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Original Article

Analysis of melatonin levels in the saliva of patients with type 2 diabetes mellitus

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Abstract

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia. Melatonin, a hormone that regulates sleep and circadian rhythms, due to its anti-inflammatory and antioxidant effects, influences the pathogenetic component of diabetes mellitus. This study includes 77 patients with type 2 diabetes who were treated at the branch "Endocrine Health Center" of the State Clinical Hospital of the Lviv Regional Diagnostic Center during January to September 2024. Patients were divided into 2 groups according to the score of the Pittsburgh Sleep Quality Index: 41 patients with a score >5, and 36 with a score <5. Melatonin levels were lower in a group of patients with poor sleep quality. Additionally, melatonin exhibits a moderate correlation with glycated hemoglobin. It is important to test melatonin levels before prescribing it to patients with diabetes to ensure individualized treatment.

Keywords: type 2 diabetes mellitus, melatonin, sleep quality, PSQI, glycated hemoglobin

Introduction

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia, which can lead to numerous significant complications. The 11th International Diabetes Federation Atlas (2025) reports that approximately 589 million people worldwide are affected by this disease. Furthermore, diabetes was responsible for 3,4 million deaths in 2024. It is important to note that over 90% of all diabetes cases are type 2 diabetes (T2D) [1]. Therefore, it is essential to find new ways to prevent or delay type 2 diabetes (T2D) and its complications.

Improving nutrition and physical activity are well-known lifestyle behavioral changes for preventing diabetes; however, the latest ADA-EASD consensus also recommends enhancing sleep at the same level [2]. Melatonin, a hormone that regulates sleep and circadian rhythms, may be a practical option. Moreover, melatonin, due to its anti-inflammatory and antioxidant effects, influences the pathogenic component of diabetes mellitus, such as oxidative stress. Melatonin, as a free radical scavenger, ameliorates oxidative stress caused by reactive oxygen and nitrogen species. It can also reduce cellular apoptosis [3]. On the other hand, *the Melatonin receptor 1B* (*MTNR1B*) gene allele G was associated with elevated fasting glucose levels and an increased risk of type 2 diabetes mellitus (T2DM) [4]. Currently, there is conflicting data regarding the impact of melatonin and *the MTNR1B* genotype on glucose metabolism, insulin secretion, and the risk of T2D [5, 6]. Considering the epidemic increase of T2D, sleep disorders, and free access to melatonin supplements as over-the-counter medicine, it is crucial to know whether it is safe and beneficial for T2D patients to consume them.

This study aims to investigate the relationship between melatonin, sleep disorders, glucose metabolism, and diabetes mellitus.

Material and methods

This study includes 77 patients with type 2 diabetes (T2D) who were treated at the "Endocrine Health

Center" branch of the State Clinical Hospital of the Lviv Regional Diagnostic Center from January to September 2024. Ethical, moral, and legal principles were observed during the work. The Commission approved the study protocol on Ethics of Scientific Research, Experimental Developments and Scientific Works of the Danylo Halytsky Lviv National Medical University.

The work was carried out within the framework of the research work of the Department of Endocrinology of the Danylo Halytskyi National Medical University: "Features of Pathogenesis, Diagnosis and Treatment of Diseases of the Cardiovascular, Digestive, Endocrine and Respiratory Systems in the Clinic and Experiment" (state registration number 0120U002142).

Criteria for inclusion of patients in the study: presence of type 2 diabetes mellitus, age 30 to 70 years, and individual voluntary consent to participate in the study.

Exclusion criteria: pregnant women, alcohol and drug addicts, severe heart, kidney and liver failure, the presence or history of mental illnesses (post-traumatic stress disorder, major depression, schizophrenia), the presence of neurological diseases (fatal familial insomnia, traumatic brain injury, multiple sclerosis).

All participants underwent examination, including measurements of height and weight. Biological characteristics included fasting and postprandial glucose levels, as well as glycated hemoglobin (HbA1c). To identify sleep disorders, patients were surveyed using the Pittsburgh Sleep Quality Index (PSQI) questionnaire. The concentration of melatonin was determined in saliva samples collected in 1 mL Eppendorf tubes at night under minimal lighting. The samples were analyzed using the enzyme-linked immunosorbent assay (ELISA) colorimetric method with a commercial Melatonin ELISA kit from Abcam.

Patients were divided into 2 groups according to PSQI score: 41 patients with a score >5, which indicates bad sleep quality and 36 with a score <5, which indicates good sleep quality. Additionally, participants were divided into groups based on sex and the level of glycated hemoglobin.

Statistical data processing was carried out using Microsoft Office Excel 2010. The data are presented as the mean (M) and standard deviation (σ), as well as the median (Me) and interquartile range (Q1; Q3) for parametric and nonparametric distributions of features, respectively.

Results

The average age of the patients was 54.3±8.27 years. The average duration of diabetes was 7 [5; 10.25] years. Among all patients (53%), there were women. The characteristics of the groups are listed in Table 1.

According to our results, melatonin level in the 2nd study group was significantly higher than in the 1st group (Figure 1).

According to our data, there is a medium negative correlation between melatonin and HbA1c. Additionally, we observe a moderate negative correlation between melatonin and the PSQI score. The results are shown in Table 2.

