences, Istanbul, Türkiye.
[3] Marmara University, Faculty of Dentistry, Department of Periodontology, Istanbul, Türkiye.

Correspondence Author: Leyla Kuru
E-mail: lkuru@marmara.edu.tr
Received: 04.01.2022 **Accepted:** 29.04.2022

ABSTRACT

Objective: Melatonin, a hormone secreted predominantly by pineal gland in a circadian manner, has antioxidant and anti-inflammatory effects. The current research is conducted to explore the influence of non-surgical periodontal therapy (NSPT) on levels of salivary melatonin in subjects with gingivitis and periodontitis.

Methods: Sixty systemically healthy participants were included in this study; the groups are as follows: gingivitis (G), chronic periodontitis (CP), generalized aggressive periodontitis (GAP) and periodontally healthy (H). NSPT was applied to G group patients for 2 sessions, to CP and GAP group patients for 4 sessions. Plaque and gingival indices, probing depth (PD), bleeding on probing (BOP), and clinical attachment level (CAL) were documented at baseline and 3 months post – treatment and early morning salivary samples were collected. ELISA was used to detect melatonin levels in saliva. Pittsburgh Sleep Quality Index (PSQI) questionnaire was performed to evaluate of sleep quality of patients.

Results: At baseline, significant difference in gingival index, PD, BOP and CAL values was detected among all groups ($p<0.05$). Following NSPT, clinical measurements improved in G, CP, and GAP groups significantly ($p<0.05$). While salivary melatonin concentration of all groups was similar at baseline ($p>0.05$), a significant elevation in the level of salivary melatonin was found only in the G group after NSPT ($p<0.05$). PSQI scores differed significantly among groups ($p<0.05$).

Conclusion: The salivary melatonin levels in the presence of gingivitis and periodontitis varied at baseline and elevated following NSPT parallel to the improvement in clinical parameters.

Keywords: Melatonin, gingivitis, periodontitis

1. INTRODUCTION

Melatonin, a natural hormone, is produced and secreted in a circadian way by retina, ovaries, gastrointestinal tract, leukocytes, lymphocytes, bone marrow and skin but predominantly the pineal gland (1). Melatonin is engaged in numerous physiologic processes, as well as regulation of circadian rhythm, control of body temperature and immunomodulation (2, 3). As melatonin controls the circadian rhythm, a two-way relationship between melatonin level and the quality of sleep is considered important (4). After its secretion, melatonin circulates in the bloodstream and diffuses passively into saliva (5, 6). Following recent discovery of its immune enhancing, anti-inflammatory and antioxidant properties against reactive oxygen species (ROS), melatonin was thoroughly studied in the medical and dental fields (6, 7). Furthermore, it has been established that melatonin may have an essential role in type I collagen synthesis and promotion of bone formation (6, 8, 9). Moreover, the remarkable efficiency and diversity of melatonin's physiological regulatory actions draw attention to prospective benefits of using it in the therapeutic prevention and treatment of bone disorders (10-12).

Periodontal disease is an inflammatory chronic condition commenced by microbial dental biofilm affecting periodontium and can be broadly categorized as gingivitis and periodontitis. Gingivitis is a biofilm induced inflammatory condition expressed by redness of gingiva, edema, and the lack of periodontal attachment loss (13). Periodontitis is a chronic inflammatory condition of periodontium that results in periodontal attachment loss, bone loss and inevitably tooth loss when not treated (14). Accumulation of microbial dental plaque containing periodontopathogen bacteria activates host immune response which results in secretion of proosteoclastogenic factors, inflammatory cytokines,

DOI: 10.33808/clinexphealthsci.1053211

and matrix metalloproteinases as well as generation of free radicals and ROS (15, 16). Furthermore, it has been reported that increased ROS levels in periodontal disease are associated with oxidative damage to the periodontal tissues and a decrease in antioxidative defense mechanisms (17-19).

Non-surgical periodontal therapy (NSPT) including oral hygiene instructions, scaling and root planing aims to stop the development of periodontal disease and to ensure optimal health and function by elimination of chronic inflammation (20). Thus, it also restores the oxidant/antioxidant balance within the periodontium (21).

