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Effect of melatonin on heart rate variability in rats with adrenaline-induced myocardial dystrophy

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Abstract. The pineal hormone melatonin actively regulates the body's adaptive reactions to changes in external environmental conditions and internal homeostasis. Melatonin, as a pharmacological agent with antioxidant properties, is widely used to correct disorders resulting from oxidative stress. The present study aimed to investigate changes in cardiac activity under the influence of this hormone, in particular, the effect of melatonin on heart rate variability in laboratory rats with a model of adrenaline-induced myocardial dystrophy. The degree of regulatory tension and neural control mechanisms and mechanisms of nervous regulation was assessed by mathematical analysis of heart rate variability, which is one of the integrative methods for evaluating the functional activity of the body's regulatory systems. The main results of the study demonstrated that autonomic regulation of the heart showed an increase in the vegetative balance index (VBI), alongside a decrease in heart rate frequency (HRF) and tension index (TI), indicating reduced sympathetic-adrenal stimulation of the heart under conditions of adrenaline-induced myocardial dystrophy. During the 10 day administration of melatonin to rats with adrenaline-induced myocardial dystrophy, an increase in autonomic activity was observed, with an emphasis on heightened parasympathetic nervous system influence on the heart, which contributed to a lower risk of arrhythmias and myocardial infarction. In particular, changes in heart rate were accompanied by HRF fluctuations ranging from 339 to 451 beats/min and an increase in TI from 1,279 to 7,942 units. Twenty-four hours post-adrenaline administration, TI and HRF decreased by 22% and 6.5%, respectively. In rats with pineal hyperfunction, the mean HRF was 414 ± 26 beats/min, TI increased by 27%, and the mean VBI increased by 14%. The observed effects of melatonin indicate that it is a potentially useful tool for preventing adrenaline-induced myocardial damage. The results of the study

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offer new possibilities for correcting the functional state of the heart and enhancing understanding of the mechanisms through which different levels of pineal gland activity influence cardiac function

Keywords: melatonin; pineal gland; tension index; heart rate; stress reactions; adrenaline induced myocardial dystrophy

Introduction

The conditions of modern reality in the country are characterised not only by the increasing pace of life but also by military events, uncertainty, social changes, and economic instability. All of these factors, coupled with the sounds of explosions, sirens, a sense of constant danger, and lack of adequate sleep and rest, as well as separation from loved ones, induce constant stress even in healthy people. It is known that stress formation occurs through the activation of the hypothalamicpituitaryadrenal complex. Any stressful event arises due to adrenaline release and is accompanied by the development of oxidative stress, which negatively affects the morphological and functional state of the heart, leading to arrhythmias, heart attacks, coronary syndromes, and hypertensive crises. The negative consequences of oxidative stress, which precede morphofunctional changes, include the intensification of free radical lipid peroxidation and the destabilisation of antioxidant defence. This process is a key factor in the development of cardiac pathologies and is therefore considered a crucial link in the pathogenesis of cardiovascular disease. The chosen research topic is highly relevant, as chronic stress has become an aspect companion of modern life, and cardiovascular disease remains the leading cause of morbidity. At the same time, the effect of melatonin on heart rate variability in rats with adrenaline-induced myocardial dystrophy has been insufficiently studied. This knowledge gap prompted the present study, as these findings may provide new opportunities for correcting the functional state of the heart and enhancing understanding of how varying levels of pineal gland activity affect cardiac function.

The pineal gland is a central endocrine organ actively involved in adaptation processes, homeostasis regulation, and stress response. The pineal hormone melatonin plays a key role in regulating the body's adaptive responses to changes in external environmental conditions and internal homeostasis. Melatonin is known to be an antioxidant with cardioprotective properties. According to V. Pishak *et al.* [1], melatonin plays an important role in blood pressure regulation. Pinealectomy in rats causes hypertension, and melatonin administration reverses this effect. Melatonin has also been found to significantly influence HRF and vascular resistance. In turn, Y-J. Song *et al.* [2] investigated the effect of melatonin supplementation on metabolic status in patients with diabetes and coronary heart disease. Their findings indicated that melatonin supplementation enhanced insulin sensitivity and improved cholesterol levels, as well as significantly reduced certain oxidative biomarkers. These results suggest that melatonin treatment may lower cardiometabolic risk in patients with diabetes and coronary heart disease. According to the research of M. Tobeiha *et al.* [3], melatonin directly interacts with the nervous system and indirectly with blood vessels and the heart. It exerts its direct effects through receptor-dependent signalling pathways, as well as indirect antioxidant actions by scavenging free radicals.

