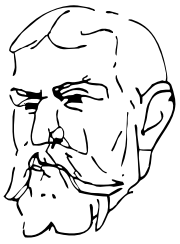
Wiadomości Lekarskie

Czasopismo Polskiego Towarzystwa Lekarskiego



Pamięci dra Władysława Biegańskiego

TOM LXXI, 2018, Nr9

Rok założenia 1928

Aluna Publishing

SPIS TREŚCI

PRACE ORYGINALNE / ORIGINAL ARTICLES

PRACA ORYGINALNA
ORIGINAL ARTICLE

PECULIAIRITIES OF THE INFLUENCE NITROGEN MONOXIDE SYNTHESIS BLOCKADE ON CIRCADIAN ORGANIZATION OF KIDNEY ACID-REGULATING FUNCTION UNDER CONDITIONS OF PINEAL GLAND HYPERFUNCTION

CHARAKTERYSTYKA WPŁYWU ZAHAMOWANIA SYNTEZY TLENKU AZOTU NA OKOŁODOBOWĄ NERKOWĄ REGULACJĘ RÓWNOWAGI KWASOWO-ZASADOWEJ W WARUNKACH NADMIERNEJ AKTYWNOŚCI SZYSZYNKI

Svitlana B. Semenenko, Svitlana U. Karatieieva, Ksenia V. Slobodian, Oksana V. Bakun, Oksana I. Yurkiv
HIGHER STATE EDUCATIONAL INSTITUTION OF UKRAINE "BUKOVINIAN STATE MEDICAL UNIVERSITY", CHERNIVTSI, UKRAINE

ABSTRACT

Introduction: In recent decades chronobiology - a science that studies the regularities of the functioning of the organism, especially biological rhythms is developing rapidly. Biorhythms are stable nonstopper lifetime fluctuations with individual amplitude-frequency characteristics. Kidneys are characterized by a clear time organization of functions too, however, the peculiarities of circadian organization and the mechanisms of the participation of intracellular messengers in particular nitrogen monoxide (NO) in biorhythmic regulation of renal functions, remain insufficiently studied

The aim of our work was to investigate the peculiairities of the influence nitrogen monoxide synthesis blockade on circadian organization of kidney acid-regulating function under conditions of pineal gland hyperfunction.

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 acid-regulating function under conditions of forced diuresis were investigated.

Results: The inhibition of the monoxide synthesis (NO) in conditions of pineal gland **(**PG) hyperfunction violated the structures of chronorhythms acid-regulating function of the kidneys. The decrease in urine pH at daytime intervals was due to a decrease in the level of hydrogen ion excretion during this period of the day. The introduction of the NO blocker against the background of the PG hyperfunction violated the structure of the acid esterification chronorhythms that are titrated. The maximum level of this indicator was recorded at 20.00 a.m. a day. The blockade of the synthesis NO on the background of the PG hyperfunction significantly reduced the level of excretion of ammonia.

Conclusions: The maximum level of excretion was 12.00 a.m., bathyphase - at 24.00 a.m. The average daily level was 1.5 mcmol/100 mcl GF and was lower relative to the control animals and animals that were in the conditions of PG hyperfunction.

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

Wiad Lek 2018, 71, 9, 1681-1684

INTRODUCTION

In recent decades chronobiology - a science that studies the regularities of the functioning of the organism, especially biological rhythms is developing rapidly [5,9]. Biorhythms are stable nonstopper lifetime fluctuations with individual amplitude-frequency characteristics [6].

The concept of circadian system of organism, functional links of which is the pineal gland (PG) and suprachiosmatic nuclei of the hypothalamus which are considered as the main generator of biorhythms of most of the organism's functions is adopted. [3].The hormone that reports information about rhythms to organs and tissues is melatonin - the main hormone of the PG. Due to the ability to restore the violation of the work of biorhythms melatonin is a powerful synchronizer of physiological functions of the body [7, 8].

Kidneys are characterized by a clear time organization of functions too [4, 11,8], however, the peculiarities of circadian organization and the mechanisms of the participation of intracellular messengers in particular nitrogen monoxide (NO) in biorhythmic regulation of renal functions, remain insufficiently studied [1, 10].

THE AIM

Aim of our work was to investigate the peculiairities of the influence nitrogen monoxide synthesis blockade on circadian organization of kidney acid-regulating function under conditions of pineal gland hyperfunction.

