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Homeostatic and Hemostatic Changes in the Blood System Under the Conditions of Experimental Hypoxia in Animals in the Early Periods of Postnatal Development

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Abstract

The main goal of this investigation was to determine the characteristic features of glucose (sugar) levels in the blood of animals of young age and sex, and to clarify to what extent they obey the daily biorhythm.

The results obtained showed that the normal level of glucose in the blood of 2-month-old male rabbits during the day is 105-108 mg%, in the blood of females 107-110 mg%, in the blood of 3-month-old males and female rabbits it ranges from 111 -118 and 114-122 mg%, respectively. The second stge of our research is experiments with hypoxia. Experiences has shown that in this case, the level of glucose in the blood fluctuates between 97-118 mg% (in 2-month-old males) and 102-117 mg% (in 2-month-old females) during the day. In 3-month-old rabbits, due to the effect of severe hypoxia, the level of glucose in the blood increases significantly in the first hours, reaches 120 ± 4.6 mg% (in males) and 124 ± 2.4 mg% (in females), and then decreases.

After short-term mild hypoxia the amount of glucose in the blood varies between 98-113 mg% in 2-month-old males, 96-115 mg% in females, 107-116 mg% in 3-month-old males, and 110-121 mg% in females. Thus, there is a statistically significant increase in glucose levels. Differences observed between male and female glycemic responses are less pronounced during mild hypoxia.

1. Introduction

The most important conditions for normal life and adaptation of the human and animal organism in a frequently changing external environment are the general homeostasis of the internal environment, blood homeostasis and its particular manifestations [1, 2]. The relative stability-homeostatic balance of the chemical composition of the internal environment of the organism - the regulation of its vital activity metabolism is very important for ensuring the effectiveness of general and specific defense-adaptive reactions to various extreme effects. Homeostasis in the body blood, lymph, tissue fluid, cerebrospinal fluid (liquor), is leaking at the levels of intracellular cytoplasm, and these fluid environments constantly affect the activity of morpho-functional systems as a single system. In the body, blood plays an exceptional role in the establishment of general homeostasis, maintaining its relative stability of the chemical composition of the cell, physiological properties and functions through various regulatory mechanisms. Glucose (sugar) is considered one of the most important homeostatic important components of blood [3, 4].

It is well known, that the level of glucose in the blood is very sensitive to the effects of a number of external and internal factors cases of falling below the limits (hypoglycemia) or rising (hyperglycemia) may occur [5]. There are many facts about this in the literature. However, there are not so many experimental or clinical research studies, dedicated to the study of the effect of a factor that has a strong effect, such as oxygen deficiency, on general carbohydrate metabolism in the body, especially on glucose homeostasis. Experimental and clinical studies of this kind have rarely been conducted

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in young human or animal bodies. There is still no consensus in the literature regarding the effect of hypoxia on blood glucose levels.

With this in mind, we conducted a study on 2- and 3-month-old rabbits of both sexes to study blood glucose homeostasis under normal and hypoxic conditions.

2. Methods

The study was performed on 3-month-old male Chinchilla rabbits (n = 24) weighing 450–470 g, kept under standard vivarium conditions and on standard feeding rations. Animals were divided into control and 3 experimental groups of 6 individuals each. The amount of glucose in the blood was determined by the express method, using a glucometer measuring device made in the USA-Canada. Blood for analysis was obtained from each rabbit from the marginal vein of the ear. A light incision was made on it with a lancet, and the blood flowing out was collected in a test tube (1.5 ml). After centrifugation of the blood, small (about 1.0 µl) volumes were taken from the plasma and applied to the test strips of the glucometer. According to his indicators, they determined the glucose content in the blood of experimental rabbits. The unit of measurement of glucose in the blood is expressed in mg/dL. In the animals of the control group, glucose was determined during the day: in the morning, at noon and in the evening, in the experimental groups - also during the day, 1, 3 and 6 hours after the application of the investigated factors - hypoxia, physical exertion and their combination. These terms are close to those that were determined for blood analysis in control individuals.

In our experiments, the amount of sugar in the blood was determined in 2- and 3-month-old rats and rabbits of both sexes.Experiments related to determination of blood glucose were performed using moderate and severe hypoxia models (15% O_2, 95% N_2).The mixture of gases in these proportions was applied once. Glucose in the blood of experimental and control animals was determined in the morning, afternoon and evening. In rats, blood was taken from the veins of the hind limbs, and in rabbits, from the ear vein.

The results of determination of blood glucose of the control and experimental groups were processed parametrically, using the Student's t-criterion, the differences between the means of the groups were considered reliable at $p < 0.05$; The measurement results are presented in the form of average value (M) and average error (m), (M ± m).

3. Results and Descutions

First, the amount of glucose in the blood of 2- and 3-month-old male and female rabbits with normal development was investigate in the study. Here, the main goal was to determine the characteristic features of glucose (sugar) levels in the blood of animals of young age and sex, and to clarify to what extent they obey the daily biorhythm. Our results are presented below in table 1.

Table 1. Changes in the amount of glucose in the blood of normal (intact) 2- and 3-month-old male and female rabbits at different times of the day (in mg%, M±m).