The cardioprotective effects of melatonin are due not only to its antioxidant properties but also to its immunomodulatory, anti-ischaemic and antihypertensive effects. In an experiment conducted by I. Yaremii *et al.* [4], daily administration of melatonin over a two-week period in rats with dexamethasone-induced diabetes led to the normalisation of certain indicators of carbohydrate metabolism in the liver. This confirms the assumption of a possible hypoglycaemic effect of melatonin in diabetes progression. Yu.O. Zolotukhina's research [5] found that patients with coronary heart disease, both those without concomitant conditions and those with diabetes mellitus, exhibit suppressed anticoagulant activity and an increased blood clotting potential, which, in turn, heightens the risk of vascular disease. This was confirmed in the research of A. Stenling [6]. C. MilletBoureima *et al.* [7] demonstrated that melatonin has a beneficial effect on the cardiovascular system (CVS) by regulating heart rate and reducing nighttime blood pressure in patients with hypertension. In addition, it may offer powerful protection for the cardiovascular system and reduce the risk of reperfusion injury following myocardial infarction. Furthermore, according to a study by A. Chrustek & D. Olszewska-Słonina [8], melatonin has a normalising effect on blood pressure, heart rate, and coronary circulation. Y.-J. Song *et al.* [2] found that melatonin can modulate cardiovascular functions such as cardiac output, blood pressure, heart rate, and seasonal rhythms. After pinealectomy, the primary source of melatonin in the bloodstream, blood pressure in rats increased, whereas melatonin administration in hypertensive rats lowered blood pressure, baroreflex response, and heart rate. A study by X. Zhang *et al.* [9] showed a beneficial effect of melatonin on mitochondrial fusion, regulated by the molecule OPA1 (optic atrophy 1), in myocardial infarction and/or reperfusion injury. It has been established that melatonin can preserve myocardial function, reduce infarct size, and prevent cardiac myocyte death in response to reperfusion stress.

Melatonin plays a crucial role in the protective effects of stress adaptation mechanisms. Y.-J. Song *et al.* [2] assessed the effect of melatonin intake on metabolic status in patients with diabetes and coronary heart disease and found that melatonin supplementation enhanced insulin sensitivity and cholesterol levels. A scientific study by A. Chrustek & D. Olszewska-Słonina confirmed that melatonin is a versatile molecule with multiple physiological

functions. It exhibits strong antioxidant properties by activating antioxidant enzymes and safeguards cells from lipid peroxidation. Therefore, melatonin, as a pharmacological agent with antioxidant properties, is widely used to correct disorders resulting from oxidative stress. However, at present, it remains unclear which factor is primary: whether genetically determined disorders of melatonin production, together with other factors, contribute to pathology formation, or whether the increased need for melatonin arises due to the disease itself, as the reserve capacity of the enzymatic (particularly antioxidant) system becomes depleted. Considering the wide range of biological activities of melatonin, including its antioxidant, antistress, and chronobiological effects, this study aimed to investigate the effects of melatonin on heart rate variability in laboratory rats with adrenaline-induced myocardial dystrophy.

Materials and Methods

The experimental component of the study was conducted on adult male Wistar rats, weighing 220-260 g, which were kept under vivarium conditions on a standard diet with exposure to natural light cycles. All stages of the study, including manipulative interventions and euthanasia, were carried out in compliance with the provisions of the "General Ethical Principles for Animal Experiments", adopted by the VII National Congress on Bioethics in 2019 [10], and following the Procedure for Carrying out Experiments and Experiments on Animals by Scientific Institutions (2012) [11], as well as the European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes (1986) [12].

