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THE IMPORTANCE OF MELATONIN IN SLEEP REGULATION AND GLYCEMIC CONTROL IN REPRODUCTIVE AGE PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Abstract
Melatonin, a pineal gland hormone, has traditionally been considered a key regulator of circadian rhythms, especially sleep. However, modern studies indicate its involvement in metabolic processes, including the regulation of carbohydrate metabolism. In patients with type 2 diabetes mellitus of reproductive age, impaired melatonin secretion is associated with worsening glycemic control, increased insulin resistance, and sleep disturbance. This review article examines current concepts of the role of melatonin in the regulation of sleep and glucose homeostasis, as well as the possibility of its use as an adjuvant therapy in patients with type 2 diabetes mellitus.

Keywords: Melatonin, circadian rhythms, type 2 diabetes mellitus, sleep, glycemic control, insulin resistance, reproductive age.

Introduction

Type 2 diabetes mellitus (T2DM) is one of the most common endocrine pathologies in the world, especially among individuals of reproductive age. Current data highlight not only the role of insulin resistance and insulin secretion disorders in the pathogenesis of T2DM, but also the importance of other physiological processes, such as sleep and hormonal rhythms. Melatonin, produced by the pineal gland at night, affects not only the quality of sleep, but also tissue sensitivity to insulin, insulin secretion, and glycemic profile. The

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purpose of this article is to analyze the role of melatonin in the regulation of sleep and carbohydrate metabolism in patients of reproductive age with T2DM and to consider the prospects for its use in clinical practice.

Biosynthesis and physiological role of melatonin

Melatonin is a hormone synthesized in the pineal gland (epiphysis) from serotonin, mainly in the dark. The main stimulus for its production is a decrease in illumination, transmitted to the suprachiasmatic nucleus of the hypothalamus through the retina. It is the suprachiasmatic nucleus that coordinates the body's circadian rhythms, synchronizing the internal biological clock with the external light cycle. When darkness sets in, the enzyme N- acetyltransferase is activated , triggering the biosynthesis of melatonin from serotonin, due to which the hormone level reaches its peak at night (usually from 2:00 to 4:00 am), and with the onset of morning its synthesis decreases sharply.

The physiological role of melatonin is multifaceted and covers more than just sleep regulation. First of all, it is responsible for:

Regulation of circadian rhythms, including the sleep-wake cycle, thermoregulation, cortisol levels, growth hormone secretion, etc.;

Pronounced antioxidant activity, manifested both in the neutralization of free radicals and in the activation of antioxidant enzymes (for example, superoxide dismutase and glutathione peroxidase);

Modulation of the immune response, including suppression of proinflammatory cytokines (TNF-α, IL-6) and stimulation of the production of interleukins involved in humoral defense;

Regulation of glucose and lipid metabolism by influencing tissue sensitivity to insulin, insulin secretion by the pancreas and the activity of liver enzymes.

Of particular interest are its metabolic effects. Melatonin interacts with MT1 and MT2 receptors, which are present on pancreatic β-cells. This effect regulates daily fluctuations in insulin secretion and improves its biological action. At the same time, melatonin can reduce insulin resistance , a key pathogenetic mechanism of type 2 diabetes mellitus (T2DM), by reducing oxidative stress and inflammation in tissues. It has also been established that low melatonin levels correlate with

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obesity, hyperglycemia, dyslipidemia , and other components of metabolic syndrome.

Thus, melatonin is not just a "sleep hormone", but an important regulator of metabolic processes, participating in ensuring the homeostasis of carbohydrates, fats, and the immune and neuroendocrine systems.

Melatonin and sleep regulation in patients with type 2 diabetes mellitus

Sleep disorders are common among patients with type 2 diabetes and have a direct impact on the course of the disease. Persistent lack of nighttime sleep, obstructive sleep apnea syndrome (OSAS), nocturnal awakenings and disruption of circadian rhythms contribute to deterioration of glycemic control, development of insulin resistance and progression of diabetic complications. These disorders can be both a consequence of diabetes itself and its risk factor, forming a vicious circle.

