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MORPHOMETRIC INDICATORS OF CHANGES IN THE CILIARY BODY OF RABBITS WITH EXPERIMENTAL HYPOPINEALISM UNDER THE INFLUENCE OF A COURSE OF MELATONIN*

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The close physiological connection of the organ of vision with the production of the hormone melatonin (M) is manifested primarily in the fact that the light fluxes in the daytime and under artificial lighting in the dark are perceived by the retina and through the retinohypothalamic pathways the signals from it are transmitted to the brain structures and suppress the production of M by the pineal gland (PG). At night, in the absence of artificial lighting, the pineal gland produces about 80% of M in the body. Under the influence of regular changes in the conditions of staying in the dark and in the light, circadian rhythms are formed in healthy person and a number of vertebrates, which is indirectly related to the work of the autonomic nervous system and is very important for the normal functioning of various organs and tissues [1–6].

The hypnotic effect of M is currently not considered the main property of this hormone. Modern studies have shown that sufficient production of M is necessary for the function of the antioxidant and immune systems of the body, affects the hormonal profile, has anticancer properties etc. It has been established that a decrease in nighttime production of M leads to disruption of many physiological functions,

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The authors assume responsibility for the published work.

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including free radical processes in the cell, and contributes to the development of atherosclerotic, trophic and oncological disorders in various tissues [7, 8].

Of great importance are the results of numerous studies that have shown the presence of M receptors in such tissues of the eye as the retina, ciliary body processes and lens epithelium. The production of M by the ciliary body processes has even been established [9–11]. Studies of the concentration of M in the aqueous humor of the eye at different intraocular pressures and the study of the relationship between M production by the pineal gland and the development of glaucoma have allowed us to establish the influence of M on the production of intraocular fluid and on the development of some types of glaucoma [12, 13].

The justification for our work was the fact that earlier, during a morphological study, we found that in the intraorbital part of the optic nerve (ON) of rabbits with experimental suppression of nocturnal melatonin production, early atherosclerotic and dystrophic processes develop, similar to those in atherosclerotic age-related atrophy of the ON [14]. Considering that the state of the ciliary body (CB) is extremely important for the trophism and functioning of the ON, it seems relevant to study the effect of course administration of M on the morphofunctional state of the CB against the background of long-term dysfunction of the pineal gland with M deficiency.

The aim of the work was to study the therapeutic effect of a course of melatonin injections on morphological changes in the ciliary body of rabbits in the early and late stages of hypopinealism formation under conditions of 24-hour light in the experiment.

MATERIALS AND METHODS

The experimental study was carried out on 55 mature male rabbits at the vivarium of the SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine» taking into account the «European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes» (Strasbourg, 1986), as well as taking into account the Law of Ukraine No. 3447-IV «On the protection of animals from cruelty» (Kyiv, 2006).

To suppress the function of the pineal gland, i.e. to simulate the state of functional hypopinealism, the animals were kept under conditions of round the clock illumination (RCI) [6]. To achieve such conditions, the lighting in the vivarium was natural during the day, and diffused artificial lighting (AL) was used at night. The measurement of the lighting intensity in the cages with rabbits, which was 30–40 lux, was carried out using a luxmeter «U-117».

The experimental animals were divided into the following groups: the control group (CG) consisted of 23 intact rabbits, which were in a vivarium with natural light and dark conditions; the group with hypopinealism (HG) consisted of 32 rabbits, which were in RCI conditions. The HG + M group consisted of 29 rabbits, which were in RCI conditions, but within 14 days before euthanasia received a course of intramuscular injections of M. Depending on the duration of the experiment, the animals were divided into subgroups: 1–2, 3–5, 8–12, 18–19, 26–28 months.

The assessment of the concentration of hormone M in the blood of control and experimental animals was carried out using enzyme-linked immunosorbent assay using standard kits (ELISA IBL GmbH, Germany). The study was carried out on a Stat Fax 303 Plus photometer (Awareness Technology INC, USA). Animals were removed from the experiment under anesthesia (sodium thiopental) in accordance with the euthanasia conditions specified in the methodological recommendations of the Ministry of Health of Ukraine [15].