Two series of experiments were conducted to study the effects of adrenaline-induced myocardial dystrophy against a background of pituitary hyperfunction, which was complicated by adrenaline-induced cardiac dystrophy. The animals were divided into four groups, with each group consisting of eight animals. Group I (control): rats were maintained under normal vivarium conditions. Group II: rats were exposed to a 10-day period of pituitary hyperfunction. Group III: rats were subjected to 10 days of adrenaline-induced myocardial dystrophy. Group IV: rats developed adrenaline-induced myocardial dystrophy against a background of pituitary hyperfunction.

According to the literature, the maximum single-administered dose of melatonin is 5 mg/kg of body weight; therefore, pituitary hyperfunction was induced by administering melatonin (VitaMelatonin, JSC "Kyiv Vitamin Plant", Ukraine) at a dose of 1 mg/kg of body weight, dissolved in 1.0 ml of solvent, once daily at 19:00 for 10 days [4]. An experimental model of cardiac pathology, specifically adrenaline-induced myocardial dystrophy (AMD), was established by administering adrenaline hydrochloride at a dose of 0.5 mg/kg as a single injection [13, 14]. To record the electrocardiogram (ECG), rats were restrained in the cervical and lumbar regions using a specialised apparatus. The animals' paws were secured with strips of adhesive plaster, and the apparatus containing the restrained animals was placed in a shielded chamber. Alcohol-treated stainless-steel needle electrodes (0.1 mm in diameter) were inserted subcutaneously into the forelimbs of the animals.

ECG recording offers additional possibilities for assessing the mechanisms involved in functional regulation, as well as the adaptive capacity of the body, which reflects the degree of dynamic balance with the environment. In this context, heart rhythm can serve as an indicator of regulatory system function, not only for the heart but also for the body as a whole. Since the cardiovascular system is the first to react to external influences, the body's adaptive response to maintaining balance with the environment manifests through increased tension in regulatory processes [15, 16].

Based on this principle, the degree of regulatory and neural control system tension was assessed through a mathematical analysis of heart rate variability (HRV). According to the literature, HRV is one of the most integrative methods for evaluating the functional activity of the body's regulatory systems, as changes in the key parameters of cardiac variability reflect both cardiac function and the impact of regulatory influences associated with autonomic nervous system activity [17, 18].

During rhythmogram recording, the following indicators were evaluated: Mode (*Mo*) – the duration of the most frequently occurring cardiac interval; Mode amplitude (*AMo*) – the number of cardiac intervals with the value of *Mo*; Variation range of cardiac intervals (ΔX) – the difference between the maximum and minimum values in the sample, and stress index. Mathematical analysis of HRV was conducted based on ECG recordings in the second standard lead at a tape speed of 100 mm/s. For analysis, 100 consecutive R-R intervals were selected. Based on the values of *Mo*, *AMo*, and ΔX, the following indicators were calculated: Regulatory system stress index, using the formula:

$$RSSI = AMo / (2\Delta X \times Mo). \quad (1)$$

Vegetative balance index (VBI) using the formula:

$$VBI = AMo / \Delta X. \quad (2)$$

Statistical analysis of the study results was conducted using the parametric method of variance statistics, specifically the Student's t-test. The arithmetic mean (M), standard deviation ($\bar{o}$), and Student's t-test (t) were determined. A difference between numerical parameters was considered statistically significant if $p < 0.05$. Statistical calculations were performed using a personal computer with the standard STATISTICA 6 software for Windows.

Results and Discussion

According to ECG recordings, the animals in the control group had a regular heart rhythm. Under conditions modelling adrenaline-induced myocardial dystrophy, the HRV parameters changed significantly. Analysis of heart rate frequency (HRF) in rats with adrenaline-induced myocardial dystrophy revealed that the average tension index (TI) ranged from 1,279 to 7,942 units, while HRF ranged from 339 to 451 beats per minute. Thus, adrenaline-induced

myocardial dystrophy had a significant effect on heart rhythm, with animals responding to myocardial dystrophy caused by epinephrine through an increased heart rate. Two hours post-adrenaline administration, the stress index decreased by 2.4%, while the heart rate decreased by 4.8%, reaching 410 ± 13.4 beats per minute. ECG recordings of rats in the experimental group, taken 24 hours post-adrenaline administration, showed a decrease in TI and HRF compared to pre-administration values by 22% and 6.5%, respectively, reaching 403 ± 14.7 beats per minute (Table 1). These changes indicate an increased influence of the sympathetic branch of the autonomic nervous system (ANS) on heart rhythm, which is mediated via the humoral pathway, primarily involving the adrenal glands.

