УДК: 612.43.45+612.618]:612.273.2:612.017.2

O.V. Yasinska

Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi

SPECIFIC CHARACTERISTICS OF TISSUE REACTION OF THE ADRENAL GLANDS HYPOBARIC HYPOXIA ACTION ACCORDING TO ALTERED PHOTOPERIOD DURATION IN IMMATURE FEMALE RATS

Keywords*: tissue proteolysis, tissue fibrinolysis, photoperiod, hypobaric hypoxia, hypoxic preconditioning, adrenal glands, immature female rats.*

Resume. *Peculiarities of the reaction of indices of proteolytic and fibrinolytic processes to hypobaric hypoxia under conditions of its independent use and hypoxic preconditioning changes, stimulated by influence of constant light, in the the adrenal glands tissues in immature female rats have been studied. It has been established that modeling of the pineal gland hypofunction by means of a constant illumination significantly influences upon the character of changes proteolysis and fibrinolysis processes in the adrenal glands tissues of immature female rats, caused by systemic hypobaric hypoxia at a combined use of the indicated influences. Hypoxic preconditioning of influences of constant lighting does not compensate shifts in biochemical indices, stimulated by altered photoperiod duration.*

Introduction

Hypoxia is one of the condition of usual mode of life and, at the same time, growth factor levels of reactive oxygen species (ROS) [8]. Structural-functional change of the adrenal glands as regulatory organ of adaptive process is a typical manifestation of organic reaction to hypobaric hypoxia. The presence of polyorganic, morpho-functional disturbances, formed at participation of the neuro-endocrine system [5, 10] and the manifestations of which depend on the age, sex and the presence of influence of other environmental factors is a peculiar feature for systemic adaptation to hypoxia. Hypoxia results in decrease of energetic potential, macroergic phosphate and pyruvate dehydrogenase content [6]. Decrease in oxygen delivery to the tissues occurs in all cases in final result [12]. The intensity of the response of organs and tissues of the body depends on the hypoxia level and sensitivity of the tissue to hypoxia [14, 15]. Possibility of the development of cross-adaptation according to hypoxia enables to use moderate hypoxic effects for the purpose hypoxic preconditioning of pathological changes caused by other factors [3, 11]. Hypobaric hypoxia influence upon expression of gene of sensitivity to hypoxia that may create protective effect under various pathologies [4]. The nature of proteolytic and fibrinolytic activity in peripheral tissues changes in the process of reaction to a variety of environmental factors, that may be both a manifestation of regenerative processes, and their involvement in the mechanisms of apoptosis [7, 9].

Specific characteristics of the reaction proteolytic and fibrinolytic activity in the adrenal glands tissues under conditions of hypoxic preconditioning of effects of the altered regime of illumination in immature female rats remain not studied.

The aim of the research

To study of specific characteristics of fibrinolytic and proteolytic processes in the tissues of the adrenal glands in immature female rats under ordinary conditions of holding and hypoxic preconditioning by systemic intermittent hypobaric hypoxia of changes, caused by permanent lighting.

Material and methods

Experiments were carried out on 48 female immature white laboratory rats aged 1 month with an average body weight of 0,052 kg. The changes of photoperiod duration were modeled by permanent day-and-night lighting (500 lux light intensity) a model of decreasing of melatonin-producing function of the pineal gland (group 2, 4 and 5). Hypobaric hypoxia was created in the flowing pressure chamber by means rarefaction of air till the value corresponding to a height of 4000 m above sea level with "lifting" velocity 0.4 km / min [13]. Under hypoxic conditions the animals were held for 2 hours daily during 14 days (group 3, 4 and 5). Photoperiod changes were introduced on the next day after hypoxic exposure, thus hypoxic preconditioning of effects of hypofunction epiphysis was used in group 4. Animals of group 5 were held at simultaneous action of hypobaric hypoxia and constant lighting. Intact rats (group 1) holding under conditions of natural light and normal atmospheric pressure, were used as control ones.

