ORIGINAL ARTICLE

Relationship of Melatonin with Chronic Periodontitis

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ABSTRACT

Aim: To determine a possible link between serum melatonin levels and chronic periodontitis, correlate serum melatonin levels with age and to analyze melatonin levels in diabetic patients with increasing severity of periodontal disease.

Methods: In this study 70 subjects were grouped into control (comprising 5 young, 5 old) the diseased group (comprising 30 young, 30 old) suffering from chronic periodontitis with CPI 3 and CPI 4. Among these diseased groups we further studied the melatonin levels of chronic periodontitis in CPI3 and CPI4, diabetic and non-diabetic and the relation of gender with melatonin levels. Serum melatonin levels were assessed using enzyme-linked immunosorbent assay (ELISA).

Results: Serum melatonin levels of the control were high as compared to diseased. Levels of melatonin were decreased in old control subjects as compared to young controls. Melatonin was decreased in code3 compared to code4. Declined levels of melatonin in females were observed as compared to males.Melatonin was high in old patients compared to young patients suffering from chronic periodontitis. Melatonin was also increased in diabetic patients with chronic periodontitis.

Conclusion: The serum melatonin levels vary in different diseased conditions and show the protective role against the infectious diseases as an antioxidant, and free radical scavenger. Therefore, melatonin could be used therapeutically in chronic periodontitis.

Keywords: Serum Melatonin, chronic periodontitis, community periodontal index (CPI), antioxidant, free radical scavenger, diabetes, age, gender,(ELISA).

INTRODUCTION

Chronic periodontitis has been well-defined as “an infective disease causing inflammation within the supporting tissues of the teeth, proceeding to the attachment and bone loss”. In chronic periodontitis the accumulation of plaque and calculus is followed by a slow-to-moderate rate of disease progression. Several local, systemic and environmental factors may influence the normal host-bacteria interaction that in turn increases the rate of disease progression[1].

Chronic periodontitis is most commonly observed in adults and may also be found in children and adolescents. The major clinical and etiologic characteristics of the disease are- microbial plaque formation, periodontal inflammation, loss of gum attachment and damage of alveolar bone. Periodontal pocket is usually a consequence of the periodontalinfection[1]. Recently some other factors have been recognized for periodontal health such as stress, a patient’s gender, hormonal influences such as androgens, estrogen, progesterone[3], genetics, nutritional state, and certain diseases, like osteoporosis or HIV[2].

Melatonin have several important roles to play in oral cavity and systemic homeostasis[4].Melatonin causes the stimulation of lymphocytes and the cytokine productions by human peripheral blood mononuclear cells via nuclear melatonin receptors[5].The action of melatonin on monocyte production can be partially due to its direct action on melatonin receptors[6]. Melatonin also accelerates the stimulation of T Cells by increasing the IL-2 production[7].

In contrast melatonin also control’s inflammation by the prevention of TNF-alpha by blocking NF-kB pathway[8]. Vascular changes realized in the retina, glomerulus, and perineural regions in people with diabetic complications also happen in the periodontium[9].The important role of diabetes in the pathogenesis of periodontal diseases is supported by a great number studies and designate periodontal diseases as the “sixth complication” of diabetes[10].This increase level of melatonin in the oral cavity may exert a defensive role in diabetic patients[18].

When oxygen is metabolized in the cytoplasm and mitochondria for the production of ATP molecules, the main source of vitality for the cell[11] free radicals and their non-radical metabolites are produced. They are also produced by the cells immune system as a result of inflammation and collectively called as reactive oxygen species (ROS) and are highly reactive[12]. In periodontal disease increase in both reactive oxygen species and nitrogen species are stated responsible for the oxidative damage in periodontitis[13].

Melatonin being a powerful antioxidant[14] and immunomodulator may have certain protective effects on the inflammation, cancer and promoting the synthesis of bone and type 1 collagen fibers[15]. Melatonin is a natural antioxidant with substantial anti-aging properties[16]. Melatonin with its antioxidant qualities plays an important role in influencing the pathogenesis of periodontal disease[17].

PATIENTS AND METHODS

A total of 70 patients were included in the study. Authorization for blood sampling was according to the University Ethical Committee and the Code of Ethics of the World Medical Association was observed[18].

