

PRACA ORYGINALNA
ORIGINAL ARTICLE**PECULIARITIES OF THE FUNCTIONING CIRCADIAN ORGANIZATION THE ION-REGULATING FUNCTION OF KIDNEY UNDER THE CONDITION OF PINEAL GLAND HYPERFUNCTION OF THE INFLUENCE NITROGEN MONOXIDE SYNTHESIS BLOCKADE****CHARAKTERYSTYKA OKOŁODOBOWEJ FUNKCJI REGULACJI WODNO-ELEKTROLITOWEJ NEREK W WARUNKACH NADCZYNNOŚCI SZYSZYNKI I ZAHAMOWANIA SYNTEZY TLENKU AZOTU****Svitlana B. Semenenko, Svitlana Y. Karatieieva, Oksana V. Bakun, Ksenia V. Slobodian, Oksana I. Yurkiv**
HIGHER STATE EDUCATIONAL INSTITUTION OF UKRAINE "BUKOVINIAN STATE MEDICAL UNIVERSITY", CHERNIVTSI, UKRAINE**ABSTRACT**

The aim of our work was to investigate the peculiarities of the functioning circadian organization the ion-regulating function of pineal gland hyperfunction of the influence nitrogen monoxide synthesis blockade.

Materials and methods: The experiments were conducted on 72 mature non-linear albino male rats with their body mass 0,15-0,18 kg. The control group included animals (n=36) kept under conditions of usual light regimen (12.00L:12.00D) during 7 days. The experimental group included animals (n=36) injected with N-nitro-L-arginine (L-NNA) in the dose of 20 mg/kg during 7 days under conditions of continuous absolute darkness (12.00D:12.00D). On the 8th day the animals were exposed to 5% water load with heated to room temperature water supplied and the parameters of the kidney ion-regulating function under conditions of forced diuresis were investigated.

Results and conclusions: The obtained results of the performed blockade nitrogen monoxide (NO) synthesis in conditions of hyperfunction of the brain epiphysis allow to conclude that the daily mean of the rate of excretion of sodium ions decreases in comparison with the animals that were kept under pineal gland (PG) hyperfunction of the filtration fraction and reabsorption of sodium ions are reduced compared to the control animals and rats which were kept under conditions of PG hyperfunction and accompanied by stable indicators of the concentration the specified cation in the blood plasma during the observation period. The action of the blockade NO synthesis in conditions of PG hyperfunction leads to a decrease in the distal transport bridge of sodium ions with a maximum in the day and night intervals of the day the position of the acro- and batiphase of the rhythm changes as compared with the control animals.

KEY WORDS: circadian rhythm, nitrogen monoxide, hyperfunction, melatonin, kidney

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INTRODUCTION

About the rhythmic organization of individual functions of the body scientists have long been known [5, 10]. In healthy people the rhythms of physiological processes are synchronized both with each other, and with the rhythms of the environment while the synchronization of biorhythms, the preservation of their phase relations provides optimal conditions for the functioning of the organism and is a sign of health [1,9]. It was established that the most important regulator of the activity of the suprachiasmatic nuclei of the hypothalamus is neurohormon melatonin which is synthesized most often in the PG in the dark period of the day [2], and acts as the main signal that coordinates the rhythms of the organism's functions with the illumination fluctuations and the ambient temperature [6].

For any biological system including for the kidneys a spatial-temporal organization of functioning is characteristic

[3, 8]. Renal effects of the epiphysis of the brain are due to the secretion of the indole melatonin [5]. Intracellular messengers NO and PG hormones in particular, were found to play an important role in the regulation of the main kidney functions and their circadian organization [4, 7].

THE AIM

Aim of our work was to investigate the peculiarities of the functioning circadian organization the ion-regulating function of pineal gland hyperfunction of the influence nitrogen monoxide synthesis blockade.

MATERIALS AND METHODS

The experiments were conducted on 72 mature non-linear albino male rats with their body mass 0,15-0,18 kg. The

animals were kept under vivarium conditions at a stable temperature and air humidity fed on a standard dietary intake. The control group included animals (n=36) kept under conditions of usual light regimen (12.00L:12.00D) during 7 days. The experimental group included animals (n=36) injected with N-nitro-L-arginine (L-NNA) in the dose of 20 mg/kg during 7 days under conditions of continuous absolute darkness (12.00D:12.00D). On the 8th day the animals were exposed to 5% water load with heated to room temperature water supplied and the parameters of the kidney ion-regulating function under conditions of forced diuresis were investigated.

