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# CURRENT STATE OF THE STUDY OF MELATONIN-DEPENDENT DISORDERS OF ENERGY METABOLISM (LITERATURE REVIEW)

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**Key words:**

*obesity, body weight, melatonin, metabolism, energy metabolism.*

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**The purpose of the work** – to analyze the current state of the study of melatonin-dependent disorders of energy metabolism.

**Conclusions.** According to the data of the scientific literary sources in obesity and metabolic syndrome the level decrease and rhythm disturbance of melatonin production are registered. Melatonin is an effective means of correcting a number of pathological changes that accompany the obesity development and energy metabolism derangement.

**Ключові слова:**

*ожиріння, маса тіла, мелатонін, метаболізм, енергетичний обмін.*

Клінічна та експериментальна патологія 2024. Т.23, №1 (87). С. 78-83.

**СУЧАСНИЙ СТАН ВИВЧЕННЯ МЕЛАТОНІН-ЗАЛЕЖНИХ РОЗЛАДІВ ЕНЕРГЕТИЧНОГО ОБМІНУ (ОГЛЯД ЛІТЕРАТУРИ)**

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**Мета роботи** – проаналізувати сучасний стан вивчення мелатонін-залежних розладів енергетичного обміну.

**Висновки.** Згідно даних наукових літературних джерел при ожирінні та метаболічному синдромі відзначається зниження рівня та порушення ритму продукції мелатоніну. Мелатонін є ефективним засобом корекції низки патологічних змін, що супроводжують розвиток ожиріння та порушення енергетичного обміну.

**Introduction**

According to scientific literary sources, recently there has been an increase in the incidence of obesity, which is a risk factor for cardiovascular diseases, type 2 diabetes, hypertension, some types of cancer and others. Excessive and poor-quality nutrition, insufficient physical activity, as well as a violation of metabolic processes is the basis of excess weight of the body. Statistical scientific data indicate that the number of obese people is increasing every year. Therefore, in recent years, the number of studies aimed at studying this problem has been increasing [1]. The obtained results of the review of scientific literary sources indicate the important role of sleep, the endogenous system of circadian rhythms and the main epiphyseal hormone melatonin in the regulation of the development and progression of obesity, which necessitates the search for means of prevention and treatment of this disease [2].

Pharmaceutical agents that are used to treat this disease at the moment are not effective enough and have many serious side effects. In this regard, scientists face an extremely urgent task aimed at finding means of prevention and treatment of obesity.

**The purpose of the work**

To analyze the current state of the study of melatonin-dependent disorders of energy metabolism.

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**Main part**

Melatonin is synthesized in the body and performs various physiological functions, is an endogenous hormone that was originally known as an effective antioxidant. Increasing attention, in recent decades, has been paid to its unique function in the regulation of energy metabolism, especially in the metabolism of glucose and lipids. According to scientific studies, melatonin lowers the level of glucose and insulin in the blood, increases sensitivity to insulin [3]. Therefore, the deficiency of this hormone contributes to the development of obesity, metabolic syndrome, and later type 2 diabetes. In the treatment of metabolic diseases, there is still no consensus among scientists regarding the possible role of melatonin as an adjunct. Additional experimental and clinical studies are needed to determine the possible risks and benefits of melatonin as a therapeutic agent [4].

To date, many scientific experimental studies have been conducted to study the incidence of obesity. The most important means of curbing excess body weight include: maintaining a balanced diet, adequate sleep, stimulation of physical activity, and drug therapy. However, current remedies do not provide the desired results, as obesity is rapidly spreading throughout the world [5]. Experimental research has established that the level of melatonin secretion can influence the process of gaining excess body weight. Melatonin, chemically

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called N-acetylmethoxytryptamine, is a naturally occurring compound that occurs in animals, plants, and microbes. In mammals, melatonin is released into the blood by the pineal gland, especially in the dark. Taking into consideration the fact that exposure to artificial blue light can suppress the secretion of melatonin, people living in modern society are much more exposed to this factor than their ancestors. Therefore, melatonin is sold in many countries of the world as a dietary supplement [6].