The relationship between periodontal status and levels of salivary melatonin is yet to be determined. The current research was conducted to explore the influence of NSPT on salivary melatonin levels in individuals with gingivitis and periodontitis.

2. METHODS

The ethical approval was obtained from the Ethics Committee of Marmara University, Faculty of Medicine, Istanbul, Turkey on 05.10.2018 (#09.2018.0673).

2.1. Study Population

Sixty systemically healthy participants consisting of 15 subjects with gingivitis (G group), 15 subjects with chronic periodontitis (CP group), 15 subjects with generalized aggressive periodontitis (GAP group), 15 volunteers with periodontal health (H group) participated in this study (22) (According to the new periodontal disease classification (23) 11 of CP patients are diagnosed as Stage III Grade B, 4 of them are Stage III Grade C; whereas 13 of GAP group patients are diagnosed as Stage III Grade C and 2 of them are Stage IV Grade C). Inclusion criteria were as follows; (i) systemically healthy, (ii) non-smoker, (iii) no antibiotic usage within 3 months, (iv) no history of periodontal treatment within 6 months, (v) no pregnancy or lactation, (vi) presence of at least 20 teeth, and (vii) no medication. Informed consent was obtained from all individuals prior to inclusion to the trial. Exclusion criteria included conditions such as systemic disorders, pregnancy, lactation, smoking habits, and medications. Flowchart of the study is demonstrated in Figure 1.

2.2. Clinical Periodontal Examination

Panoramic radiography and intraoral photographs were taken from each participant. Following medical and dental history, thorough periodontal examination was performed by the same clinician (KK). Plaque index (PI) (24), gingival index (GI) (25), probing depth (PD), bleeding on probing (BOP), and clinical attachment level (CAL) were documented on six aspects per tooth via a periodontal probe (PCPUNC15, Hu-Friedy, Ins. Co., USA) at baseline and 3 months post – treatment.

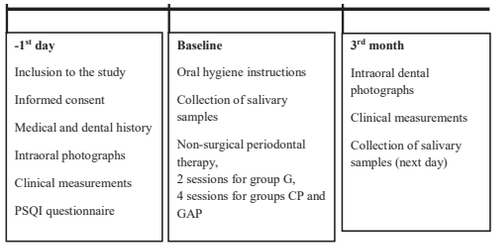

Figure 1. *Flowchart of the study.*

2.3. Salivary Sample Collection

All participants were instructed to refrain from consuming sustenance after 12:00 am prior to the salivary sample collection at baseline and 3 months following the treatment. All subjects were admitted to the clinic at 8:30 am on the day of sample collection. The unstimulated salivary samples were collected via spitting into a sterile glass beaker after accumulation on the floor of the mouth (26). The samples were then transferred to sterile tubes and were stored at −80°C until the day of assay.

2.4. Non-surgical Periodontal Therapy

At baseline, oral hygiene instructions were given, scaling and root planing with ultrasonic and hand instruments (WOODPECKER® Cavitron, Guilin Woodpecker Medical Ins. Co., China, EverEdge®; Gracey, 5/6, 7/8, 11/12, 13/14, Hu-Friedy Ins. Co., USA), was performed. Subjects in the G group received 2 sessions of NSPT, while patients in the CP and GAP groups underwent 4 sessions of NSPT under local anesthesia.

2.5. Determination of Melatonin Levels

On the day of assay, frozen salivary samples were thawed at room temperature and centrifuged at 3000 rpm for 20 min, the supernatant was taken and transferred immediately to a new propylene tube. The melatonin levels were determined by radioimmunoassay per manufacturer's instructions (RE54041, IBL GmbH, Hamburg, Germany).

2.6. Assessment of Sleep Quality

For assessment of sleep quality, subjects were instructed to complete Pittsburgh Sleep Quality Index (PSQI) questionnaire (Figure 2) at baseline. According to the PSQI, scores varies from 0 to 21 and scores higher than or equal to 5 indicate low quality of sleep (27).