The following day after the completion of experimental influence all animals were decapitated under slight diethyl ether narcosis. The tissues of the adrenal glands was taken out on cold immediately after the decapitation and the weighted samples were homogenized in 2.0 ml of cooled borate buffer (pH 9.0). The homogenate was used in biochemical analysis. Determination of the total, enzymatic and non-enzymatic fibrinolysis in the adrenal glands tissues was performed according azofibrin lysis ("Simko Ltd", Ukraine) [7], proteolytic activity was determined according azoalbumin, azokazein and azokol lysis [1].

Statistical analysis of the results was performed by the method of variational statistics using Student's test.

Experiments have been carried out in compliance with the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasbourg, 1986).

Discussion of the Results

Modeling of chronic hypobaric hypoxia under conditions of natural light in immature female rats resulted in a significant restructuring of the nature of the processes of proteolysis in the tissue of the adrenal glands (Table 1). In particular, lysis of low molecular weight proteins (LMWP) in the tissue of the adrenal glands decreased by 29% in comparison with the control, lysis of hight molecular weight proteins (HMWP) - by 27.9%. Lysis of collagen mostly decreased the - by 43.5% compared with the group that was under conditions of normoxia.

Processes of proteolysis in the tissues of the adrenal glands of females were undergone of opposite changes by application of constant light. Thus, LMWP lysis increased by 13.4%, lysis of azokazein - by 14.4%, in comparison with the control one, and only lysis of collagen underwent tendencies to decrease. Simultaneous action of hypobaric hypoxia and constant lighting led to increase of proteolysis indices concerning all kinds of protein molecules by 25%, and hypoxic preconditioning effect of a permanent lighting coused the most of all experimental groups increase the intensity of proteolysis, particularly in regard to macromolecular proteins. At the same time, lysis of collagen remained insignificantly higher in comparison with the control one, as in the experiment without preconditioning. Draws attention that intensity of tissue proteolysis significantly increases under conditions of constant illumination both with hypoxia and against a background of normoxia, that may be an evidence of intensification of elimination of oxidation-modified protein molecules, formed by reduction of antioxidant potential of tissue at melatonin deficiency.

The total fibrinolytic activity (TFA) in the tissues of the adrenal glands of immature females at the actions of a systemic hypobaric hypoxia increased by 34.4% due to enzymatic fibrinolytic activity (EFA), the growth rate of which reached 82.2%, whereas non-enzymatic fibrinolytic activity (NFA) index decreased by 22.8% (Table .2). However, the

Table 1

Reaction of proteolytic process in the adrenal glands tissues of immature female rats under conditions of hypobaric hypoxia and modified duration of photoperiod (M±m)

№ of group	Conditions of research		Lysis of LMWP, мкg azoalbumin/1g of tissue per 1 hour	Lysis of HMWP, мкg azocasein/1g of tissue per 1hour	Lysis of collagen, мкg azocol/1g of tissue per 1hour
1	Natural lighting, normoxia, n=10	M±m	115,9±3,901	104,6±5,317	12,42±1,722
2	Natural lighting, hypoxia, n=10	M±m	82,145±6,400	75,448±5,287	7,022±0,704
		p	0,003	0,006	0,014
3	Permanent lighting, normoxia, n=10	M±m	131,4±4,238	119,7±6,679	11,46±0,666
		p	0,026	0,072	0,261
4	Permanent lighting with hypoxic preconditioning, n=8	M±m	155,1±7,864	139,7±6,870	14,21±1,043
		p	0,001	0,003	0,065
		p_1	0,048	0,112	0,086
		p_2	0,000	0,000	0,000
5	Permanent lighting, hypoxia (simultaneously) n=10	M±m	145,1±5,864	134,7±6,030	13,27±1,087
		p	0,001	0,003	0,362
		p_1	0,052	0,104	0,098
		p_2	0,000	0,000	0,000