Table 1. Heart rate variability indicators in rats with adrenal-induced myocardial dystrophy

HRV indicators	Before adrenaline administration of	After 2 hours	After 1 day
HRF (beats per minute)	431 ± 14	410 ± 13.4	403 ± 14.7
TI (units)	4,716 ± 467	4,605 ± 381	3,681 ± 460
VBI (units)	1,255 ± 222	1,652 ± 238 $p_1 > 0.05$	1,073 ± 160 $p_2 > 0.05$

Notes: p_1 – comparison with values before adrenaline administration; p_2 – comparison of values observed after 24 hours with those recorded two hours post-adrenaline administration

Source: developed by the authors based on their research

The authors concur with researchers who suggest that phosphoinositide secondary mediators play a role in the formation of limiting systems that mitigate the destructive effects of stress factors, in this case, adrenaline. It is possible that in addition to functional regulation at the systemic level (brain-myocardium), the myocardium itself can counteract negative effects through the selfregulation and oscillatory properties of secondary mediator systems. This process may block adverse effects at the stage of intracellular signalling [19, 20]. The data obtained suggest that epinephrine administration induces changes that result in autonomic regulation disorders. It can be hypothesised that a key trigger in this process is a reduction in melatonin production by the pineal gland.

Testing for adrenaline sensitivity 10 days after administration showed some alterations in HRV parameters; however, these changes were not statistically significant. Two hours post-administration, TI increased by 2%, whereas after 24 hours, it decreased by 30% and 32%, respectively, compared to the baseline level recorded at the two-hour mark. HRF decreased by 10.5% two hours postepinephrine administration. Meanwhile, VBI increased by 27% within two hours but subsequently decreased by 5% over the following 24 hours, relative to pre-administration values. Thus, mathematical analysis of heart rate variability indicated a reduction in TI and HRF, alongside an increase in VBI, two hours post-adrenaline administration. Analysis of heart rate in rats with an experimental model of pituitary hyperfunction revealed an average heart rate of 414 ± 26 beats per minute, with TI increasing by 27% to 5,981 ± 410 units, and VBI rising by 14% to 1,741 ± 197 units (Table 2).

Table 2. Results of mathematical analysis of heart rate in rats under the influence of adrenalineinduced myocardial dystrophy against a background of hypermelatoninaemia

ECG parameters	Before adrenaline administration	After 2 hours	After 1 day
HRF (beats per minute)	414 ± 26	369 ± 18	365 ± 28
TI (units)	5,981 ± 410	2,435 ± 300 $p < 0.01$	3,431 ± 424 $p < 0.001$
VBI (units)	1,741 ± 197	898 ± 77 $p < 0.01$	1,086 ± 100

Notes: p – significant difference between values before adrenaline administration and two hours post-administration within the same group of animals

Source: developed by the authors based on their research

ECG recordings taken two hours post-adrenaline injection in this group of animals revealed a sharp decrease in the stress index and a moderate reduction in heart rate. The average HRF decreased by 10 beats per minute, while the TI value decreased by 47% relative to baseline levels. The TI reduction was statistically significant ($p < 0.001$) compared with both the baseline value and the preadministration TI value recorded in this group ($p < 0.01$). Notably, despite this substantial decline in TI and only a slight reduction in HRF, VBI dropped sharply to 898 ± 77 units. This decrease was significant ($p < 0.01$) compared to control animals. ECG recordings taken 24 hours post-epinephrine administration revealed a further slight reduction in heart rate and an increase in TI and VBI.