One of the main risk factors for morbidity and mortality from many chronic diseases, including cardiovascular, type 2 diabetes and some types of cancer, is a body mass index of more than 30 kg/m<sup>2</sup>. The problem is growing dangerously not only in high-income countries, but also in poorer regions of the world, and among population groups of both sexes and all age groups [7]. Reducing the prevalence of obesity and developing new strategies for its treatment and the medical complications that arise from the disease is clearly a public health priority. The mechanisms underlying the pathogenesis of obesity and related chronic diseases are being intensively investigated to combat this global pandemic [8].

In recent years, studies of chronobiorhythms have raised awareness of the effects of circadian rhythms on obesity. A circadian system exists to synchronize and regulate the daily rhythm of physiological and behavioral processes such as eating/fasting and wakefulness/sleep. Circadian disturbances due to shift work, continuous exposure to light and changes in diet can negatively affect the energy balance and increase the risk of excess body weight [9].

A wide range of physiological processes in humans is regulated by the endogenous circadian clock, which receives information from external and internal input signals to synchronize peripheral clocks with these input signals [10]. The pineal hormone melatonin, which is related to all physiological systems of the body, fulfills its functional integrative role in the activity of the central nervous system, sleep and wake cycles, energy metabolism and thermoregulation, immune, reproductive, endocrine, cardiovascular, respiratory and excretory systems. The body adapts the integrative, physiological, regulatory role of melatonin to modern environmental problems. It synchronizes the physiology and behavior of the organism with daily and annual photoperiodic cycles [11].

Melatonin, originally known as an effective antioxidant, is an endogenous hormone that is found in the body and performs various physiological functions. It is able to absorb highly toxic hydroxyl radicals and stimulate the activity of a large number of antioxidant enzymes. A sharp decrease in the secretion of melatonin leads to a change in the quantity and quality of night sleep. If the external lighting does not decrease to a physiologically critical level, melatonin will not begin to be produced even in young people, which happens, for example, when falling asleep with a light source [12]. Violations of melatonin secretion do not always arise from lighting conditions, but can naturally occur during physiological aging of a person, which is associated with calcification of pinealocytes – functioning cells of the pineal gland that synthesize melatonin. This process

has received the conventional name «melanopause», although from the point of view of physiology, as the body ages, there is not a sudden cessation of melatonin secretion by the pineal gland, but its slow decrease [13].

A decrease in the synthesis of melatonin and the development of disturbances in the «sleep-wake» system leads, in particular, to insomnia, which is a natural attribute of human aging, and to an increase in the number of calcium deposits. However, as mentioned, the consequences of melatonin deficiency are not limited to the development of circadian rhythm disorders and insomnia in people of any age. A deficiency of the sleep hormone also leads to a number of other hormonal and metabolic negative consequences, which is associated with its universal physiological effects, which are very diverse [14].

Taking into account that the synthesis of the epiphyseal hormone melatonin is directly correlated with the length of daylight and circadian rhythms, its systemic hormonal response consists of the coordination of behavioral and physiological adaptation to the geophysical day and seasonal changes in the environment. Circadian rhythms are determined by the daily regularity of melatonin synthesis, as well as the contrast between day and night levels of its synthesis. Therefore, at present, more and more chronobiological studies indicate the importance of observing the timing of meals and the need to develop special diets in which the consumption of the main nutrients is clearly related to circadian activity. Scientists have proven that skipping the first meal increases the risk of obesity and its complications [15].

Innate and adaptive immunity is also regulated by melatonin. Its antioxidant properties are associated with reduced susceptibility to infections and weight gain in obese patients, through modulation of the immune response, which has significant beneficial effects on inflammation and metabolic status. Obesity is associated with low melatonin levels, so melatonin-based drugs can reduce body weight, correct metabolic profile, and improve immune responses and anti-inflammatory stimuli [16].