Table 2

Reaction of fibrinolytic process in the adrenal glands tissues of immature female rats under conditions of hypobaric hypoxia and modified duration of photoperiod (M±m)

№ of group	Conditions of research		TFA, мкg azofibrin/ 1 g of tissue per 1 hour	NFA, мкg azofibrin/ 1 g of tissue per 1 hour	EFA, мкg azofibrin/ 1 g of tissue per 1 hour
1	Natural lighting, normoxia, n=10	M±m	20,13±1,139	9,170±0,608	10,96±0,660
2	Natural lighting, hypoxia, n=10	M±m	27,05±2,036	7,079±0,510	19,97±1,853
		p	0,005	0,020	0,001
3	Permanent lighting, normoxia, n=10	M±m	21,08±0,390	10,47±0,334	10,62±0,202
		p	0,224	0,056	0,335
4	Permanent lighting with hypoxic preconditioning, n=8	M±m	20,78±0,410	9,74±0,434	11,83±0,302
		p	0,055	0,095	0,064
		p_1	0,072	0,495	0,002
		p_2	0,059	0,001	0,004
5	Permanent lighting, hypoxia (simultaneously) n=10	M±m	23,08±1,385	10,45±0,913	12,62±0,563
		p	0,048	0,099	0,060
		p_1	0,072	0,495	0,002
		p_2	0,048	0,001	0,002

Note in tables 1 i 2: p – criterion of probability of difference in comparison with group 1; порівняно з групою 1; p_1 - criterion of probability of difference in comparison with group 3; p_2 - criterion of probability of difference in comparison with group 2

observed increase of TFA in adrenal tissues under conditions of constant illumination was insignificant. Application of preconditioning of the effects of permanent lighting by hypoxia brought nearer the indices of fibrinolytic activity of the adrenal tissue to the indices of the control group, that may be indication of compensatory preconditioning effect of interval hypobaric hypoxia on damaging impact of permanent lighting. Pronounced changes in the tissues of the adrenal glands, probably testifies to reactivity of local fibrinolysis in them due to active participation of the hypothalamic-pituitary-adrenal axis to regulation of adaptation [2].

Detected peculiarities of the reaction of the tissues proteolysis and fibrinolysis indices in the adrenal glands in immature female rats to the applied factors and their combinations, indicate different intensity of the process of adaptation under various conditions. Conseqences of hypobaric hypoxia influence in case of hypoxic preconditioning of photoperiodic changes are leveled by hypofunction of the pineal gland, that result in "normalization" of indices, that is their approaching to the control ones. However, this may be also indicate of disturbance of adaptation process, that subsequently may lead to the development of pathology.

Conclusions

1. Modeling of the decreased melatonin-producing function of the pineal gland by application of constant lighting resulted in significant increase of the activity of proteolytic processes in the tissues of the adrenal glands in immature female rats, that may testify to intensification of elimination of oxidation-modified proteoxidant capacity according to melatonin deficiency.

2. The observed TFA increasing in tissues of the adrenal glands under conditions of hypoxia by 34.4% was caused by credible increase in enzymatic fibrinolysis by 82.2 % at simultaneously reducing the intensity of NFA by 22.8 %.

3. Hypoxic preconditioning of permanent lighting influence make the indices of fibrinolytic activity of adrenal tissues closer to the level of indices of animals under natural lighting, that may be indication of compensatory preconditioning effect of interval hypobaric hypoxia on damaging impact of permanent lighting. At the same time, changes in proteolytic processes in the tissues of the adrenal glands, caused by hypofunction of pineal gland, failed to be compensated by mean of hypoxic preconditioning.

Perspectives of the research

Mechanisms of parcipitation of fibrinolysis and

proteolysis processes in their interaction with the processes of peroxidation of lipids and proteins and their role in ensuring adrenal glands reaction under conditions of hypoxic preconditioning of the damaging effects of the modified duration of photoperiod by moderate hypobaric hypoxia at different stages of preconditioning require further investigation and profound analysis.