2.7. Statistical Analysis

Demographic and clinical data were entered in a spreadsheet application and statistical analysis were completed using Statistical Package for the Social Sciences (SPSS® 20.0, Chicago, IL, USA). A p value<0.05 was considered as statistically significant. To test the normality, the Kolmogorov-Smirnov

test was done. Data were analyzed first by *Kruskal–Wallis* test among groups, and when significant difference was detected, *Mann–Whitney U* test with *Bonferroni* correction was applied for pair-wise comparison. *Wilcoxon* test was performed to analyze differences between the two time intervals.

Pittsburgh Sleep Quality Index

During the past month;

1. When have you usually gone to bed? ……
2. How long (in minutes) has it taken you to fall asleep each night? ……...
3. What time have you usually gotten up in the morning? ……
A. How many hours of actual sleep did you get at night? ……
B. How many hours were you in bed? ……

4. During the past month, how often have you had trouble sleeping because you	Not during the past month (0)	Less than once a week (1)	Once or twice a week (2)	Three or more times a week (3)
A. Cannot get to sleep within 30 minutes				
B. Wake up in the middle of the night or early morning				
C. Have to get up to use the bathroom				
D. Cannot breathe comfortably				
E. Cough or snore loudly				
F. Feel too cold				
G. Feel too hot				
H. Have bad dreams				
I. Have pain				
J. Other reason(s), please describe, including how often you have had trouble sleeping because of this reason(s)				
5. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?				
6. During the past month, have you had trouble staying awake while driving, eating, or engaging in social activity?				
7. During the past month, how much of a problem has it been for you to keep up enthusiasm to get things done?				
8. During the past month, how would you rate your sleep quality overall?	Very good (0)	Fairly good (1)	Fairly bad (2)	Very bad (3)

Scoring

Component 1	#9 Score	**C1 …**
Component 2	#2 (<15min (0), 16-30min (1), 31-60min (2), >60min (3)) + #5a Score (if sum is equal 0=0; 1-2=1; 3-4=2; 5-6=3)	**C2 …**
Component 3	#4 Score (>7(0), 6-7(1), 5-6(2), <5(3)	**C3 …**
Component 4	(total # of hours asleep)/(total # of hours in bed) x 100	**C4 …**
Component 5	# sum of scores 5b to 5j (0=0, 1-9=1, 10-18=2, 19-27=3)	**C5 …**
Component 6	#6 Score	**C6 …**
Component 7	#7 Score + #8 Score (0=0; 1-2=1; 3-4=2; 5-6=3)	**C7 …**

Add the seven component scores together = Global PSQI score …

Figure 2. *PSQI questionnaire (24).*

3. RESULTS

3.1. Demographic Data and Clinical Parameters

Demographic data are presented in Table 1.

Table 1. *Demographic data of healthy individuals and patients.*

	H group n=15	G group n=15	CP group n=15	GAP group n=15	*p*
Gender N (%)					
Female	9 (60)	9 (60)	6 (40)	8 (53.3)	0.658*
Male	6 (40)	6 (40)	9 (60)	7 (46.7)	
Age (years)					
Mean ± SD	30.27 ± 5.90	26.20 ± 5.16	38.27 ± 5.86†‡	32.47 ± 4.26‡	<0.0001**
Min – Max	23.0 – 45.0	22.0 – 40.0	30.0 – 51.0	27.0 – 40.0	

H: Healthy, G: Gingivitis, CP: Chronic Periodontitis, GAP: Generalized Aggressive Periodontitis, SD: Standard deviation
**Chi-square test, **Kruskal-Wallis test; †different from H group, p<0.05; ‡different from G group, Mann-Whitney U, p<0.05*