It is possible that the administration of epinephrine enhances sympathetic nervous system function, and in the presence of hypermelatoninaemia, parasympathetic nervous system activity is increased, thereby reducing the risk of arrhythmias and myocardial infarction. Melatonin administration may also reduce the intensity of energy metabolism

and, consequently, oxygen consumption. In addition, this effect of melatonin could activate the stress-limiting system in a manner similar to opioid peptides and phosphoinositide systems, ultimately enhancing myocardial resistance to catecholamine-induced stress. With the artificial activation of adrenoceptor structures through adrenaline administration, melatonin may trigger feedback mechanisms that enhance parasympathetic nervous system activity, thereby reducing the risk of arrhythmias, preventing pathological foci, and minimising the likelihood of myocardial infarction.

In contemporary scientific research, the role of the pineal gland has gained increasing significance in understanding the mechanisms of neurohumoral regulation of cardiac function. This growing interest stems from the well-established cardioprotective effects of melatonin. Thus, the results of this study suggest that melatonin administration in the context of AMD exerts an antiischaemic effect, promoting the restoration of cardiac function, enhancing parasympathetic nervous system activity, and mitigating dystrophic manifestations [21, 22].

Mathematical analysis of heart rate under conditions of hypermelatoninaemia in AMD revealed a decrease in HRF and TI in rats two hours after adrenaline administration. However, after 24 hours, the heart rate remained at the two-hour level, while the stress index had increased. This trend did not align with ECG control values following epinephrine administration. Meanwhile, VBI decreased over the 24-hour period. Epinephrine administration may enhance sympathetic nervous system function, while pineal hyperfunction promotes increased parasympathetic nervous system activity, thereby reducing the risk of arrhythmias and myocardial infarction. These data may be attributed to melatonin administration leading to heightened parasympathetic tone, inhibition of free radical reactions, and reduced myocardial electrical instability.

With pineal gland hyperfunction, melatonin production increases, leading to a reduction in sympathetic-adrenal system activity, metabolic rate, and oxygen consumption. Daily fluctuations in autonomic nervous system activity play a crucial role in this process. Thus, the results obtained in this experiment indicate that one of the key advantages of pineal gland hyperfunction, which maximises melatonin's cardioprotective effects, is the predominant role of parasympathetic processes in cardiac adaptation mechanisms under conditions of AMD. The timely and sufficient activation of melatonin enhances the efficiency of compensatory and adaptive responses, thereby increasing myocardial resistance. These findings are consistent with studies conducted by Ukrainian, American, and Chinese researchers. Studies by Y.-J. Song *et al.* [2] have demonstrated that melatonin exerts an antihypertensive effect and alleviates hypertension caused by continuous exposure to light. Similarly, V. Kolesnikova & A. Radchenko [23] found that melatonin affects cardiac function and plays a role in oxidative stress mechanisms. According to V.P. Pishak *et al.* [1], melatonin acts directly on the paraventricular nucleus and the hypothalamic-pituitary-adrenal axis, modulating the baroreflex set point, reducing sympathetic tone, and increasing parasympathetic tone within the medulla oblongata, which regulates heart rate.

The dynamic changes of heart rate variability values in AMD under conditions of pituitary gland hyperfunction exhibited a consistent pattern, characterised by a decrease in heart rate, TI, and VBI (Fig. 1). Comparative analysis of these data and the observed trends suggests that these changes may be attributed to adrenoceptor desensitisation and reduced baroreceptor sensitivity, resulting from structural and metabolic alterations in the myocardium. Such processes may obscure the progressive impairment of neurohumoral regulation. These results also suggest an increase in sympathetic nervous system activity as part of a compensatory response. The decrease in primary HRV parameters highlights the close interrelation between extracardiac heart rate regulation and the functional state of the myocardium during the progression of AMD and the effects of melatonin.