For a comprehensive morphological study, the enucleated eyeballs of animals were fixed in a solution of neutral formalin, after which they were subjected to standard histological wiring and embedded in paraffin. Serial sections $4–5\times10^{-6}$ m thick were stained with hematoxylin with eosin, according to Mallory, and pikrofuksin according to Van Gieson (to identify components of the connective tissue), followed by survey microscopy to assess the general condition of the tissues under study, as well as with subsequent morphometric studies [16].

Histological and morphometric studies were carried out on an Olympus BX-41 microscope using Olympus DP-Soft (Version 3.1) and Microsoft Excel software [17]. Morphometric analysis was performed using the «fields» method [18]. The results obtained were processed by methods of mathematical statistics using elements of variational and alternative analyzes [19].

RESULTS AND THEIR DISCUSSION

Under the influence of RCI, after just 1 month of the experiment, the M concentration in blood at night decreased to 62.26 ± 5.27 pmol/L, compared to the control (369.45 ± 14.35 pmol/L; $p < 0.005$). Such a reduced level of M was maintained throughout the experiment.

After 1–2 months of the experiment in the HG+M_{1-2} subgroup, during a general microscopy of the tissues of the iris and ciliary body, circulatory disorders are revealed in the form of dilation and vascular congestion (Fig. 1). Average relative area of vessels (ARAV) was 6.61 ± 0.25% (7.80 ± 0.27% in HG_{1-2}, $p < 0.05$) (Table 1), average vascular wall thickness (AVWT) was 50.71 ± 1.30 $\times 10^{-6}$ m (59.20 ± 1.21 $\times 10^{-6}$ m in HG_{1-2}, $p < 0.05$) (Table 2). The average optical density of vascular endothelial cell nuclei DNA was 0.0809 ± 0.0037 conventional units (CU) in the green part of the spectrum on preparations stained according to Feulgen-Rossenbeck, which was significantly higher than the value of the HG_{1-2} subgroup (0.0503 ± 0.0038 CU, $p < 0.005$). The average optical density of endothelial cytoplasm RNA was 0.537 ± 0.017 CU in the green part of the spectrum on preparations stained according to Brachet, which was not statistically different from the values of the HG_{1-2} subgroup (0.541 ± 0.016 CU) (Table 3).

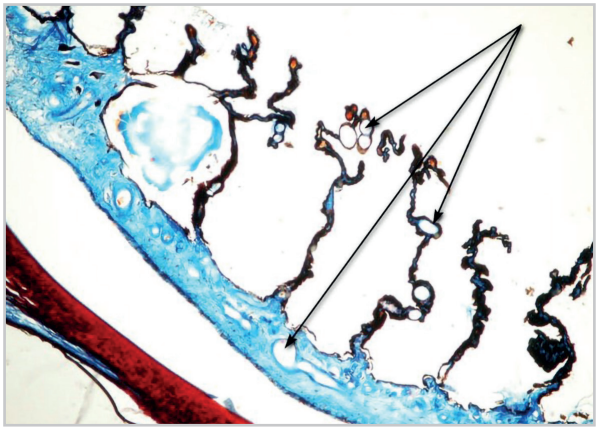

Fig. 1. Rabbit from subgroup HG + M_{1-2}. The vessels of the iris and ciliary body are sharply dilated (cystic in places), full-blooded, which indicates severe circulatory disorders. Mallory staining, ×100.

After 3–5 months of the experiment after a course of M administration in the HG + M_{3-5} subgroup, survey microscopy of the iris and CB tissues revealed an increase in dyscirculatory disorders in the form of vasodilation. These changes are most pronounced in the vessels of

Table 1

Average relative area of vessels (%) in the iris and ciliary body in animals exposed to 24-hour lighting, as well as in animals receiving a course of melatonin

Group CG subgroups	ARVA (%)	Group HG subgroups	ARVA (%)	Group HG + M subgroups	ARVA (%)
CG_{1-2}	4.51 ± 0.21	HG_{1-2}	7.80 ± 0.27^	HG + M_{1-2}	6.61 ± 0.25^°
CG_{3-5}	4.70 ± 0.19	HG_{3-5}	17.71 ± 0.43^*	HG + M_{3-5}	15.32 ± 0.37^°*
CG_{8-12}	4.51 ± 0.20	HG_{8-12}	11.52 ± 0.49^*	HG + M_{8-12}	10.21 ± 0.28^°*
CG_{18-19}	4.22 ± 0.17	HG_{18-19}	4.01 ± 0.19*	HG + M_{18-19}	4.10 ± 0.19*
CG_{26-28}	3.81 ± 0.11*	HG_{26-28}	3.42 ± 0.15^*	HG + M_{26-28}	3.43 ± 0.13^*

Notes:

^ the difference between the two means is significant when compared with the CG group ($p < 0.005$);

° the difference between the two means is significant when compared with the HG group ($p < 0.005$);

* the difference between the two means is significant when compared with the 1–2 months period of the experimental study ($p < 0.005$);

ARAV – average relative area of vessels (%).