Table 2. *Clinical parameters of study population at baseline and 3rd month.*

		H group n=15 Mean±SD Min-Max Median	G group n=15 Mean±SD Min-Max Median	CP group n=15 Mean±SD Min-Max Median	GAP group n=15 Mean±SD Min-Max Median	*p**
PI	**Baseline**	0.12 ± 0.059 0.02 – 0.25 0.10	1.72 ± 0.30† 1.18 – 2.21 1.70	2.02 ±0.37†‡ 1.43 – 2.69 1.94	1.75 ±0.43† 1.05 – 2.48 1.56	<0.0001
	3rd month	-	0.12 ± 0.095 0.03 – 0.32 0.095	0.17 ± 0.17 0.01 – 0.68 0.12	0.23 ± 0.15 0.02 – 0.47 0.25	0.232
	p**	-	0.001	0.001	0.001	
GI	**Baseline**	0.12 ±0.059 0.03 – 0.22 0.11	1.67 ± 0.27† 1.14 – 2.19 1.66	1.84 ± 0.18† 1.44 – 2.11 1.89	1.97 ± 0.16†‡ 1.69 – 2.22 1.98	<0.0001
	3rd month	-	0.13 ± 0.10 0.04 – 0.42 0.13	0.22 ± 0.10‡ 0.02 – 0.48 0.21	0.34 ± 0.14‡ 0.08 – 0.61 0.30	<0.0001
	p**	-	0.001	0.001	0.001	
PD	**Baseline**	1.91 ±0.14 1.71 – 2.17 1.92	2.59 ± 0.29† 2.22 – 3.44 2.50	3.64 ± 0.64†‡ 2.99 – 5.54 3.53	4.43 ± 0.51†‡§ 3.72 – 5.82 4.34	<0.0001
	3rd month	-	2.08 ± 0.24 1.70 – 2.58 2.06	2.62 ± 0.40‡ 2.09 – 3.64 2.63	3.00 ± 0.37‡§ 2.56 – 4.01 2.88	<0.0001
	p**	-	0.001	0.001	0.001	
BOP	**Baseline**	5.80 ± 2.59 1.71 – 2.17 5.95	68.25 ± 17.94† 39.88 – 91.70 74.44	82.69 ± 16.33†‡ 44.05 – 100.00 89.4	90.97 ± 9.70†‡ 68.70 – 100.00 95.1	<0.0001
	3rd month	-	11.37 ± 6.18 4.17 – 19.64 10.12	12.38 ± 3.25§ 4.94 – 16.67 13.58	17.29 ± 6.36‡§ 7.30 – 25.93 17.36	<0.0001
	p**	-	0.001	0.001	0.001	
CAL	**Baseline**	1.92 ± 0.15 1.71 – 2.17 1.92	2.59 ± 0.30† 2.20 – 3.45 2.50	3.88 ± 0.64†‡ 3.23 – 5.79 3.72	4.84 ± 0.62†‡ 4.05 – 5.99 4.83	<0.0001
	3rd month	-	2.12 ± 0.24 1.77 – 2.60 2.06	3.10 ± 0.52‡ 2.40 – 4.48 3.18	3.90 ± 0.51‡§ 3.18 – 4.64 3.73	<0.0001
	p**	-	0.001	0.001	0.001	

*H: Healthy, G: Gingivitis, CP: Chronic Periodontitis, GAP: Generalized Aggressive Periodontitis, PI: plaque index, GI: gingival index, PD: probing depth, BOP: bleeding on probing, CAL: clinical attachment level, SD: Standard deviation*Kruskal-Wallis test, **Wilcoxon test, †different from H group, Mann-Whitney U, p<0.05; ‡different from G group, Mann-Whitney U, p<0.05; §different from CP group, Mann-Whitney U, p<0.05*

The clinical measurements of study population at baseline and 3rd month are displayed in Table 2. At baseline, PI and GI values of the treatment groups were significantly greater than the H group, as expected (p<0.001). PD, BOP and CAL values of the G group were detected to be higher than the H group and lower than the CP and GAP groups, significantly (p<0.001). Following NSPT, all clinical values improved significantly in all treatment groups (p<0.01). Following treatment, GI, PD, BOP and CAL values were found to be the highest in the GAP group, followed by the CP and G groups, respectively (p<0.001). At 3rd month, PI values were found to be similar in all groups (p>0.05).

As presented in Table 3, at baseline, significant difference in salivary melatonin concentrations among groups was detected (p<0.01), where the lowest concentration of salivary melatonin was found in the G group (p<0.05). After NSPT, melatonin level in saliva increased only in the G group, significantly (p<0.05). Change in melatonin level in saliva was significantly different in the G group (p<0.001)

Regarding the PSQI scores, a significant difference was detected in sleep quality among groups. As displayed in Table 4, the G group presented greater PSQI scores than the H and GAP groups (p<0.05), and also the highest percentage (%53.3) of patients with bad sleep quality.