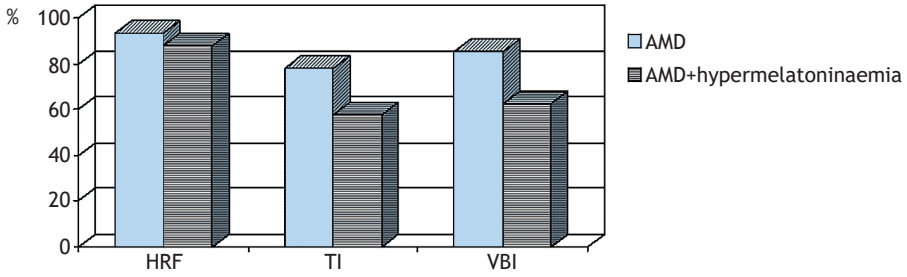

Figure 1. Dynamics of changes in the indicators of mathematical analysis of heart rate under conditions of AMD and AMD + hypermelatoninaemia

Notes: 100% of the values represent indicators in control animals

Source: developed by the authors based on their research

This reduction in heart rate variability suggests a shift in autonomic balance towards increased parasympathetic dominance. Such mechanisms underlying heart rate variability reduction may result from two primary factors: a decrease in the amplitude of autonomic tone oscillations and reduced sinus node sensitivity to autonomic influences.

The results obtained by the present study indicate that melatonin administration under conditions of AMD exerts a general corrective effect by restoring the functional state of the heart. This finding aligns with the studies of M. Tobeiha *et al*. [3], which demonstrated melatonin's role in heart regeneration and its protective effects against cardiac dysfunction. In addition, the absence of significant changes in heart rate, which characterises the central mechanism of heart function, indicates that the observed changes occur at the local level. In other words, these changes take place within the myocardium and are realised at the cellular level rather than within central regulatory circuits.

These results are further supported by the studies of N.O. Bezkorovayna *et al*. [24], found that 10-day exposure to continuous illumination (500 lux) induces a significant increase in parasympathetic influence on heart rate and bradycardia in females, while in males, it leads to an increase in heart rate accompanied by a decrease in parasympathetic influence on the heart. The development of adrenaline-induced myocardial necrosis in females under continuous illumination is associated with cardio-intervalometer dynamics similar to those observed under light-balance conditions, with greater parasympathetic activity within the ANS and a corresponding increase in sympathetic activity. In males, under similar conditions, the ANS response to the development of myocardial necrosis differs from that observed under balanced lighting conditions and demonstrates parasympathetic involvement in heart rhythm regulation while exhibiting sympathetic dominance [24].

The results of the present study indicate that melatonin contributes to reducing oxidative stress under conditions of AMD and normalising the studied parameters. Melatonin demonstrated its antiischaemic effect, significantly improving the functional state of the rat heart in the experiment conducted by T. Senoner & W. Dichtl [25]. For example, studies by F.Gd. Amaral & J. CipollaNeto [26] have shown that the benefits of melatonin's potent protective properties are associated with its ability to lower oxidative stress and reduce the risk of damage following myocardial infarction. Additionally, melatonin functions as a scavenger of reactive oxygen species within mitochondria, thereby providing a beneficial effect in coronary heart disease. According to other studies, notably M. Cherska *et al*. [27], the mechanisms through which melatonin affects vascular tone have been identified, specifically its interaction with its own receptors, its influence on adrenergic pathways of muscle contraction, and its ability to block serotonergic stimulation.

Thus, the findings of this study confirm that melatonin administration under conditions of adrenaline-induced myocardial dystrophy exerts a general corrective effect. It promotes the restoration of the functional state of the heart at the cellular level without significantly affecting central regulatory mechanisms. Melatonin exhibits an anti-ischaemic effect by reducing oxidative stress and improving cardiac function, which corroborates previous studies confirming its role in lowering the risk of damage following myocardial infarction and its involvement in vascular tone regulation.

Conclusions

Based on studies investigating the autonomic regulation of the rat heart under the influence of melatonin in the context of adrenaline-induced myocardial dystrophy, this study has demonstrated the physiological role of melatonin in modulating autonomic status and functional changes in the heart. These effects are attributed to its antioxidant, anti-ischaemic, and stress-protective properties. The dynamics of the studied parameters indicate the adaptive mechanisms of the rat heart, which involve the autonomic nervous system. A comparison with similar parameters in rats with adrenalineinduced myocardial dystrophy led to the following conclusions.