Literatura. 1.Веремеенко К.Н. Белковые ингибиторы плазмы крови - регуляторы активности протеолитических ферментов / К.Н. Веремеенко // Системная энзимотерапия. Теоретические основы, опыт клинического применения. -К.: МОРИОН, 2000. - С. 21-53. 2.Вишневский А. А. Эндокринные и мессенджерные системы при адаптации к условиям высокогорья/ А. А.Вишневский, Д. З.Закиров, В. М.Яковлев и др. // Пробл. эндокринол.-2003.-Т.49, № 1.-С.53-56. 3.Горбань Е.Н. Влияние хронической гипоксической тренировки на урони стабильных метаболитов в крови, тканях сердца и аорты взрослых и старых крыс в отдалённые сроки после облучения / Е.Н. Горбань, Е.В. Подъяченко, Н.В. Топольникова //Пробл. старения и долголетия.- 2013.-Т.22, прилож. - С.21-22. 4.Горбань Е.Н. Уровни экспрессии мРНК HIF-1α И HIF-3α в ткани сердца взрослых и старых крыс после однократного облучения и предшествующей интервальной гипоксической тренировки / Е.Н. Горбань, Т.И. Древицкая, Н.В. Топольникова // Современные аспекты геронтологии и гериатрии: от теории к практике: научн.-практ. конф. и школа, посвящ. 90-летию со дня рождения акад. В.В. Фролькиса: Мат. конф. (Киев, 26-27 мая 2014 года). - К., 2014. - С.45-46. 5.Заморський І.І. Вплив мелатоніну на рівень кортикостерону і пролактину в плазмі крові щурів за різної довжини фотоперіоду та гострої гіпоксії/ І.І.Заморський, В.П.Пішак, Г.І.Ходоровський// Ендокринологія.-2000.-Т.5, № 1.-С. 22-28. 6.Карпов Л.М., Можливість корекції вітамінами групи В та їх похідними енергетичного обміну у мишей в умовах гіпобаричної гіпоксії / Л.М. Карпов, Л.Г.Савлучинська, Н.В. Полтавцева, Л.А. Прєснова, В.В. Пєнов // Вісник Харківського національного університету ім.В.Н. Каразіна. Серія: біологія. Вип. 18, № 1079, 2013.- С. 24-28. 7.Кухарчук О.Л. Патогенетична роль та методи корекції інтегративних порушень гормонально-месенджерних систем регуляції гомеостазу натрію при патології нирок: Автореф. дис. ... д-ра мед. наук: 14.03.05 / .Л. Кухарчук. - Одеса, 1996.-37 с. 8.Лукьянова Л.Д. Роль биоэнергетических нарушений в патогенезе гипоксии// Патол.физиол. и эксперим.терапия. - 2004. - № 2. - С. 2-11. 9.Мойбенко А.А., Досенко В.Е., Нагибин В.С. Ферментативные механизмы апоптоза // Патолог. физиология и эксперим. терапия.-2005.-№3.-С.17-26. 10.Сазонтова Т.Г., Архипенко Ю.В. Роль свободнорадикальных процесов и редокс-сигнализаии в адаптации организма к изменению уровня кислорода // Росс. физиол. журнал им. И.М. Сеченова.-2005.-Т.91, №6.-С.636-656. 11.Топольникова Н.В. Влияние интервальной гипоксической тренировки на показатели углеводного и липидного обменов у взрослых и старых крыс после однократного облучения / Н.В. Топольникова, Е.Н. Горбань, Е.В. Подъяченко // Современные аспекты геронтологии и гериатрии: от теории к практике: научн.-практ. конф. и школа, посвящ. 90-летию со дня рождения акад. В.В. Фролькиса: Мат. конф. (Киев, 26-27 мая 2014 года). - К., 2014. - С.85-86. 12.Шевченко Ю.Л. Гипоксия. Адаптация, патогенез, клиника. / Ю.Л. Шевченко - СПб, ООО "ЭЛБИ", 2000. - 384 с. 13.Ясінська О.В. Особливості фотоперіодичних змін прооксидантних процесів, антиоксидантної системи та надниркових залоз за умов екзогенної гіпоксії: автореф. дис. на здобуття наук. ступеня канд. мед. наук: спец.14.03.03 "Нормальна фізіологія" / О.В.Ясінська.-Вінниця, 2007.-24 с. 14.Groenendaal F. Selection of babies for intervention after birth asphyxia / F. Groenendaal, L.S. de Vries // Semin. Neonatale.-2000.-Vol.5, N1.- P.17-32. 15.Zayour Dany Endocrine changes in a rat model of chronic hypoxia mimicking cyanotic heart disease / Zayour Dany, Azar Sami T., Bitar Fadi F. // Endocr.Res.-2003.- 29, № 2. - С.191-200.

