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Research Article

THE ROLE OF MELATONIN IN DIABETIC PATIENTS

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ABSTRACT

Diabetes mellitus (DM) and complications associated with diabetes are one of the leading causes of death worldwide. The International Diabetes Federation (IDF) has estimated that 592 million people will suffer from diabetes by 2035. Therefore, it is vital to find a new biomolecule that can further help in the treatment of diabetes. For several decades, a persistent interest in the biological properties of melatonin (MT) has been maintained in biological science and medicine. In recent years, a lot of information has appeared about its participation in maintaining energy homeostasis and the genesis of diabetes mellitus. The purpose of this review is to study the pathogenetic mechanism of melatonin in diabetes mellitus.

KEYWORDS

Melatonin, diabetes mellitus, gestational diabetes

INTRODUCTION

According to the WHO, up to 15% of the world's population suffers from sleep disorders, this is a lifestyle problem that gradually progresses towards exaggerated activity at night and a sedentary lifestyle during the day, which leads to disruption of the circadian rhythm. A disturbed circadian rhythm is strongly associated with impaired glucose tolerance (IGT) and an increased risk of developing type 2 diabetes (DM2). Melatonin, the main sleep hormone secreted by the pineal gland, peaks at night in the human body. Melatonin has antioxidant, anti-inflammatory, and anti-aging properties and plays a key role in various sleep disorders. According to the literature, the role of melatonin in insulin secretion and

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glucose homeostasis has been demonstrated in recent decades [1,2].

Biological features of melatonin include the fact that, MT synthesis in pinealocytes goes through several stages starting material serves tryptophan, which through serotonin and N-acetylserotonin is converted to the final hormone. The key enzymes of its synthesis are N-acetyltransferase and hydroxyindole-omethyltransferase. MT is secreted mainly into the cerebrospinal fluid, from where it enters the vascular channel and is carried by the blood throughout the body [3,4]. In various brain structures and peripheral organs, the effects of the hormone are realized through specific receptors (mainly of the MP1 and MP2 types). Secondly, the formation of epiphyseal MT, regardless of the species characteristics of animals, is maximally expressed in the dark and minimally in the light periods of the day. This made it possible to count the epiphysis an important chronotropic gland that provides due to close morphofunctional ties with the circadian pacemaker (suprachiasmatic nuclei of the hypothalamus) circadian oscillations various physiological functions. MT has established a reputation as a natural chronobiotic and universal adaptogenic hormone [5]. The effects of regional MT, like the epiphyseal one, are realized through specific MR identified in all organs of the gastrointestinal tract. However, if in the gastric mucosa and in the pancreas the density of MP1 reveals a clear circadian rhythm with maximum values in dark period, then MP2 does not have such a rhythm. The wide distribution in the body made it possible to consider that extra-epiphyseal MT plays a role the key role of the paracrine signaling molecule, regionally coordinating cellular functions [6]. MT circulating in the blood can act as typical hormone, reaching far located target cells. Involvement of MT in the regulation of carbohydrate metabolism and its contribution to the pathogenesis of diabetes is realized, obviously, in several ways, but the main the role, in all likelihood, is played by direct interference with the function of the cellular elements of the islets Langerhans through specific receptors present on the membrane surface of β- and α-cells both rodents and humans. However, in β-cells MP2 mRNA was found, and in α-cells - MP1[5,7].

According to a number of authors, the similarity of the circadian rhythms of melatonin and insulin secretion is associated with differences in the biological actions of these hormones. In the human body, the minimum level of insulin is observed at night, it is known that the main function of insulin - the control of metabolism after eating, should not be realized at night, this physiological process is the opposite of melatonin. Melatonin ensures the synchronization of metabolic processes during nocturnal sleep, that is, the time programmed for fasting in a person, and can have an inhibitory effect on insulin production [8]. Thus, it seems likely that melatonin contributes to the creation of the most optimal regimen of energy metabolism in conditions of low secretion and high insulin sensitivity at night.

Effect of melatonin on the development of DM.

Melatonin is an integral part of the homeostatic mechanism in the body. It signals whether light or darkness prevails. Interestingly, melatonin has been associated with both type 1 diabetes (DM1) and type 2 diabetes. Elevated plasma melatonin levels and decreased insulin levels are seen in type 1 DM and similarly in type 2 DM caused by insulin resistance. In type 1 diabetes, melatonin production is increased, while the loss of β-cells reduces insulin production, leading to hyperglycemia. In type 2 DM, melatonin depletion leads to an increase in the expression of melatonin membrane receptor mRNA, while insulin resistance enhances an increase in insulin levels, which

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leads to depletion of β-cells and an increase in glucagon levels, leading to hyperglycemia [9,10]. However, there are conflicting reports on melatonin and the risk of type 2 DM associated with either an increase or decrease in melatonin signaling, leading to the association of melatonin with DM. In addition, genomic studies have shown that rare variants of the melatonin 1b receptor (MTNR1B) are also associated with impaired glucose tolerance and an increased risk of type 2 DM [11,13].

Melatonin and complications of diabetes

Nduhirabandi F. et al., in their studies described MT is involved not only in pathogenesis diabetes mellitus, but also in the prevention of its complications. MT reduces the risk of developing cardiovascular disorders that occur in animals when modeling with DM. In the isolated cardiac muscle of rats with alimentary obesity, in which the content of insulin and triglycerides in plasma increases, gross morphological changes were observed during ischemia-reperfusion. If the animals were previously regularly injected with MT, then such shifts were much less pronounced [12].

Melatonin in the development of gestational diabetes mellitus

Gestational diabetes mellitus (GDM) is a common problem among pregnant women, the prevalence of GDM provokes its adverse consequences for mother and child, and it is necessary to study the features underlying the development of this pregnancy.

During pregnancy, hyperinsulinemia and insulin resistance is a physiological process, and there is an increased sensitivity to insulin as a result of the restructuring of metabolic processes in the focus of the parturient, aimed at ensuring the arbitrary delivery of nutrients to the developing fetus. At this stage, there is an increase in insulin biosynthesis, an increase in its secretion stimulated by glucose, and an increase in the mass of pancreatic β-cells [17]. According to the literature, the circadian rhythm of melatonin secretion determines the successful course of pregnancy and the birth of a healthy child. MT during pregnancy performs a number of positive actions on the fetus and the woman in labor. Firstly, they stimulate antioxidant enzymes, thereby providing stable protection against free radical damage at the cellular and tissue levels in a single mother-placenta-fetus system [18].

In GDM, melatonin deficiency increases the transport of glucose to the fetus, while oxidative stress is observed due to a decrease in the removal of free radicals, an increase in oxidative metabolism. The formation of oxidative stress types will be a direct consequence of hyperglycemia leading to various diabetic embryopathies [19,20]. Current literature suggests that the melatonin receptor 1B (MTNR1B) gene polymorphism may influence insulin secretion and pancreatic activity causing GDM.

CONCLUSION

Thus, melatonin, a pineal gland hormone with antioxidant and anti-inflammatory properties, is involved in the development of DM associated with circadian arrhythmia. Decreased melatonin levels and a functional relationship between melatonin and insulin are implicated in the pathogenesis of diabetes. In addition, treatment with exogenous melatonin in cell lines, rodent models, and diabetic patients has shown a powerful effect in alleviating diabetes and other related complications. This highlights the role of melatonin in glucose homeostasis.

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