Table 3. *Salivary melatonin levels at baseline, 3 months after NSPT and change (Δ)*

		H group n=15 Mean±SD Min-Max Median	G group n=15 Mean±SD Min-Max Median	CP group n=15 Mean±SD Min-Max Median	GAP group n=15 Mean±SD Min-Max Median	*p**
Melatonin pg/mL	**Baseline**	3.21 ± 3.99‡ 0.60 – 11.69 0.91	0.92 ± 0.82 0.36 – 3.75 0.71	2.14 ± 1.26‡ 0.79 – 5.13 2.00	1.56 ± 0.80‡ 0.34 – 3.04 1.44	0.002
	3rd month	-	3.35 ± 3.25¶ 0.47 – 11.58 2.63	2.22 ± 1.76 1.00 – 7.31 1.68	1.50 ± 0.78 0.49 – 3.18 1.16	0.234
	Δ (0-3)	-	2.42 ± 3.27 0.03 – 10.86 0.94	0.08 ± 1.48‡ -1.74 – 4.52 0.18	-0.06 ± 0.93‡ -2.12 – 1.46 0.15	<0.0001

H: Healthy, G: Gingivitis, CP: Chronic Periodontitis, GAP: Generalized Aggressive Periodontitis, PI: plaque index, GI: gingival index, PD: probing depth, BOP: bleeding on probing, CAL: clinical attachment level, SD: Standard deviation

**Kruskal-Wallis test, ‡different from G group, Mann-Whitney U, p<0.05; ¶different than baseline, Wilcoxon test, p<0.05*

Table 4. *PSQI scores of all participants at baseline.*

		H group n=15	G group n=15	CP group n=15	GAP group n=15	*p*
PSQI **Mean ± SD** **Min – max** **Median**		2.93 ± 1.87‡ 0.00 – 6.00 3.00	5.47 ± 2.83 1.00 – 11.00 5.00	3.80 ± 2.54 0.00 – 9.00 3.00	3.13 ± 2.42‡ 0.00 – 8.00 3.00	0.048*
Sleep quality	**Good N (%)**	11 (73.3)	7 (46.7)	9 (60)	11(73.3)	0.368**
	Bad N (%)	4 (26.7)	8 (53.3)	6 (40)	4 (26.7)	

H: Healthy, G: Gingivitis, CP: Chronic Periodontitis, GAP: Generalized Aggressive Periodontitis, PI: plaque index, GI: gingival index, PD: probing depth, BOP: bleeding on probing, CAL: clinical attachment level, SD: Standard deviation

**Kruskal-Wallis test, p<0.05; **Chi–Square test; ¥ different from G group, Mann-Whitney U test, p<0.05*

4. DISCUSSION

The principal cause of periodontal disease is microbial dental biofilm which triggers inflammatory process on host immune response. Periodontal diseases are worsened by an overproduction of ROS leading to cellular damage (28). Melatonin, a hormone produced and secreted in a circadian manner mainly by the pineal gland, has been discovered in saliva (6) and recently received remarkable attention in periodontal research because of its anti-inflammatory and antioxidant properties. Recent findings have focused on melatonin levels in different periodontal conditions such as periodontal health, G, and periodontitis, and revealed decreased levels of melatonin in both saliva and serum in periodontal diseases (7, 29-32). Furthermore, the only study evaluating the effect of NSPT on melatonin levels discovered that NSPT resulted in marked improvement of low salivary melatonin levels in subjects with periodontitis (33). However, the outcome of NSPT in relation to salivary melatonin levels of individuals with different periodontal diseases is yet to be explored. For all we know, the current study is the first study conducted to evaluate the influence of NSPT on salivary melatonin levels in subjects with gingivitis and periodontitis in accordance with PSQI scores.

Periodontal status and healing can be affected by existing systemic disorders and environmental factors such as smoking, antibiotic usage, previous periodontal treatment, pregnancy, and lactation (34-36). Melatonin diffuses into the blood immediately after its secretion (2) . Ophthalmic diseases, spinal cord injuries, liver and kidney diseases may also alter melatonin levels as well as some medications such as beta-blockers, nonsteroidal anti-inflammatory drugs, antiepileptic drugs, and antidepressants (37). Therefore, in this study participants with conditions affecting the periodontal status and/or melatonin levels were excluded.