The experiments were conducted with 4 hour interval during the day. The level of were the concentration of sodium ions in the urine, excretion and concentration of sodium ions, sodium/potassium ratio, filtration fraction of sodium ions, absolute and relative reabsorption of sodium ions, clearance of sodium ions and sodium-free water, proximal and distal transport of sodium ions, concentration index of sodium ions studied. The results were statistically processed by means of "Cosinor-analysis" method and parametric methods of variation statistics. The diagnostics of functional peculiarities was based on the analysis of changes of the following characteristics: daily mean, amplitude, acrophase, and circadian rhythm curve shape. Individual chronograms for every animal obtained were distributed by the principle of maximal acrophase identity and intersecting for every group of chronograms daily mean, amplitude and phase structure (by the interval of time between acro- and bathyphase) were calculated by "Cosinor-analysis" method. All the stages of the experiment were carried out keeping to the major requirements of the European Convention on Human Attitude to Animals.

The experimental data obtained were processed on personal computers with the program package EXCE-2003 (Microsoft Corp., USA). The values of arithmetic mean sampling (\bar{x}), its dispersion and mean error (S_x) were calculated. To detect probable differences of the results in the experimental and control groups of animals Student (t) coefficient was determined, after that probability of sampling differences (p) and mean confidence interval by the tables of Student distribution were detected. The values were considered reliable with $p < 0,05$.

RESULTS AND DISCUSSION

Kidney functions in the control animals are subordinated to accurate circadian organization. Daily rhythms of the parameters of kidney ion-regulating function reflect similar changes of the renal processes [10]

The investigations of the ion-regulating function of the kidneys showed that both the blockade of the NO synthesis, and the dysfunction of the PG, lead to sharp violations of the structure of the chronorhythms of renal transport of sodium ions.

The injection of L-NNA against the background of PG hyperfunction resulted in a sharp increase in sodium urez. The daily mean significantly exceeded the average daily

values in the control animals and rats who underwent a blockade of NO synthesis under normal light conditions but was 5 times lower than that of animals kept in conditions of constant darkness (Table I).

The amplitude of the rhythm was likely to decrease and was $24.5 \pm 0.52\%$ (Table I). The maximum concentration of sodium ions in the urine was observed at 8.00 a.m., the second increase is about 16.00 a.m. The batiphase of rhythm was at 4.00 a.m. The excretion of sodium ions and their concentration in the urine had a symmetrical character (Fig. 1, Table I).

Despite the high level of sodium urez when L-NNA was administered under hyperfunctional conditions the concentration of cation in plasma was significantly different from that of control animals as well as on the rates of animals that received L-NNA against the background of the normal light regime ((Fig. 2). Instead under conditions of PG hyperfunction an increase in the concentration of sodium ions in the blood plasma was observed (Table I).

Compared with the control values the average daily level of relative reabsorption of sodium ions in animals that was administered L-NNA under the background of PG hyperfunction significantly decreased and amounted to 99.1% (Table I).

Increasing sodium thinning in conditions of inhibition of NO synthesis blockade resulted in a disturbance of sodium/potassium urine (Table 1). The average daily level of the indicator significantly increased compared to the animals that were administered L-NNA under normal light conditions, and control rats. The maximum level of sodium/potassium rhythm was at 16.00 a.m. and decreased from 8.00 a.m. to 12.00 a.m.

Observations on changes in the chronorhythm of the concentration index of sodium ions during the day showed that the administration of L-NNA resulted in an increase in the concentration index of sodium ions in animals that were under conditions of modeling PG hyperfunction (Table I).

Regarding the distal reabsorption of the cation in the conditions of PG hyperfunction the minimum value of distal reabsorption was recorded at about 12.00 a.m., and at the introduction of L-NNA at the background of PG hyperfunction of the batiphase were noted at 24.00 a.m. (Fig. 3, Table I).

The average daily mean of the indicator was significantly lower compared to other observation groups although the structure of the rhythm was in complete inversion relative to the studied groups.

CONCLUSIONS

The obtained results of the performed blockade NO synthesis in conditions of hyperfunction of the brain epiphysis allow to conclude that the daily mean of the rate of excretion of sodium ions decreases in comparison with the animals that were kept under hyperfunction of the brain epiphysis the filtration fraction and reabsorption of sodium ions are reduced