Seventy subjects were comprised of 10 controls (5 young subjects from age of 20-40 and 5 old subjects from

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age of 41-60) and 60 diseased suffering from chronic periodontitis were (grouped as 30 young subjects from age of 20-40 and 30 old subjects from age of 41-60). Seventy subjects were categorized into five groups as follows:

1. Young controls (5 subjects) and Old controls (5 subjects)
2. Young Diseased (30 subjects) and Old Diseased (30 subjects)
3. Gender (20 female and 20 male)
4. Diabetic (12 subjects) and non-diabetic (12 subjects)
5. According to the severity of the disease code 3(28 subjects) and code 4(28 subjects)

Dental and medical history of all patients was in accordance with criteria of the WHO. The periodontal status was assessed by the CPI (Community Periodontal Index).

The inclusion criteria involved the patients suffering from chronic periodontitis, age, gender, severity of disease (code 3 and code 4) diabetic and non-diabetic subjects. Exclusion criteria included the presence of a systemic neurological disorder (e.g. epilepsy or schizophrenia), existence of disease with possible effects on the immune system (e.g. chronic infections or cancer) and the treatment with any drug that could alter melatonin levels[19].

All the subjects underwent an oral examination including medical and dental assessment. Periodontal disease severity was assessed using the CPI.

A specifically designed lightweight CPI probe with a 0.5 mm ball tip was used, having a black band between 3.5 and 5.5 mm and rings at 8.5 and 11.5 mm from the ball tip.

After CPI next step was to draw the blood from subjects. Patients came between 8.00 am to 11.00 am to the department. They were seated for 30 minutes before sampling.The level of melatonin starts declining after 11:00 am. We collected the samples from 8:00 am to 11:00 am. The blood for serum was drawn from the median cubital vein, inside of the cubital fossa. Blood was collected in red capped vacutainers, centrifuged for 5 minutes at 3500 rpm. Then the serum was separated and was frozen at -20 ^{o}C until further use. Serum melatonin was determined by commercial, ELISA, RE54021 (IBL International GmbH, Hamburg Germany). An automated immunoanalyzer was used.

Statistical Analysis: Independent t-test was applied to find out the significance of the parameters and the Pearson's correlation test was applied to findout the correlation between the groups.

RESULTS

The results of Table I show that the serum melatonin level in diseased patients (34.44 ± 1.47; P <0.001) suffering from chronic periodontitis with Community Periodontal Index CPI 3 and CPI4 was significantly reduced when compared to young control (50.26 ± 2.83; P<0.001) subjects.

It was observed in this study that the serum melatonin levels were increased in young control subjects (56.84 ± 2.96; P <0.05) as compared to old control subjects (43.68 ± 2.39; P <0.05) (Table II).

The data given in Table III indicates that the serum melatonin was decreased in young diseased subjects (28.22±1.30; P <0.001) compared to old diseased (40.65 ± 2.10; P <0.001) subjects suffering from chronic periodontitis with Community Periodontal Index CPI 3 and CPI 4.

The results given in Table IV of the present study showed that the serum melatonin level was reduced significantly in female (32.71 ± 3.25; P<0.05) when it was compared with male serum melatonin level (42.69 ± 1.95; P<0.05). Both groups were suffering from chronic periodontitis.

Table V indicated that the serum melatonin was found significantly increased in diabetic patients with chronic periodontitis (50.44±7.12; P <0.05) than that of non-diabetic patients with chronic periodontitis (24.68 ± 0.625; P <0.05). The chronic periodontitis patients were compared in the Community Periodontal Index between CPI 3 and CPI 4 (Table VI). The serum melatonin levels were significantly decreased in the patients (33.65 ± 2.08; P <0.05) with CPI 3 and increased in the patients (44.65 ± 3.22; P <0.05) with CPI 4.

Table I: Serum melatonin level in diseased subjects compared to control subjects

	Control	Diseased
N	10	60
Mean	50.26	34.44
SE	2.83	1.47

Table II: Serum melatonin in young control subjects than old control subjects.

	Control Young	Diseased Old
N	5	5
Mean	56.84	43.68
SE	2.96	2.39

Table III: Serum melatonin levels in young diseased and old diseased patients.

	Control Young	Diseased Old
N	30	30
Mean	28.22	40.65
SE	1.30	2.10

Table IV: Serum Melatonin level in female and male.

	Female	Male
N	20	20
Mean	32.71	42.69
SE	3.25	1.95

Table V: Serum melatonin levels in diabetic and non-diabetic patients.