NSPT aims the establishment of biologically acceptable root surfaces, resolution of gingival inflammation, reduction in PD, gain of CAL through oral hygiene instructions, supragingival and subgingival calculus removal and root surface debridement (20, 38-40). At baseline, clinical measurements showed significant difference among groups parallel to the severity of the periodontal disease, as expected. PI scores of all treatment groups were greater than the healthy individuals at baseline ($p<0.05$), however, plaque control of all patients improved significantly following NSPT which can be explained by the efficacy of oral hygiene instructions. NSPT resulted in improvement of GI and PI scores, reduction in PD and BOP and CAL gain, in all treatment groups ($p<0.05$), as supported by previous studies (41, 42).

Data obtained from this study indicated that the salivary melatonin levels were lower in the presence of periodontal disease than the healthy individuals, similar to the studies investigating melatonin levels in periodontal health and disease (7, 29-32, 43), although no significance was reached in the present study. Almughrabi et al. (32) compared salivary melatonin levels among healthy individuals, G, CP and GAP patients and reported an association between melatonin concentration and severity of periodontal disease, where the lowest melatonin level in salivary samples was detected in GAP patients and the highest in healthy individuals. Similar to this finding, our result demonstrated the highest melatonin level in healthy individuals. However, the lowest salivary melatonin levels observed in the G group contradicted with previous studies (31, 32). This may be explained by lower scores of PSQI of the G group indicating bad quality of sleep. Cutando *et al.* (31) reported that concentrations of melatonin in saliva decreased as the periodontal status deteriorated. Parallel with this result, a tendency to decrease in melatonin from health to severe periodontitis was found in our study, although not significant ($p>0.05$). Further investigations with larger study population are required to confirm this relationship.

After successful NSPT, salivary melatonin level significantly elevated only in the G group ($p<0.05$) without any substantial change in the CP and GAP groups ($p>0.05$). However, the first study investigating impact of NSPT on melatonin levels by Bertl *et al.* reported elevated melatonin levels in salivary samples in periodontitis following NSPT (33), contradicting with the data from the present study. For all we know, current research is the first in evaluating the influence of NSPT on salivary melatonin levels in subjects diagnosed as gingivitis. In our study, improvement of salivary melatonin levels following NSPT in the G group suggested that gingival inflammation can be resolved and reversed by non-surgical treatment approach in subjects with gingivitis whereas in subjects with periodontitis, in order to achieve complete periodontal healing surgical treatment might be necessary. Further clinical trials with enlarged study population are needed to discover the influence of NSPT on melatonin levels in the presence of different periodontal diseases and the role of melatonin in periodontal pathogenesis.

The small-scale sample size, the lack of evaluation of other antioxidant and/or oxidant biomarkers, the lack of melatonin treatment as an adjunct to NSPT, and the lack of PSQI scores at 3rd month post-treatment limited the study.

5. CONCLUSION

The current study indicates that salivary melatonin may be a factor in periodontal pathogenesis and NSPT may induce improvement of decreased melatonin levels in the presence of periodontal disease. Further investigations with larger scale are required to fully elaborate the three-way association between melatonin levels in saliva, its effect on periodontal condition and NSPT.

ACKNOWLEDGEMENTS

Funding

This study was supported by Marmara University, Scientific Research Projects Unit (#SAG-C-DRP-120.619.0228).

Conflict of Interest

None.

REFERENCES

[1] Reiter RJ. Pineal melatonin: cell biology of its synthesis and of its physiological interactions. Endocr Rev 1991; 12(2): 151-180.

[2] Cagnacci A, Elliott J, and Yen S. Melatonin: a major regulator of the circadian rhythm of core temperature in humans. J Clin Endocrinol Metab 1992; 75(2): 447-452.

[3] Arzt ES, Fernández-Castelo S, Finocchiaro LM, Criscuolo ME, Díaz A, Finkielman S, and Nahmod VE. Immunomodulation by indoleamines: serotonin and melatonin action on DNA and interferon-γ synthesis by human peripheral blood mononuclear cells. J Clin Immunol 1988; 8(6): 513-520.