Table 2

Average vascular wall thickness (×10^{-6} m) in the iris and ciliary body of animals exposed to 24-hour illumination, as well as in animals given a course of melatonin

Group CG subgroups	AVWT (×10^{-6} m)	Group HG subgroups	AVWT (×10^{-6} m)	Group HG+M subgroups	AVWT (×10^{-6} m)
CG_{1-2}	51.31 ± 1.22	HG_{1-2}	59.20 ± 1.21^	$HG + M_{1-2}$	50.71 ± 1.30°
CG_{3-5}	66.12 ± 2.71*	HG_{3-5}	87.61 ± 3.90^*	$HG + M_{3-5}$	81.14 ± 3.81^*°
CG_{8-12}	92.60 ± 4.21*	HG_{8-12}	136.33 ± 5.51^*	$HG + M_{8-12}$	133.82 ± 5.32^*
CG_{18-19}	101.91 ± 4.42*	HG_{18-19}	177.51 ± 7.32^*	$HG + M_{18-19}$	173.01 ± 6.91^*
CG_{26-28}	107.22 ± 5.21*	HG_{26-28}	217.42 ± 8.72^*	$HG + M_{26-28}$	207.92 ± 8.6^*

Notes:
^ the difference between the two means is significant when compared with the CG group ($p < 0.005$);
° the difference between the two means is significant when compared with the HG group ($p < 0.005$);
* the difference between the two means is significant when compared with the 1-2 months period of the experimental study ($p < 0.005$).
AVWT — average vascular wall thickness.

Table 3

Average optical density of DNA in endothelial cell nuclei, on preparations stained according to Feulgen-Rossenbeck (conventional units) in animals kept under conditions of RCI, as well as in animals receiving a course of melatonin administration

Group CG subgroups	AOD DNA (CU)	Group HG subgroups	AOD DNA (CU)	Group HG+M subgroups	AOD DNA (CU)
CG_{1-2}	0.0612 ± 0.0041	HG_{1-2}	0.0503 ± 0.0038^	$HG+M_{1-2}$	0.0809 ± 0.0037^°
CG_{3-5}	0.0654 ± 0.0032	HG_{3-5}	0.0448 ± 0.0029^*	$HG+M_{3-5}$	0.0662 ± 0.0033*°
CG_{8-12}	0.0689 ± 0.0023	HG_{8-12}	0.0386 ± 0.0018^*	$HG+M_{8-12}$	0.0432 ± 0.0021^*°
CG_{18-19}	0.0676 ± 0.0021	HG_{18-19}	0.0393 ± 0.0019^	$HG+M_{18-19}$	0.0428 ± 0.0020^
CG_{26-28}	0.0577 ± 0.0025	HG_{26-28}	0.0587 ± 0.0027*	$HG+M_{26-28}$	0.0573 ± 0.0024*

Notes:
^ the difference between the two means is significant when compared with the CG group ($p < 0.005$);
° the difference between the two means is significant when compared with the HG group ($p < 0.005$);
* the difference between the two means is significant when compared with the 1–2 months period of the experimental study ($p < 0.005$);
CU — conventional units;
AOD DNA — average optical density of DNA.

the terminal sections of the ciliary processes, where the capillaries have paretically dilated walls, a sharp slowdown in blood flow up to stasis and the phenomenon of erythrocyte sludge (Fig. 2). The ARAV of the CB in rabbits of the HG + M_{3-5} subgroup was 15.32 ± 0.37% (see Table 1), which is significantly higher than this indicator in animals of the CG_{3-5} subgroup (4.70 ± 0.19%; $p < 0.005$) and significantly lower than this indicator in the HG_{3-5} subgroup (17.71 ± 0.43%; $p < 0.005$). AVWT was 81.14 ± 3,81×10^{-6} m (87.61 ± 3,90 ×10^{-6} m in HG_{3-5}, $p < 0.05$).