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 con-

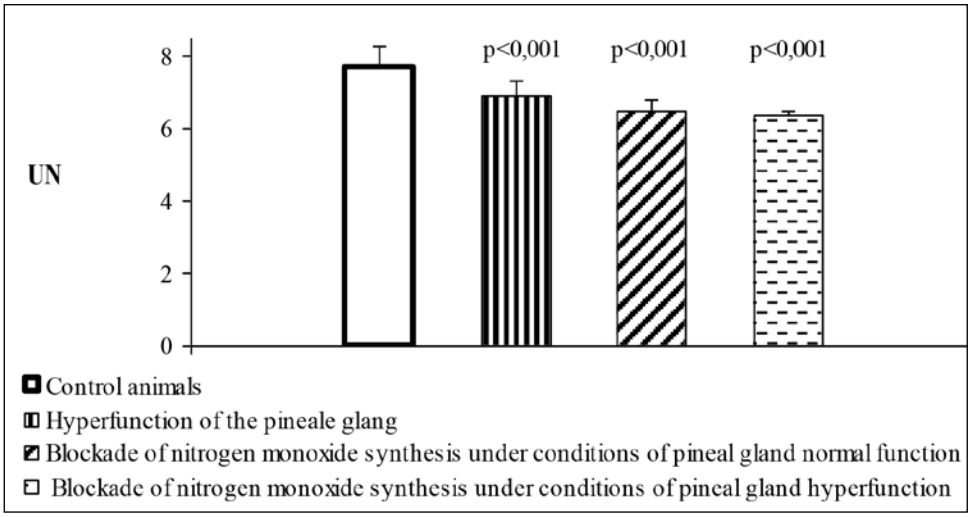


Fig. 1. Daily mean levels of pH in urine (UN) in rats exposed to the blockade of NO synthesis under conditions of pineal gland hyperfunction

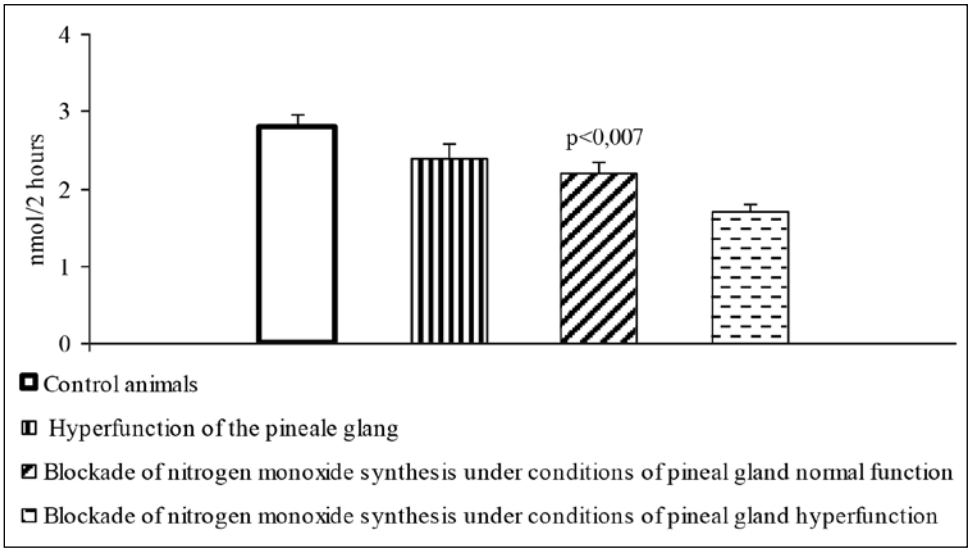


Fig. 2. Daily mean levels of excretion of hydrogen ions in urine (nmol/2 hours) in rats exposed to the blockade of NO synthesis under conditions of pineal gland hyperfunction

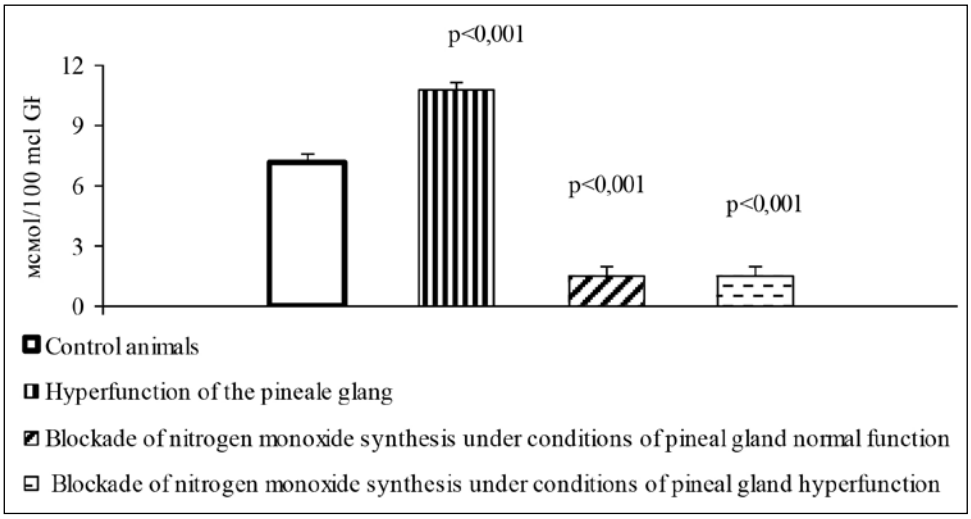


Fig. 3. Daily mean levels of titrating acids secretion (mcmol/100 mcl GF) in rats with blockade of nitrogen monoxide synthesis under conditions of pineal gland hyperfunction