[4] Åkerstedt T, Fröberg JE, Friberg Y, and Wetterberg L. Melatonin excretion, body temperature and subjective arousal during 64 hours of sleep deprivation. Psychoneuroendocrinology 1979; 4(3): 219-225.

[5] Laakso M, Porkka-Heiskanen T, Alila A, Stenberg D, and Johansson G. Correlation between salivary and serum melatonin: dependence on serum melatonin levels. J Pineal Res 1990; 9(1): 39-50.

[6] Cutando A, Gómez-Moreno G, Arana C, Acuña-Castroviejo D, and Reiter RJ. Melatonin: potential functions in the oral cavity. J Periodontol 2007; 78(6): 1094-1102.

[7] Gómez-Moreno G, Guardia J, Ferrera M, Cutando A, and Reiter R. Melatonin in diseases of the oral cavity. Oral Dis 2010; 16(3): 242-247.

[8] Park KH, Kang JW, Lee EM, Kim JS, Rhee YH, Kim M, Jeong SJ, Park YG, and Hoon Kim S. Melatonin promotes osteoblastic differentiation through the BMP/ERK/Wnt signaling pathways. J Pineal Res 2011; 51(2): 187-194.

[9] Nakade O, Koyama H, Ariji H, Yajima A, and Kaku T. Melatonin stimulates proliferation and type I collagen synthesis in human bone cells in vitro. J Pineal Res 1999; 27(2): 106-110.

[10] Konečná B, Chobodová P, Janko J, Baňasová L, Bábíčková J, Celec P, and Tóthová Ľ. The Effect of Melatonin on Periodontitis. Int J Mol Sci 2021; 22(5): 2390-2401.

[11] Ahmed E, Shaker OG, Yussif N, and Ghalwash DM. Effect of locally delivered melatonin as an adjunct to nonsurgical therapy on GCF antioxidant capacity and MMP-9 in stage ii periodontitis patients: A randomized controlled clinical trial. Int J Dent 2021; 2021(1): 1-10.

[12] Lu X, Yu S, Chen G, Zheng W, Peng J, Huang X, and Chen L. Insight into the roles of melatonin in bone tissue and bone-related diseases. Int J Mol Med 2021; 47(5): 1-19.

[13] Trombelli L, Farina R, Silva CO, and Tatakis DN. Plaque-induced gingivitis: Case definition and diagnostic considerations. J Clin Periodontol 2018; 45(20): 44-67.

[14] Tonetti MS, Greenwell H, and Kornman KS. Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. J Periodontol 2018; 89(1): 159-172.

[15] Brook I. Microbiology and management of periodontal infections. Gen Dent 2003; 51(5): 424-428.

[16] Gustafsson A and Åsman B. Increased release of free oxygen radicals from peripheral neutrophils in adult periodontitis after Feγ-receptor stimulation. J Clin Periodontol 1996; 23(1): 38-44.

[17] Akalin FA, Toklu E, and Renda N. Analysis of superoxide dismutase activity levels in gingiva and gingival crevicular fluid in patients with chronic periodontitis and periodontally healthy controls. J Clin Periodontol 2005; 32(3): 238-243.

[18] Sculley DV and Langley-Evans SC. Salivary antioxidants and periodontal disease status. Proc Nutr Soc 2002; 61(1): 137-143.

[19] Kimura S, Yonemura T, and Kaya H. Increased oxidative product formation by peripheral blood polymorphonuclear leukocytes in human periodontal diseases. J Periodont Res 1993; 28(3): 197-203.

[20] Heitz-Mayfield L, Trombelli L, Heitz F, Needleman I, and Moles D. A systematic review of the effect of surgical debridement vs. non-surgical debridement for the treatment of chronic periodontitis. J Clin Periodontol 2002; 29(3): 92-102.

[21] Wei D, Zhang XL, Wang YZ, Yang CX, and Chen G. Lipid peroxidation levels, total oxidant status and superoxide dismutase in serum, saliva and gingival crevicular fluid in chronic periodontitis patients before and after periodontal therapy. Aust Dent J 2010; 55(1): 70-78.

[22] Armitage GC. Development of a classification system for periodontal diseases and conditions. Ann Periodontol 1999; 4(1): 1-6.