The autonomic regulation of the heart, as assessed by mathematical analysis of heart rate, revealed an increase in VBI values alongside a decrease in HRF and TI values. This pattern indicates a reduction in sympathetic-adrenal stimulation of the heart under conditions of adrenaline-induced myocardial dystrophy. Mathematical analysis of the heart rate in rats with an experimentally induced model of pituitary hyperfunction showed that the average heart rate was 414 ± 26 beats per minute. The average TI increased by 27% to 5,981 ± 410 units, while the average VBI increased by 14% to 1,741 ± 197 units. Given the above findings, these differences may indicate that changes reflecting autonomic balance mechanisms and their influence on adaptive and compensatory responses under adrenaline stress occurred with the vagus nerve playing a dominant role. Experimental data highlight the importance of studying the effects of melatonin in cardiovascular conditions such as myocardial ischaemia, chronic hypoxic heart injury, and atherosclerosis. Therefore, the timely diagnosis of melatonin production disorders, along with its potential therapeutic use in stressful situations, underscores the importance of these measures. In this context, circadian rhythm disturbances – which are crucial for maintaining normal myocardial function – further emphasise the need to investigate melatonin's role in stress and myocardial pathology. The study of heart rate variability is essential for a more precise determination of regulatory mechanisms. This will facilitate the development of effective preventive and therapeutic measures.

The results of this study indicate the need to investigate sex-related differences in heart rate variability. Furthermore, melatonin appears to be a promising agent for the prevention of adrenalineinduced myocardial damage. Future research should focus on examining the effects of melatonin deficiency on heart rate parameters during the development of adrenaline-induced myocardial dystrophy in male and female rats.

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Conflict of Interest

None.

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Вплив мелатоніну на варіабельність серцевого ритму у щурів на тлі адреналінової міокардіодистрофії

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Анотація. Активне керування адаптивними реакціями організму на зміни зовнішніх умов середовища і внутрішнього гомеостазу відбувається за участі гормону епіфіза мелатоніну. Мелатонін як фармакологічний препарат із антиоксидантними властивостями широко використовують для корекції розладів, що виникають внаслідок оксидативного стресу. Це дослідження було спрямоване на вивчення змін серцевої активності під впливом даного гормону, зокрема впливу мелатоніну на варіабельність серцевого ритму у лабораторних щурів, які мали модель адреналінової дистрофії міокарда. Ступінь напруги регуляторних механізмів та механізмів нервової регуляції оцінювали за математичним аналізом варіабельності ритму серця, який є одним із інтегративних методів оцінювання функціональної активності регуляторних систем організму. Основні результати дослідження показали, що вегетативна регуляція серця виявила збільшення значення показника вегетативного балансу (ПВБ) при зниженні значень частоти серцевих скорочень (ЧСС) та індексу напруженості (ІН), що свідчить про зниження симпато-адреналової стимуляції серця в умовах адреналінової міокардіодистрофії. Протягом 10-денного введення мелатоніну щурам на тлі розвитку адреналінової міокардіодистрофії спостерігалося підвищення вегетативної активності з акцентом на посилення впливу парасимпатичної нервової системи на серце, що сприяло зниженню ризику аритмій і розвитку інфаркту міокарда. Зокрема, зміни ритму серця супроводжувалися коливаннями ЧСС від 339 до 451 уд./хв. і підвищенням індексу напруженості від 1279 до 7942 од. Через 24 години після введення адреналіну ці показники знижувалися на 6,5 % і 22 %, відповідно. У щурів із гіперфункцією епіфіза середнє значення ЧСС становило 414±26 уд./хв., ІН збільшився на 27 %, а середня величина ПВБ – на 14 %. Виявлені ефекти мелатоніну свідчать, що він є потенційно корисним засобом для запобігання індукованих адреналіном пошкоджень міокарда. Результати дослідження відкривають нові можливості у корекції функціонального стану серця та дозволять розширити рамки розуміння механізмів впливу різної функціональної активності епіфізу на функціональний стан серця

Ключові слова: мелатонін; епіфіз; індекс напруження; серцевий ритм; стресові реакції; адреналінова міокардіодистрофія