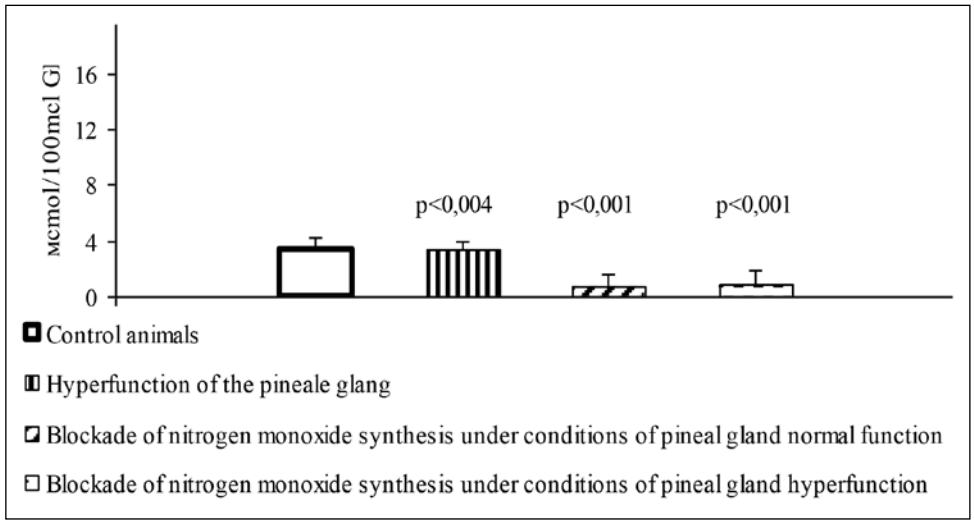


Fig. 4. Daily mean levels of ammonia excretion (mcmol/100 mcl GF) in rats exposed to the blockade of nitrogen monoxide synthesis under conditions of pineal gland hyperfunction

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 acid-regulating functions in albino rats ($\bar{x} \pm S_{\bar{x}}$)

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 (%)
pH of urine, UN	7,7±0,08	2,5±0,61	6,4±0,11 p<0,001	4,2±0,09 p<0,01
Excretion of hydrogen ions, mmol/2 hours	2,8±0,25	19,5±1,71	1,7±0,21 p<0,01	48,4±2,51 p<0,001
Excretion of hydrogen ions, mmol/100 mcl GF	0,5±0,06	31,3±1,52	0,6±0,05	19,6±1,02 p<0,001
Excretion of titrating acids, mcmol/2 hours	18,6±0,89	27,9±1,11	2,7±0,43 p<0,001	40,8±2,61 p<0,001
Excretion of titrating acids, mcmol /100 mcl GF	3,4±0,06	34,9±1,41	0,9±0,05 p<0,001	37,3±1,82
Ammonia excretion, mcmol/2 hours	37,9±1,61	27,1±2,12	4,4±0,56 p<0,001	43,4±1,81 p<0,001
Ammonia excretion, mcmol/100 mcl GF	7,1±0,32	33,1±1,82	1,5±0,14 p<0,001	18,8±1,51 p<0,001
Ammonium coefficient, UN	2,1±0,07	13,2±1,02	1,7±0,11	20,0±1,11 p<0,01

Notes: p – reliable difference between the parameters of the experimental and control animals;
n – number of animals

trol 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 acid-regulating function under conditions of forced diuresis were investigated.

The experiments were conducted with 4 hour interval during the day. The level of pH in urine, hydrogen ion excretion, titrating acids, ammonia, and ammonium coefficient were 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 (x), its dispersion and mean error (Sx) 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

The suppression of NO synthesis with the background of PG hyperfunction disrupted the structures of the chronorhythms of the acid-regulating function of the kidneys.