ОСОБЕННОСТИ РЕАГИРОВАНИЯ ТКАНЕЙ НАДПОЧЕЧНИКОВ НЕПОЛОВОЗРЕЛЫХ САМОК КРЫС НА ДЕЙСТВИЕ ГИПОБАРИЧЕСКОЙ ГИПОКСИИ В УСЛОВИЯХ ИЗМЕНЕННОЙ ДЛИТЕЛЬНОСТИ ФОТОПЕРИОДА

Е.В. Ясинская

Резюме. Изучены особенности реагирования показателей протеолитических и фибринолитических процессов в тканях надпочечников неполовозрелых самок крыс на действие гипобарической гипоксии в условиях самостоятельного её применения и гипоксического прекондиционирования изменений, обусловленных влиянием постоянного освещения. Установлено, что моделювание гипофункции эпифиза путём постоянного освещения значительно влияет на характер изменений процессов протеолиза и фибринолиза в тканях надпочечников неполовозрелых самок крыс, вызванных системной гипобарической гипоксией при условии одновременного применения указанных влияний. Гипоксическое прекондиционирование влияний постоянного освещения не компенсирует сдвиги биохимических показателей, обусловленные изменением длительности фотопериода.

Ключевые слова: тканевой протеолиз, тканевой фибринолиз, фотопериод, гипобарическая гипоксия, гипоксическое прекондиционирование, надпочечники, неполовозрелые самки крыс.

ОСОБЛИВОСТІ РЕАГУВАННЯ ТКАНИН НАДНИРКОВИХ ЗАЛОЗ СТАТЕВОНЕЗРІЛИХ САМИЦЬ ЩУРІВ НА ДІЮ ГІПОБАРИЧНОЇ ГІПОКСІЇ ЗА ЗМІНЕНОЇ ТРИВАЛОСТІ ФОТОПЕРІОДУ

О.В. Ясінська

Резюме. Вивчені особливості реагування показників протеолітичних та фібринолітичних процесів у тканинах надниркових залоз статевонезрілих самиць щурів на дію гіпобаричної гіпоксії за умов самостійного її застосування та гіпоксичного прекондиціонування змін, зумовлених впливом постійного освітлення. Встановлено, що моделювання гіпофункції епіфіза шляхом постійного освітлення значно впливає на характер змін процесів протеолізу та фібринолізу в тканинах надниркових залоз статевонезрілих самиць щурів, викликаних системною гіпобаричною гіпоксією за поєднаного застосування зазначених впливів. Гіпоксичне прекондиціонування впливів постійного освітлення не компенсує зсуви в біохімічних показниках, зумовлені зміненою тривалістю фотоперіоду.

Ключові слова: тканинний протеоліз, тканинний фібриноліз, фотоперіод, гіпобарична гіпоксія, гіпоксичне прекондиціонування, надниркові залози, статевонезрілі самиці щурів.

Вищий державний навчальний заклад України "Буковинський державний медичний університет", м. Чернівці

Clin. and experim. pathol.- 2015.- Vol.14, №4 (54).-P.194-197.

Надійшла до редакції 23.11.2015
Рецензент – проф. І.І. Заморський