The average level of glycated hemoglobin was 9.28±2.14. According to this indicator, patients were divided into two groups: those with optimal and suboptimal diabetes control (with a glycated hemoglobin level ≤8%) – 25 people (32%), and those with unsatisfactory control – 52 people (68%). In the first group, 5 people (20%) had low melatonin levels, 13 people (52%) had normal melatonin levels, and 7 people (28%) had elevated melatonin levels, respectively. In the second group, 8 people (15%) had low melatonin levels, 32 people (62%) had normal melatonin levels, and 12 people (23%) had elevated melatonin levels, respectively. Among women, 12 patients (29%) had high levels, 7 patients (17%)

Table 1: Clinical characteristics of the groups included in the study.

Characteristics	Group 1 M±m	Group 2 M±m	P-value
Age, years	53.8±7.5	55.5±7.96	p>0.05
Weight, kg	89.35±17.47	92.94±16.13	p>0.05
BMI, kg/m²	31.14±5.0	31.52±5.06	p>0.05
Score of PSQI	7.88±2.22	3.38±1.12	p<0.01*
Fasting glucose, mmol/L	10.18±3.7	10.05±3.83	p>0.05
Postprandial glucose, mmol/L	9.35±4.3	11.09±4.6	p>0.05
Melatonin (pg/mL)	10.09±7.02	20.68±12.01	p<0.01*

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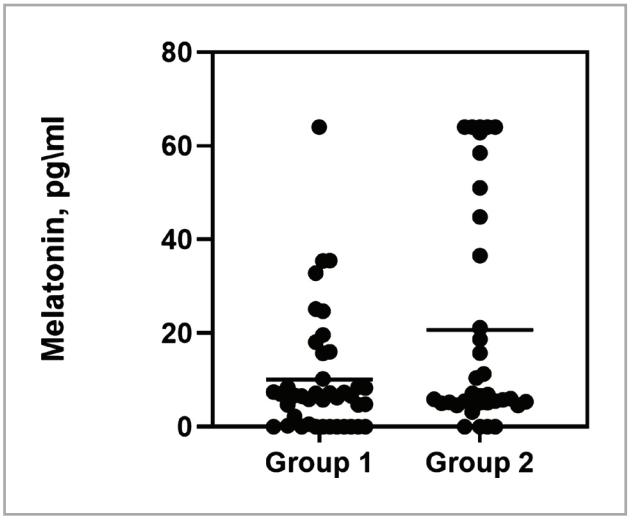

Figure 1: Dispersion of participants according to melatonin levels.

had low levels, and 22 patients (54%) had normal levels. Among men, 5 patients (14%) had high levels, 8 patients (22%) had low levels, and 23 patients (64%) had normal levels.

Discussion

Salivary biomarkers have begun to be used in clinical settings for diagnosing or monitoring systemic diseases, including type 2 diabetes (T2D). The benefit of these biomarkers is the non-invasive nature of saliva sampling that does not require trained medical personnel [7]. On the other hand, due to xerostomia and lower salivary flow, it may make it harder for T2D patients to collect enough saliva samples compared to the general population [8].

A recent study found that patients with type 2 diabetes (T2D) and obesity have lower melatonin levels. Also, poor sleep quality was observed in T2D patients using short-acting insulin analogues and those with diabetic retinopathy, and obese individuals [9].

It has been suggested that melatonin impacts glucose metabolism by affecting both beta-cell insulin secretion and insulin sensitivity. It is well-documented that pancreatic alpha and beta cells express melatonin receptors MT1 and MT2, and evidence suggests that melatonin's action on these pancreatic melatonin receptors modulates insulin secretion and glucagon release in a diurnal fashion [10, 11].

There is a suggestion that melatonin improves glucose tolerance and insulin sensitivity in nocturnal rodents, while in humans, this impact is less clear. Timing may be a key factor in the influence of melatonin on glucose metabolism, and individuals should avoid eating when melatonin levels are high [12]. The question of the effect of melatonin on insulin secretion and glucose regulation remains open.

The timing model developed by Garaulet M *et al.* suggests that low melatonin levels during mealtimes support high glucose tolerance, whereas high melatonin levels during fasting promote β-cell repair. Thus, an abnormally high melatonin state during mealtimes, as observed in night-eating populations, shift workers, or those taking exogenous melatonin, may lead to dysregulation of glucose metabolism, thereby increasing the risk of type 2 diabetes. In addition, abnormally low melatonin levels or reduced melatonin receptor signaling during the night (as may occur in carriers of rare loss-of-function mutations in MTNR1B) may limit β-cell repair and chronically increase the risk of type 2 diabetes [13].

Further studies would be necessary to fully evaluate the association between various subgroups of T2D patients (divided by treatment and complications), melatonin levels, sleep quality, and the possibility of melatonin use in patients with diabetes and its complications.

Limitations of the current study include the low number of participants.

Table 2: Correlation of melatonin levels, HbA1c and Score PSQI in subjects with bad (group 1) and good (group 2) quality.

Variable		Melatonin (pg/mL)	
		Group 1	Group 2
HbA1c	R	-0.327	-0.323
	P	0.003	0.04
Score PSQI	R	-0.36	-0.29
	P	0.03	0.007

Conclusion

Melatonin levels were lower in a group of patients with bad sleep quality. Additionally, melatonin exhibits a moderate correlation with HbA1c. It is important to test melatonin levels before prescribing it to patients with diabetes to ensure individualized treatment.

Conflict of interest

The authors declare no conflict of interest.

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