After a course of M administration in the HG + M_{8-12} subgroup in the vessels of the iris and CB, signs of circulatory disorders persist, however, they are less pronounced both in comparison with animals of the HG_{8-12} subgroup. The ARVA was 10,21 ± 0,28% (11,52 ± 0,49% in HG_{8-12}, $p < 0.05$) (see Table 1), AVWT was 133.82 ± 5.32×10^{-6} m (136.33 ± 5.51 ×10^{-6} m in HG_{8-12}, $p < 0.5$, and 92.60 ± 4.21×10^{-6} m in CG_{8-12}, $p < 0.005$) (see Table 2). The AOD DNA of vascular endothelial cell nuclei was 0.0432 ± 0.0021 CU (0.0386 ± 0.0018 CU in HG_{8-12}, $p < 0.5$, and 0.0689 ± 0.0023 CU in

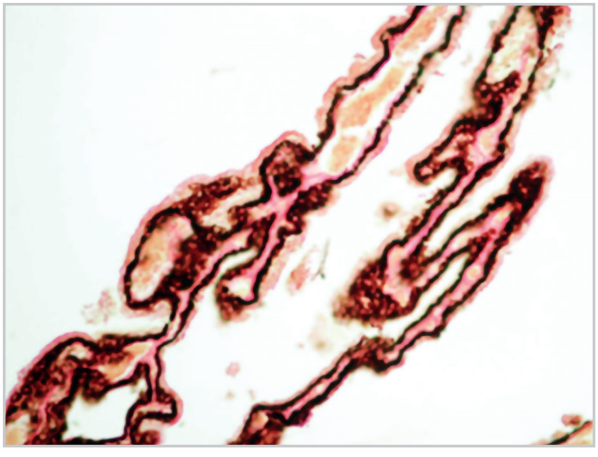

Fig. 2. Rabbit from the subgroup HG + M_{3-5}. In the processes of the ciliary body, pronounced discirculatory disorders are observed: paretic dilatation and congestion of capillaries up to stasis and sludge of red blood cells. Hematoxylin and eosin staining, ×200.

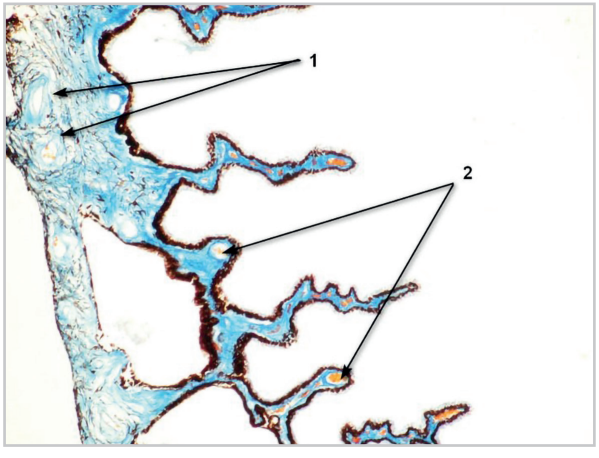

Fig. 3. Rabbit from subgroup HG + M_{8-12}. Moderate thickening of the walls of individual small-caliber arterioles is revealed (1). Dilation and focal plethora of the vessels of the iris and terminal sections of the ciliary processes are also detected (2). Mallory staining, ×100.

Table 4

Average optical density of RNA in the cytoplasm of endothelial cells, on preparations stained by the Brachet method (conventional units) in animals kept under conditions of RCI, as well as in animals receiving a course of melatonin

Group CG subgroups	AOD RNA CU	Group HG subgroups	AOD RNA CU	Group HG + M subgroups	AOD RNA CU
CG_{1-2}	0.533 ± 0.015	HG_{1-2}	0.541 ± 0.016	$HG+M_{1-2}$	0.537 ± 0.017
CG_{3-5}	0.567 ± 0.018	HG_{3-5}	0.594 ± 0.018	$HG+M_{3-5}$	0.591 ± 0.019
CG_{8-12}	0.563 ± 0.019	HG_{8-12}	0.772 ± 0.015^*	$HG+M_{8-12}$	0.678 ± 0.013^*°
CG_{18-19}	0.543 ± 0.011	HG_{18-19}	0.737 ± 0.014^	$HG+M_{18-19}$	0.674 ± 0.012^°
CG_{26-28}	0.545 ± 0.012	HG_{26-28}	0.655 ± 0.011	$HG+M_{26-28}$	0.651 ± 0.010^