	Diabetic	Non diabetic
N	12	12
Mean	50.44	24.68
SE	7.12	0.625

Table VI: Serum melatonin contents in CPI 3 and CPI 4 patients.

	CPI 3	CPI 4
N	28	28
Mean	33.65	44.65
SE	2.08	3.22

DISCUSSION

Data from the present study indicated that the amount of serum melatonin levels which were (P< 0.001) declined significantly in patients with chronic periodontitis, had Community Periodontal Index CPI 3 and CPI 4. According

to the finding of Cutandoet al[19] as the severity of periodontal disease increased, the salivary melatonin level gets declined,showing that melatonin may act to prevent the body from external bacterial infection by combating with free radicals. Srinath et al[17] also reported that the salivary and gingival cervicular fluid melatonin levels were decreased in patients suffering from chronic patients showing the protective role of melatonin against periodontitis. Gomez-Moreno et al[20] also observed that the patients with periodontitis had significantly (P<0.000) decrease plasma and saliva melatonin levels than healthy control patients. Subsequently, Gomez-Moreno et al[21] explained by experimental evidences that melatonin could have valuable effects in certain oral pathologies comprising periodontal disease, herpes viral infections, candida, oral inflammatory process, xerostomia , oral ulcers and oral cancer. The destruction caused by the toxic derivatives of oxygen is reduced by the melatonin. So melatonin could be used as a co-adjuvant in the treatment of certain oral diseases. Rai[22] also found that the salivary melatonin level declination could be related to the ability of melatonin being an antioxidant immunostimulating and increasing the differentiation of osteoblastic activity. He further explained that melatonin as an anti –aging agent protects the body from infection and inflammation.

In this research the level of serum melatonin was high in young control adults as compared to the old control adults showing a significant (P<0.05) declination of melatonin level as the age proceeds. The previous studied of Zeitzer etal[23]andFourtillan et al[24] also showed that the plasma melatonin of different age groups manifested consistent decrease as aging progressed. As the aging process proceeds, there is decrease in body's respond to the stress because stress increases with aging and reduces the melatonin level. This shows the fighting role of melatonin against the free radicals. Another reasonfor the decrease of melatonin with the passage of age is the calcification of the pineal gland. As a result the circulating melatonin level declines in the body[25].

Data of this study also showed that the serum melatonin level was raised significantly (P<0.001) in old patients suffering from chronic periodontitis with CPI 3 and CPI 4 when compared to young patients with same conditions. Cutandoetal[18] found out a significant increase in melatonin levels of older patients having chronic periodontitis. Therefore the increased melatonin level in periodontal disease might be followed to the increase in the free radical generation in this pathological process. Results of Cutando et al[21] also showed a significant higher levels of melatonin in older patients having worse periodontal damages in chronic periodontitis.

In the present study, when male patients with chronic periodontitis were compared with female patients, the serum melatonin level of the female subjects were decreased significantly (P<0.05) as compared to male subjects. This might be because of thehormonal changes in female and furtherresearch is required to fully elucidate therelationship between serum melatonin level and gender. The findings of Cutandoet al[19] are different from our findings. According to himGender had no correlation with serum melatonin level.

According to the present studies when the diabetic patients were compared with non-diabetic patients, both suffering from chronic periodontitis, the serum melatonin level of diabetic patients had significantly (P<0.05) increased level than the non-diabetic patients. Cutandoet al[18] also observed that the diabetic patients, with the Community Periodontal Index CPI 3 and CPI 4 had peak values of melatonin. Hence, higher melatonin levels might protect the body organs from oxidative stress.

The data collected from this study indicated that the serum melatonin level of the subjects suffering from chronic periodontitis with CPI 3 had significantly (P<0.05) decreased level of melatonin when compared to the patients with CPI 4. This increased level of melatonin in oral activity showed the protective role of melatonin[15]. Likewise, Gomez-Moreno et al[20] reported that with higher Community Periodontal Index value (3 or 4), the plasma melatonin level was increased suggesting that melatonin might act as a protector against periodontal infection. Cutandoet al[18] also showed that the melatonin levels were increased to highest values at CPI 4.

CONCLUSION

It can be concluded from the present study that the melatonin inhibits the damage of supporting tissues of the teeth, and enhances the immune system to fight against the inflammation of gums. Melatonin also has the ability of remolding of bone formation and stops the osteoclastogenesis in chronic periodontitis. Further research is required inthis field of medicine to evaluate the therapeutic effects of melatonin in the dentistry.

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