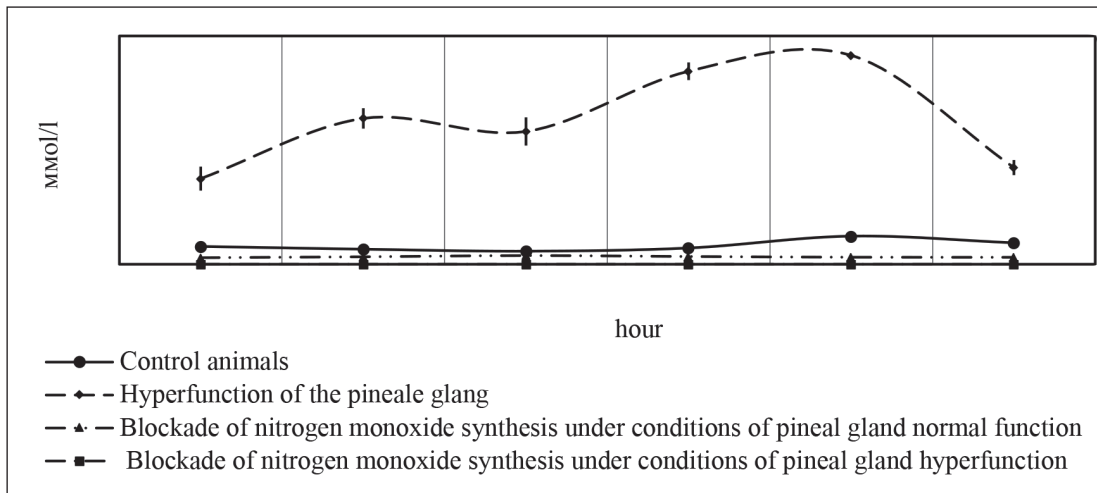


Fig. 1. Chronorhythms of concentration of sodium ions in urine (mmol/l) in rats exposed to the blockade of NO synthesis under conditions of pineal gland hyperfunction

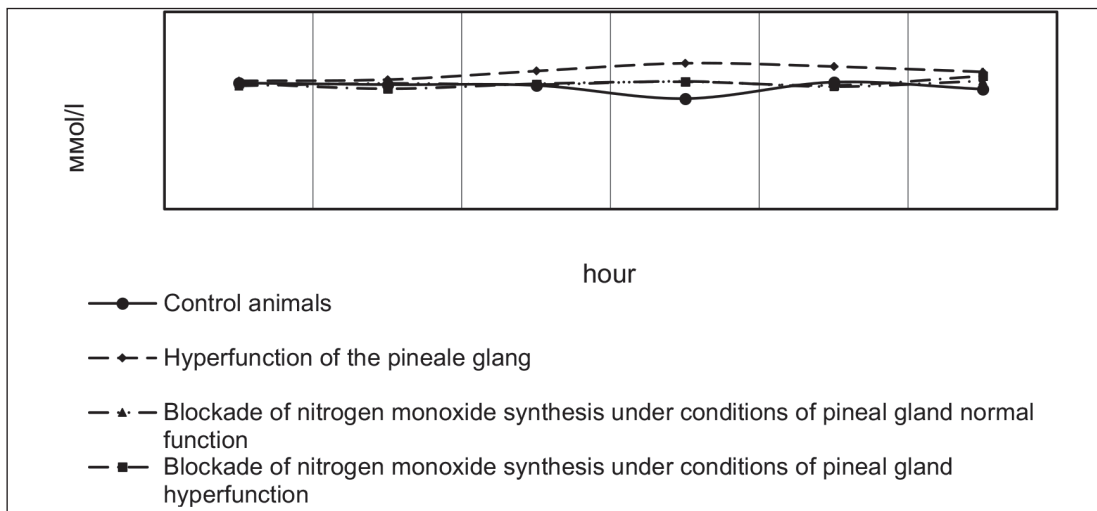


Fig. 2. Chronorhythms of concentration of sodium ions in the plasma (mmol/l) in rats exposed to the blockade of NO synthesis under conditions of pineal gland hyperfunction