Notes:
^ the difference between the two means is significant when compared with the CG group ($p < 0.005$);
° the difference between the two means is significant when compared with the HG group ($p < 0.005$);
* the difference between the two means is significant when compared with the 1–2 months period of the experimental study ($p < 0.005$);
CU — conventional units;
AOD RNA — average optical density of RNA.

CG_{8-12}, $p < 0.005$) (see Table 3). The average optical density of endothelial cytoplasm RNA was 0.537 ± 0.017 CU, this indicator was similar to that in the HG_{8-12} subgroup (0.541 ± 0.016 CU, $p > 0.05$) (Table 4).

After 18–19 months of the long-term RCI and course administration of melatonin in animals of the HG + M_{18-19} subgroup, a survey microscopy revealed thickening of the walls of small arteries and veins, as well as arterioles due to sclerosis (Fig. 4), which leads to significant an increase in the average thickness of the vascular wall to 173.01 ± 6.91×10^{-6} m (see Table 2) compared with the control subgroup CG_{18-19} (101.91 ± 4.42×10^{-6} m; $p < 0.05$), but this the indicator did not differ statistically from the indicator of the HG_{18-19} subgroup (177.51 ± 7.32×10^{-6} m; $p > 0.05$).

After 26–28 months of the experiment, survey microscopy of the iris and CB tissues revealed pronounced sclerosis of the walls of small arteries and veins, as well as the microvascular retina vessels — arterioles, capillaries and venules (Fig. 5). The average vascular wall

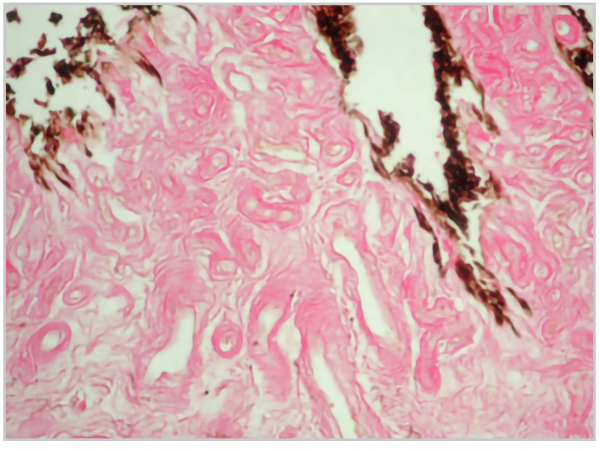

Fig. 4. Rabbit from the subgroup HG + $M_{18\text{-}19}$. Iris: in loose connective tissue there are small arteries, arterioles, as well as small veins with thickened, sclerotic walls. Hematoxylin and eosin staining, ×200.

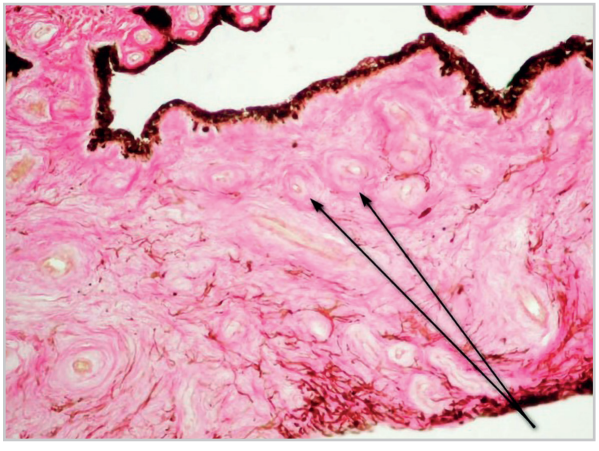

Fig. 5. Animal from subgroup HG + $M_{26\text{-}28}$. In the iris, there is a sharp thickening of the arteriole walls due to sclerosis and hyalinosis; in addition, there are signs of sclerotization in the connective tissue of the iris. Hematoxylin and eosin staining, ×200.