[23] Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, Flemmig TF, Garcia R, Giannobile WV, and Graziani F. Periodontitis: Consensus report of workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol 2018; 89(1): 173-182.

[24] Silness J and Löe H. Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand 1964; 22(1): 121-135.

[25] Löe H. The gingival index, the plaque index and the retention index systems. J Periodontol 1967; 38(6): 610-616.

[26] Navazesh M. Methods for collecting saliva. Ann N Y Acad Sci 1993; 694(1): 72-77.

[27] Buysse DJ, Reynolds CF, Monk TH, Berman SR, and Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989; 28(2): 193-213.

[28] Liu C, Mo L, Niu Y, Li X, Zhou X, and Xu X. The role of reactive oxygen species and autophagy in periodontitis and their potential linkage. Front Physiol 2017; 8(1): 439-452.

[29] Cutando A, Gómez-Moreno G, Villalba J, Ferrera MJ, Escames G, and Acuña-Castroviejo D. Relationship between salivary melatonin levels and periodontal status in diabetic patients. J Pineal Res 2003; 35(4): 239-244.

[30] Srinath R, Acharya AB, and Thakur SL. Salivary and gingival crevicular fluid melatonin in periodontal health and disease. J Periodontol 2010; 81(2): 277-283.

[31] Cutando A, Galindo P, Gómez-Moreno G, Arana C, Bolanos J, Acuña-Castroviejo D, and Wang HL. Relationship between salivary melatonin and severity of periodontal disease. J Periodontol 2006; 77(9): 1533-1538.

[32] Almughrabi O, Marzouk K, Hasanato R, and Shafik S. Melatonin levels in periodontal health and disease. J Periodont Res 2013; 48(3): 315-321.

[33] Bertl K, Schoiber A, Haririan H, Laky M, Steiner I, Rausch W, Andrukhov O, and Rausch-Fan X. Non-surgical periodontal therapy influences salivary melatonin levels. Clin Oral Investig 2013; 17(4): 1219-1225.

[34] Haber J, Wattles J, Crowley M, Mandell R, Joshipura K, and Kent RL. Evidence for cigarette smoking as a major risk factor for periodontitis. J Periodontol 1993; 64(1): 16-23.

[35] Preber H and Bergstrom J. Cigarette smoking in patients referred for periodontal treatment. Scand J Dent Res 1986; 94(2): 102-108.

[36] Page RC, Offenbacher S, Schroeder HE, Seymour GJ, and Kornman KS. Advances in the pathogenesis of periodontitis: summary of developments, clinical implications and future directions. Periodontol 2000 1997; 14(1): 216-248.

[37] Rzepka-Migut B and Paprocka J. Melatonin-Measurement methods and the factors modifying the results. A systematic review of the literature. Int J Environ Res Public Health 2020; 17(6): 1916-1934.

[38] Caffesse RG, Mota LF, and Morrison EC. The rationale for periodontal therapy. Periodontol 2000 1995; 9(1): 7-13.

[39] Cobb CM. Non-surgical pocket therapy: mechanical. Ann Periodontol 1996; 1(1): 443-490.

[40] Delatola C, Adonogianaki E, and Ioannidou E. Non-surgical and supportive periodontal therapy: predictors of compliance. J Clin Periodontol 2014; 41(8): 791-796.

[41] Cobb CM. Non-surgical pocket therapy: Mechanical. Ann Periodontol 1996; 1(1): 443-490.

[42] Badersten A, Nilvéus R, and Egelberg J. Scores of plaque, bleeding, suppuration and probing depth to predict probing attachment loss 5 years of observation following nonsurgical periodontal therapy. J Clin Periodontol 1990; 17(2): 102-107.

[43] Ghallab N, Hamdy E, and Shaker O. Malondialdehyde, superoxide dismutase and melatonin levels in gingival crevicular fluid of aggressive and chronic periodontitis patients. Aust Dent J 2016; 61(1): 53-61.

How to cite this article: Kundak K, Yarat A, Dogan B, Kuru L. Effect of Non-surgical Periodontal Therapy on Salivary Melatonin Levels. Clin Exp Health Sci 2022; 12: 1032-1039. DOI: 10.33808/clinexphealthsci.1053211