The role of melatonin in obesity is mainly related to improved oxidative stress signaling, modulation of adipokine secretion. In addition, melatonin's role in modulating obesity by controlling the circadian rhythm has recently been implicated as a key mechanism of lipid and glucose metabolism dysfunction in adipose, muscle, and liver tissues. By directly influencing the morphology and activity of the thymus, as well as modulating oxidative stress and inflammation during infections, melatonin may also regulate the immune system. The close relationship between melatonin and the regulation of the immune response is coordinated by Toll-like receptors, which are rhythmically activated throughout the day. Their expression can be strongly modulated by melatonin, as their signaling is strongly inhibited by melatonin [17].

Deregulation of physiological and behavioral central and peripheral circadian rhythms, which contributes to obesity-related metabolic disturbances, is characterized by chronodestruction. Feelings of hunger, satiety, and weight gain can be strongly influenced by eating and

sleeping schedules, which are appropriate synchronizers of the human biological clock and in which melatonin plays an important role. The scientific community has increased its attention to the molecular mechanisms involved in the etiopathogenesis of obesity in order to treat better patients with obesity and its associated complications [18].

First of all, to assess the development of obesity, in experimental conditions, anthropometric indicators are used, on the basis of which the body mass index is calculated, the weight of organs, abdominal and peritoneal fat, histology and histochemistry of organs and tissues are also investigated. An increase in the body weight 10-25 % is considered to be moderate obesity, and 40 % or more is considered as severe obesity [19].

In addition, it is recommended to determine the level of leptin, ghrelin, adiponectin and insulin resistance of cells in order to evaluate the effectiveness of the researched treatment and preventive measures. Therefore, today in the world medicine, one of the most important tasks of preventive measures regarding excessive body weight is considered to be the prevention of the development of hormonal and metabolic complications of excessive accumulation of adipose tissue [20].

During the day, melatonin synthesis is blocked, so the daily cycles of melatonin synthesis coordinate adaptive physiological processes at night and form the prerequisites for the body's daytime range of adaptation. Depending on the change of season, the daily rhythms of melatonin secretion modulate the physiological activity of the central nervous and endocrine systems. It has been established that maternal melatonin regulates the physiological processes and behavioral reactions of the fetus, which allows the child to adapt to the daily and seasonal circadian rhythm after birth [21].

Due to the development of clinical complications, obesity leads to a decrease and even loss of working capacity, frequent hospitalization of this population group. The polyetiological and polypathogenetic nature of disorders is indicated by studies accumulated as a result of the study of the metabolic processes of various nutrients in obesity [22]. In addition to that, an important role is given to the processes of free radical oxidation of lipids. The main function of melatonin is the modulating effect on the circadian organization of physiological processes and ensuring the synchronization of the body's biological rhythms with the rhythms of the environment. In particular, there are data that this hormone has an antioxidant effect, which lies in binding free radicals, increasing the activity of antioxidant enzymes and potentiating the action of other endogenous antioxidants [23].

Today, melatonin drugs are often prescribed for various sleep disorders due to incoherence of biological rhythms, such as night work, long-distance flights, incorrect daytime routine, sleeping with the light switched on. Melatonin also has antidepressant properties, so it is taken to improve mood [24, 25].

However, much less is known about the effects of melatonin, related to its influence on carbohydrate and fat metabolism, the lymphatic and immune systems, the processes of vital activity and cell death, which requires

further research to clarify the current state of the study of melatonin-dependent disorders of energy metabolism.

## Conclusions

1. According to the data of scientific literary sources, in obesity and metabolic syndrome, there is a decrease in the level and disruption of the rhythm of melatonin production.

2. Melatonin is an effective means of correcting a number of pathological changes that accompany the development of obesity and impaired energy metabolism.

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