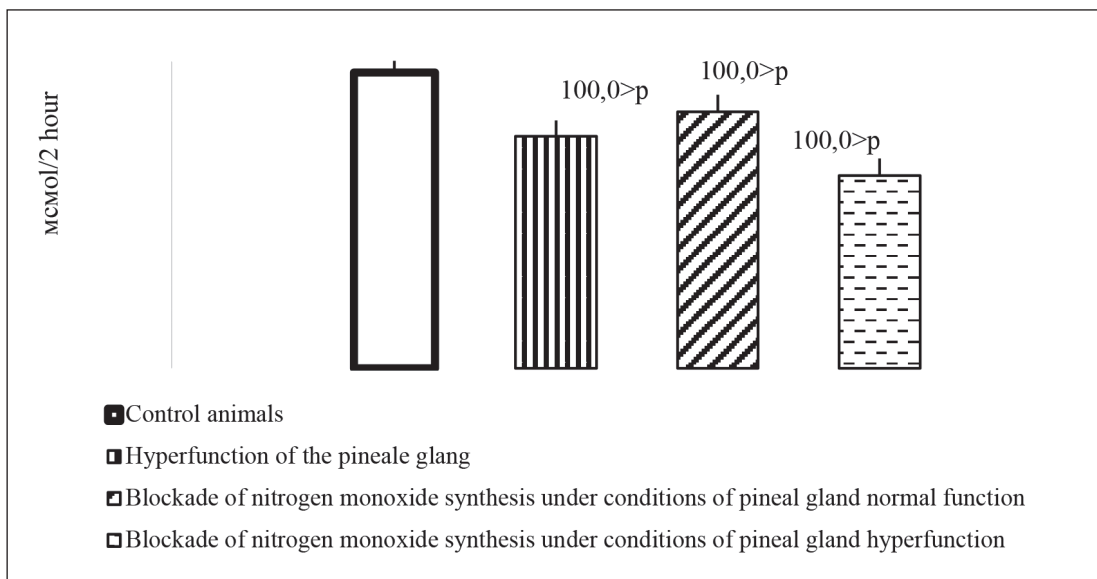


Fig. 3. Daily mean levels of distal transport of sodium ions (mcmol/2 hour) in rats exposed to the blockade of NO synthesis under conditions of pineal gland hyperfunction

Table I. Influence of nitrogen monoxide synthesis blockade under conditions of pituitary gland hyperfunction on mesor (daily mean) and amplitude of the rhythms of the kidney ion-regulating functions in albino rats ($\bar{x} \pm S_x$)

Parameters	Control animals (n=36)		Blockade of nitrogen monoxide synthesis under conditions of pineal gland hyperfunction (n=36)	
	Mesor (daily mean)	Amplitude (%)	Mesor (daily mean)	Amplitude (%)
Concentration of sodium ions in the urine, mmol/l	3,9±0,19	29,2±1,61	6,4±0,26 p<0,001	24,5±0,52 p<0,01
Excretion of sodium ions, мсmol/2 hours	12,2±1,62	32,5±2,61	12,7±3,77	45,7±2,33 p<0,005
Excretion of sodium ions, мсmol/100 mcl GF	2,2±0,14	26,9±1,91	4,5±0,41 p<0,001	33,4±2,43
Concentration of sodium ions in the plasma, ммol/l	123,7±3,82	5,0±1,21	127,7±1,37 p<0,05	3,4±0,43
Sodium/potassium ratio, un	0,3±0,05	41,7±1,51	0,9±0,02 p<0,001	11,3±0,51 p<0,001
Filtration fraction of sodium ions, ,мсmol/min	77,1±3,18	19,1±1,02	39,4±1,54 p<0,001	9,09±0,83 p<0,001
Absolute reabsorption of sodium ions, мсmol/min	76,9±2,35	9,0±0,82	39,3±2,86 p<0,001	42,4±1,51 p<0,001
Relative reabsorption of sodium ions, %	99,9±0,02	0,1±0,01	99,1±0,07 p<0,001	1,5±0,01 p<0,001
Clearance of sodium ions, ml/2 hours	0,1±0,01	28,3±2,41	0,1±0,02	48,2±2,11 p<0,001
Clearance of sodium-free water, ml/2 hours	3,1±0,09	18,8±0,42	1,9±0,05 p<0,01	47,9±1,81 p<0,001
Proximal of sodium ions, ммol/2 hours	8,9±0,17	20,2±0,41	4,5±0,19 p<0,001	42,4±2,11 p<0,001
Distal transport of sodium ions, мсmol/2 hours	385,4±13,46	21,1±0,41	251,1±8,45 p<0,001	47,1±2,21 p<0,001
Proximal of sodium ions, мсmol/100 mcl GF	11,8±0,29	4,2±0,41	12,1±0,13	3,8±0,09
Distal transport of sodium ions, мсmol/100 mcl GF	0,6±0,07	32,4±0,41	0,7±0,06	19,5±0,81 p<0,001
Concentration index of sodium ions, un	0,1±0,01	34,4±0,41	0,1±0,11	25,3±0,11 p<0,001

Notes:

p – reliable difference between the parameters of the experimental and control animals;

n – number of animals

compared to the control animals and rats which were kept under conditions of PG hyperfunction and accompanied by stable indicators of the concentration the specified cation in the blood plasma during the observation period. The action of the blockade NO synthesis in conditions of hyperfunction of the brain's epiphysis leads to a decrease in the distal transport bridge of sodium ions with a maximum in the day and night intervals of the day the position of the acro- and batiphase of the rhythm changes as compared with the control animals.

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Authors' contributions:

According to the order of the Authorship.

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Svitlana B. Semenenko

Higher State Educational Institution of Ukraine

"Bukovinian State Medical University"

2, Theatralna sq., 58002 Chernivtsi, Ukraine

tel: +380505277151

e-mail: semenenko.svitlana@bsmu.edu.ua

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