thickness increased to 207.92 ± 8.61×10^{-6} m (see Table 2) compared to the animals of the previous experimental period and the control subgroup (173.01 ± 6.91×10^{-6} m and 107.22 ± 5.21×10^{-6} m; $p < 0.005$) and did not statistically differ from the indicator in the $HG_{26\text{-}28}$ subgroup (217.42 ± 8.72×10^{-6} m, $p > 0.05$). The AOD DNA of vascular endothelial cell nuclei was 0.0573 ± 0.0024 CU (0.0587 ± 0.0027 CU in $HG_{26\text{-}28}$, $p > 0.05$, and 0.0577 ± 0.0025 CU in $CG_{26\text{-}28}$, $p > 0.05$) (see Table 3). The average optical density of endothelial cytoplasm RNA was 0.651 ± 0.010 CU, which was not statistically different from the values of the $HG_{26\text{-}28}$ subgroup (0.655 ± 0.011 CU) (see Table 4).

CONCLUSIONS

Morphological and morphometric studies have shown that animals with hypopinealism, which developed as a result of being in the conditions of the RCI, in the early stages of the experimental study (up to 5–8 months) exhibited pronounced circulatory disorders in the iris and ciliary body. The vessels are sharply dilated and hyperemic. In the paretically dilated capillaries of the ciliary crown processes, there is a slowdown in blood flow up to stasis and sludge of erythrocytes. Against the background of circulatory disorders in the CB, analysis DNA and RNA of the vascular endothelium showed a consistently high level of morphofunctional activity of the endothelial cells, which was recorded almost throughout the entire experimental study. After 12 months of the experimental study, circulatory changes in the CB of animals are replaced by sclerotic ones. We also observed sclerotic changes in the animals of the control group, interpreting them as gerontological processes. However, it should be noted that under RCI conditions, vascular sclerosis occurs earlier and is much more pronounced than in the animals of the control group. Thus, in rabbits kept under RCI conditions for 26–28 months, sclerosis of the connective tissue itself is observed, the average thickness of the vascular wall exceeds the similar indicator in the CG by 1.5 times. In addition, the qualitative composition of the affected vessels also changes. In the animals of the control group, we observed only sclerosis of the walls of small arteries, and in the animals that were under RCI conditions, in the late stages of the experiment, in addition to sclerotic changes in small arteries, we observe sclerosis of small veins and vessels of the microcirculatory bed (arterioles, capillaries, venules), in individual arterioles and capillaries, hyalinosis is detected. Thickening of the walls of small arteries and veins due to sclerosis leads to a significant increase in the AVWT index. Desolation of the vessels is characterized by a significant decrease in the ARAV index. Based on the results of the morphometric

analysis, it can be concluded that a course of melatonin administration reduced edema and vascular disorders in the CB of rabbits in the early stages of hypopinealism formation in an experiment with RCI up to 5–8 months. In the late stages of hypopinealism formation during 12–28 months of the RCI, apparently due to irreversible atherosclerotic changes in the vessels, the melatonin course did not have a therapeutic effect.

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MORPHOMETRIC INDICATORS OF CHANGES IN THE CILIARY BODY OF RABBITS WITH EXPERIMENTAL HYPOPINEALISM UNDER THE INFLUENCE OF A COURSE OF MELATONIN

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There is a close physiological connection between the organ of vision and the pineal gland, which is manifested in the fact that under the influence of light falling on the retina, signals are transmitted along the retinohypothalamic pathways to the brain and, reaching the pineal gland, inhibit the production of the hormone melatonin (M). It was found that a decrease in nighttime production of M leads to disruption of free-radical processes in the cell, disruptions in the immune and endocrine systems, etc. As a result, pathological changes develop in various tissues of the body. Modern studies have identified M in such eye tissues as the retina, ciliary body (CB), and lens epithelium. A connection has also been established between M production, production of intraocular fluid by the ciliary body, intraocular pressure and the development of certain types of glaucoma.

The aim of the work was to investigate the features of morphological changes in the ciliary body of rabbits under the influence of the course of melatonin injections at different times of manifestation of experimental hypopinealism, which developed against the background of 24-hour lighting.