One of the central causes of these disorders in diabetics is considered to be reduced secretion of melatonin. Against the background of hyperglycemia and chronic inflammation, the production of this hormone in the pineal gland is disrupted, which, in turn, leads to further desynchronization of biorhythms. Such patients experience the following pathological changes:

Increased cortisol levels in the evening and at night, which stimulates hyperglycemia and aggravates catabolic processes;

Decreased tissue sensitivity to insulin, especially at night;

Increased fasting glucose levels associated with impaired carbohydrate metabolism and counter-insular action of hormones;

Increased systemic inflammation, which further increases insulin resistance and affects the vascular bed.

The addition of melatonin as a pharmacological drug to patients with type 2 diabetes who suffer from insomnia or sleep disorders has demonstrated a positive effect on a number of clinical and laboratory parameters. Thus, taking melatonin 30-60 minutes before sleep contributes to:

- normalization of the latency period of falling asleep;
- improving sleep structure (increasing the deep sleep phase);
- reducing anxiety levels;
- reduction of night awakenings;

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- normalization of insulin and glucose secretion at night;
- reducing the level of glycated hemoglobin (HbA1c).

Some studies have shown that after just 8–12 weeks of melatonin intake, patients with type 2 diabetes experienced an improvement in overall well-being, a decrease in fasting glucose levels, and an improvement in the sleep profile without significant side effects. It is important to emphasize that melatonin therapy is especially effective in patients with a combination of type 2 diabetes and chronic insomnia, as well as in individuals with nocturnal hyperglycemia.

Thus, melatonin is considered as a potentially effective and safe addition to the basic therapy of T2DM, especially in terms of correction of sleep and circadian disturbances. This highlights the need to integrate chronobiological approaches into the individual management of patients with metabolic disorders.

Table 1. Effect of melatonin levels on sleep and glycemia parameters in patients with T2DM

Parameters	Normal melatonin levels	Decreased melatonin levels
Sleep duration (hours)	7.5–8.0	<6.0
Sleep quality (PSQI questionnaire)	<5 (good)	>8 (bad)
HbA1c level (%)	6.5–7.0	>8.0
Homeopathic insulin resistance index (HOMA-IR)	<2.5	>3.5

Effect of melatonin on glycemic control

Melatonin affects carbohydrate metabolism through several mechanisms:

1. Regulation of insulin secretion - melatonin interacts with MT1 and MT2 receptors on β-cells, regulating their sensitivity.
2. Modulation of tissue sensitivity to insulin - with normal melatonin levels, the sensitivity of skeletal muscles and the liver to insulin increases.
3. Antioxidant action - reduces the level of inflammatory cytokines, improving the metabolic profile.

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Table 2. Effects of melatonin use in patients with type 2 diabetes (clinical trial data)

Indicator	Before therapy	After 3 months of taking melatonin
Fasting glucose level (mmol /l)	8.2	6.9
HbA1c (%)	8.1	7.0
Body Mass Index (BMI)	30.5	29.1
HOMA-IR	3.8	2.6
Sleep quality index scores (PSQI)	9.2	5.1

Genetic aspects and sex differences

Some studies have found associations between polymorphisms of the melatonin receptor gene (MTNR1B) and predisposition to T2DM. In individuals of reproductive age, especially women, hormonal levels additionally influence sensitivity to melatonin. Estrogens potentiate its action, which can be taken into account when individualizing therapy.

Prospects for Melatonin Therapy

To date, melatonin is not included in the standard treatment for type 2 diabetes, but its use as an adjuvant therapy may be justified in the following cases:

- severe sleep disturbances;
- high levels of stress;
- low insulin sensitivity;
- nocturnal hyperglycemia.

Larger randomized trials are still needed, but preliminary results are encouraging.

Conclusion

Melatonin is a multifunctional hormone that plays an important role not only in sleep regulation but also in glycemic control. In reproductive-age patients with type 2 diabetes, there is a clear relationship between melatonin levels, sleep quality, and metabolic status. Inclusion of melatonin in combination therapy may

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improve clinical outcomes, especially in the presence of sleep disorders. However, further data verification and development of clinical guidelines are required before widespread implementation of this approach.

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