The daily mean of urine pH was characterized by high amplitude with a rise in the level of 20.00 a.m., a minifase accounted for 16.00 a.m. The average daily level was lower than the control and indices of animals that were under conditions of PG hyperfunction (Fig. 1, Table 1). The decrease in urine pH at daytime intervals was due to a decrease in the level of excretion of hydrogen ions during this period of the day and at night the figure did not differ from that in animals that blocked of the NO synthesis in conditions of normal light mode. Under the blockade of NO synthesis, there was a decrease in the excretion of hydrogen ions against the background of increased excretion of sodium ions, indicating violation of the work of sodium-hydrogen antiport (Fig. 2, Table I).

The introduction of the blocker of NO against the background of the PG hyperfunction disrupted the structure of the chronorhythmic patterns of excretion of titrated acids. The maximum level of this indicator was registered at 20.00 a.m. a day. In the periods from 12.00 a.m. to 24.00 a.m. the level of the indicator was higher than that of animals that was administered L-NNA against the background of the usual light regime. The average daily level significantly decreased and the amplitude by contrast increased with respect to the values of control animals (Fig. 3, Table I).

This applies to ammonia excretion also. The blockade of NO synthesis under conditions of PG hyperfunction significantly reduced the level of ammonia excretion. At the same time the maximum level of output fell to 12.00 a.m., buttyphase - at 24.00 a.m. The average daily level was 1.5 mcmol/100 mcl GF and was lower than control animals and rats that were under PG hyperfunction. The average daily level was 1.5 mcmol/100 mcl GF and was lower than control animals and rats that were under PG hyperfunction (Fig. 4, Table I).

CONCLUSIONS

Consequently the results of the performed blockade NO synthesis under conditions of hyperfunction the brain epiphysis indicate that the level of excretion the titrated acids over the course of the day decreases compared to control animals and rats which were kept under conditions of PG hyperfunction. This led to a decrease in urine pH with a rather high rhythm amplitude. It should be noted that the daily average level of ammonia excretion has decreased significantly, relative to control animals and rats with PG hyperfunction and the average daily level of ammoniacal factor has decreased in relation to the studied observation groups.

REFERENCES

1. Bondar T. N. Systema L-arhynyn/oksyd azota y ymmunytet. Eksperymentalna i klinichna medytsyna. 2009; 4-7.
2. Эрyfyzarnыi hormon melatonyn y khronycheskaia bolezn pochek. N. N. Kaladze, E. Y. Slobodian, A. L. Hovdaniuk. Zdorovia dytyny. 2015; 2 (61):183 – 184.
3. Lytvynenko H. Y. Khronofarmakolohycheskye svoistva melatonyna. H. Y. Lytvynenko. Biull. эksperym. byol. y med. 2010; 30 (6): 82-92.
4. Natochyn Yu. V. Vodno-solevoi homeostaz - rol refleksov, hormonov, ynkretynov, autakoydov. Yu. V. Natochyn. Fyzyol.zh. 2011; 57 (5): 13-15.
5. Orlova N. Y. Tsyrkadyannыe rytmы u detei pubertatnoho vozrasta: podkhodы y faktы. N. Y. Orlova, T. S. Pronyna. Alm. «Nov. yssled. 2014; (1): 40-47.
6. Tymchenko H. M. Khronolohichnyi pasport yak zasib optymizatsii rezhymu dnia studentiv klasychnoho universytetu. H. M.Tymchenko. SCIENCERISE. 2014; 4, (1; 4): 27-33.
7. Age-related effect of melatonin on permeability transition pore opening in rat brain. Krestinina O. V., Odinokova S. V. Baburina Y. I., Azarashvili T. S. Biochem Sup Ser A Memb Cell Biol. 2013; 3 (4): 286-23.
8. Bryukhanov V. M. The kidney role in regulation of circade rithms of the organism. V. M. Bryukhanov, A. J. Zvereva. Nephrology. 2010; 14 (3): 17-31.
9. Chronophysiological features of Central hemodynamic in women of reproductive age. Agadzhanyan N. A., Brunin D. V., Radysh I. V. [et al.]. Technol Liv Sys. 2014; 11 (1): 3-6.
10. Effect of hypoosmotic shock on the volume of renal collecting duct epithelial cells of brattleboro rats with hereditarily defective vasopressin synthesis. Ilyaskin A. V., Baturina G. S., Katkova L. E. [et al.]. Doklady RAN. 2013; .453 (1): 102-105.
11. Peguliairities of melatonin effect on chronorhytmic organization of kidney acid-regulating function influenced by nitrogen monoxide synthesis blockade under conditions of pineal gland hypofunction. Semenenko S., Tymofiychuk I., Boreyko L. [et al.]. Georgian medical news. 2017; 10 (271): 117-122.

Authors' contributions:
According to the order of the Authorship.
Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Svitlana B. Semenenko
tel.: +380505277151
e-mail: semenenko.svitlana@bsmu.edu.ua

Received: 11.08.2018
Accepted: 27.11.2018