Materials and methods. The experimental study was carried out on rabbits in compliance with the «European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes» (Strasbourg, 1986) and Law of Ukraine «On the Protection of Animals from Cruelty» No. 3447-IV (Kyiv, 2006). The formation of hypopinealism in animals was achieved by exposing them to 24-hour lighting. The groups were: the control group (CG) — 23 intact animals, which were in vivarium with natural change of day and night; a group with hypopinealism (HG) — 32 rabbits that were in the round-the-clock illumination (RCI); the HG + M group — 29 rabbits that were in the RCI, but before being withdrawn from the experiment, received a course of injections of M for 14 days. Depending on the duration of the experiment, subgroups were identified: 1–2, 3–5, 8–12, 18–19, 26–28 months. When conducting a morphological study of the CB of enucleated eyes of rabbits, morphometric analysis was used using the «field» method. To determine the M content in the blood during the day and night, an enzyme immunoassay was used.

Results. Nighttime melatonin levels in blood decreased under RCI conditions to 62.26 ± 5.27 pmol/L (control: 369.45 ± 14.35 pmol/L; $p < 0.005$).

After 1–2 months of experiment in the HG+$M_{1\text{-}2}$ subgroup, the average vascular wall thickness (AVWT) indicator (50.71 ± 1.30×10^{-6} m) decreased compared to $HG_{1\text{-}2}$ (59.20 ± 1.21×10^{-6} m; $p < 0.005$) and the indicator was similar to $CG_{1\text{-}2}$ (51.31 ± 1.22×10^{-6} m, $p < 0.005$); the average relative area of the vessels (ARAV) indicator (6.61 ± 0.25 %) was lower than the $HG_{1\text{-}2}$ indicator (7.80 ± 0.27 %; $p < 0.005$), and significantly exceeds the indicator $CG_{1\text{-}2}$ (4.51 ± 0.21 %; $p < 0.005$). According to morphological and morphometric analysis, after 18–19 months of experimentation in the CB, circulatory disorders completely disappear and pronounced sclerotic changes increase. After 26–28 months in the subgroup HG + $M_{26\text{-}28}$ the indicator of AVWT increased (207.92 ± 8.6×10^{-6} m), not differing from the $HG_{26\text{-}28}$ indicator (217.42 ± 8.72×10^{-6} m; $p > 0.05$), but remaining higher than the $CG_{26\text{-}28}$ indicator (107.22 ± 5.21×10^{-6} m; $p < 0.005$). The ARAV indicator decreases to 3.43 ± 0.13 % ($p < 0.005$) and is similar to the indicators of subgroups $CG_{26\text{-}28}$ and $HG_{26\text{-}28}$ (3.81 ± 0.11 % and 3.42 ± 0.15 %; $p > 0.05$).

Conclusions. Thus, according to morphometric and morphological indices, the course of melatonin injections used up to 5 months of the experiment reduces reactive edema and vascular disorders characteristic of the early stages of hypopinealism formation under round-the-clock illumination conditions. After 26–28 months of round-the-clock illumination, the course of melatonin does not have a therapeutic effect on morphological changes in the ciliary body, apparently due to irreversible sclerotic changes in the vessels.

Keywords: pineal gland, hypopinealism, vascular disorders, dyscirculatory disorders, injections of melatonin, ciliary body.

МОРФОМЕТРИЧНІ ПОКАЗНИКИ ЗМІН ЦИЛІАРНОГО ТІЛА КРОЛІВ З ЕКСПЕРИМЕНТАЛЬНИМ ГІПОПІНЕАЛІЗМОМ ПІД ВПЛИВОМ КУРСУ МЕЛАТОНІНУ

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Природна зміна дня і ночі, тобто чергування інтенсивного впливу світла і темряви через сітківку на структури центральної нервової системи, забезпечує ритмічність вироблення в пінеальній залозі (епіфіз) гормону мелатоніну (М) і формування добових ритмів. Вночі концентрація М в крові найвища, а денне світло пригнічує продукцію М. Зменшення нічної продукції М призводить до порушення багатьох фізіологічних процесів, у тому числі вільнорадикальних процесів у клітині, та сприяє розвитку патологічних змін у різних тканинах організму. Мелатонін виявлено в таких тканинах ока, як сітківка, відростки циліарного тіла та епітелій кришталика. Також було встановлено, що М бере участь у виробленні внутрішньоочної рідини циліарним тілом.

Метою роботи було дослідити особливості морфологічних змін циліарного тіла (ЦТ) кролів під впливом курсу ін'єкцій мелатоніну в різні терміни прояву експериментального гіпопінеалізму, який розвинувся на фоні цілодобового освітлення (ЦО).

Матеріали та методи. Експериментальне дослідження проводили на кролях відповідно до Закону України «Про захист тварин від жорстокого поводження» № 3447-IV (Київ, 2006 р.) та «Європейської конвенції про захист хребетних тварин, які використовуються для піддослідних та інших цілей». Наукові цілі» (Страсбург, 1986). Гіпопінеалізм у тварин досягався шляхом утримання їх в умовах ЦО. Групи становили: контрольна (КГ) — 23 інтактні тварини, які перебували в умовах природної зміни дня і ночі; група з гіпопінеалізмом (ГГ) — 32 кролики, які перебували в умовах ЦО; група ГГ + М — 29 кроликів, які перебували в умовах ЦО, але перед виведенням з експерименту отримували курс ін'єкцій М протягом 14 днів. Залежно від тривалості експерименту виділено підгрупи: 1–2, 3–5, 8–12, 18–19, 26–28 міс. Концентрацію М в крові визначали імуноферментним методом. Проведено морфологічне дослідження енуклеованих очних яблук тварин з морфометричним аналізом методом «полів».

Результати. Під впливом ЦО нічна продукція М знизилася до 62,26 ± 5,27 пмоль/л порівняно з контролем (369,45 ± 14,35 пмоль/л; $p < 0,005$).

Через 1–2 місяці ЦО після курсу ін'єкцій М зменшувались дисциркуляторні розлади у ЦТ, що підтверджуються тим, що показник середньої відносної площі судин (СВПС) при морфометричному дослідженні в підгрупі ГГ + $М_{1-2}$ (6,61 ± 0,25%) нижчий за показник $ГГ_{1-2}$ (7,80 ± 0,27%; $p < 0,005$), хоча і значно перевищує показник $КГ_{1-2}$ (4,51 ± 0,21%; $p < 0,005$); показник середньої товщини судинної стінки (СТС) (50,71 ± 1,30×10^{-6} м) був подібним до показника $КГ_{1-2}$ (51,31 ± 1,22×10^{-6} м, $p < 0,05$), а вірогідно знизився порівняно з $ГГ_{1-2}$ (59,20 ± 1,21×10^{-6} м; $p < 0,005$).

Через 26–28 місяців у підгрупі ГГ + $М_{26-28}$ показник СВПС знижується до 3,43 ± 0,13% і є подібним до показників груп $КГ_{26-28}$ та $ГГ_{26-28}$ (3,81 ± 0,11% та 3,42 ± 0,15%; $p > 0,05$). Показник СТС підвищився (207,92 ± 8,6×10^{-6} м), не відрізняючись від показника $ГГ_{26-28}$ (217,42 ± 8,72×10^{-6} м; $p > 0,05$), але залишаючись вищим за показник $КГ_{26-28}$ (107,22 ± 5,21×10^{-6} м; $p < 0,005$).

Висновки. Як свідчать результати нашого морфологічного та морфометричного дослідження, у тварин з дефіцитом мелатоніну через 18-19 місяців цілодобового освітлення в циліарному тілі повністю зникають явища гіперемії судин і дисциркуляторних розладів, з'являються виражені склеротичні зміни. Відмічається значне потовщення стінок дрібних артерій і вен внаслідок склерозу, що призводить до значного підвищення показника середньої товщини судинної стінки. Запустіння судин характеризується значним зниженням індексу середньої відносної площі судин. Курс ін'єкцій мелатоніну зменшує набряк і судинні розлади на ранніх етапах формування гіпопінеалізму в експерименті з цілодобовим освітленням до 5 місяців. Через 26-28 місяців цілодобового освітлення, мабуть, у зв'язку з незворотними склеротичними змінами в судинах, курс мелатоніну не має терапевтичного ефекту.

Ключові слова: пінеальна залоза, гіпопінеалізм, васкулярні розлади, дисциркуляторні розлади, екзогенний мелатонин, циліарне тіло.