Age and sex of animals	Time intervals and analysis indicators		
	Morning 10^{00}-11^{00} hours	in the afternoon 13^{00}-14^{00} hours	in the evening 16^{00}-17^{00} hours
2-month-old male rabbits (n=6)	106±4,2	108±4,6	105±3,6
2-month-old female rabbits	108±5,0	110±4,4	107±5,2

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(n=6)			
3-month-old male rabbits (n=6)	111±3,3	118±2,4	112±3,0
3-month-old female rabbits (n=6)	116±2,0	122±3,1	114±2,6

The obtained results showed that the normal level of glucose in the blood of 2-month-old male rabbits during the day is 105-108 mg%, in the blood of female rabbits it is 107-110 mg%, in the blood of 3-month-old male and female rabbits, it varies between 111-118 and 114-122 mg%, respectively. When we pay attention to our results, it is known that glucose homeostasis in normal 3-month-old male and female rabbits is expressed with different indicators compared to that in 2-month-old male and female rabbits. In relatively old animals, the level of glucose is high and fluctuates in a wider range. As in the first age group, gender-related differences are observed in this indicator in the second age group; Quantitative values of glucose in 3-month-old females were slightly higher than in males of the same age, but this difference was not statistically significant. Referring to such facts, it can be assumed that in the early stages of postnatal ontogenesis, the demand for glucose in the body gradually increases due to age dynamics. According to some studies, the amount of glucose in the blood can reach 140-160 mg% and higher in old rabbits [6, 7]. The relevant dynamics of glucose circulating in the blood and delivered to the tissues under normal conditions is of considerable interest for experimental studies.

Another regularity is noticeable here. The amount of glucose in the blood in 2-month-old male and female individuals is close to or at the same level in the morning, afternoon and evening. In other words, the biorhythm is not clearly noticeable in the daily dynamics of this homeostatic component. But in 3-month-old rabbits, the concentration of sugar in the blood changes during the day in such a way that the signs of daily biorhythms are reflected more clearly. It can be assumed that the reason for this, as mentioned in some literature data, is the strengthening of diurnal biorhythms in the secretion of some hormones (for example, glucocorticoids) in connection with sexual maturity in rabbits already at the age of 3 months, and the behavioral forms that are important for life activity are more stable, the environment and the internal environment are more stable it leads to more harmony in the background of mutual relations.

The second stage of our research is experiments with hypoxia. During the experiments, glucose analysis was performed on 2 and 3-month-old rabbits. First, 2-month-old and then 3-month-old animals of both sexes were exposed to moderate (mild) hypoxia for 20 minutes in an environment of 85% nitrogen and 15% oxygen in a barochamber. After hypoxia, glucose in their blood was determined in the morning, afternoon and evening according to the above procedure. The obtained experimental results are given in tables 2 and 3.

Table 2. Quantification of daily changes in blood glucose levels in 2- and 3-month-old rabbits exposed to 20 minutes of moderate hypoxia (in mg%, M±m, n= 6).

Age and sex of animals	Time intervals and analysis indicators		
	Morning 10^{00}-11^{00} hours	in the afternoon 13^{00}-14^{00} hours	in the evening 16^{00}-17^{00} hours
2-month-old male rabbits	113±5,2	104 ± 3,8	98 ± 2,6

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(n=6)	p<0,01		p<0,05
2-month-old female rabbits (n=6)	115±4,0 p<0,05	106 ± 2,6	96 ± 3,0 p<0,05
3-month-old male rabbits (n=6)	116±3,4 -	118 ± 4,2 -	107 ± 5,3 -
3-month-old female rabbits (n=6)	119±6,5 -	121 ± 5,0 -	114 ± 2,6 -

Note: The difference between practice and norm indicators p<0.05 is considered statistically reliable (norm indicators are given in table 1).

Table 3. Daytime dynamics of glucose content in the blood of 2- and 3-month-old rabbits after 20 minutes of severe hypoxia (in mg%, M±m, n=6)

Age and sex of animals	Time intervals and analysis indicators		
	Morning 10^{00}-11^{00} hours	in the afternoon 13^{00}-14^{00} hours	in the evening 16^{00}-17^{00} hours
2-month-old male rabbits (n=6)	118±7,3 p<0,01	103 ± 2,6	97 ± 4,5 p<0,05
2-month-old female rabbits (n=6)	127±5,0 p<0,01	107 ± 3,5 -	102 ± 3,1 -
3-month-old male rabbits (n=6)	120±4,6 p<0,05	116 ± 4,0 -	108 ± 3,7 -
3-month-old female rabbits (n=6)	124±2,4 p<0,05	119 ± 1,8 -	110 ± 2,0 -

Note: As shown in Table 2.

The analysis of the results of our experiments showed that early postnatal development periods, as we observed in this experiment, glucose homeostasis in the animal refers to the physiological parameters sensitive to the effect of hypoxia. Susceptibility is noticeable even in the mild form of hypoxia. During its effect, interesting changes occur in the amount of glucose in the blood.

After short-term mild hypoxia, an important empirical fact that is noticeable when we pay attention to the changes in the amount of glucose during the day in 2- and 3-month-old male and female rabbits (see table 3.2.2) is that the obtained physiological indicator is significantly different compared to the norm. In this case, the amount of glucose in the blood varies between

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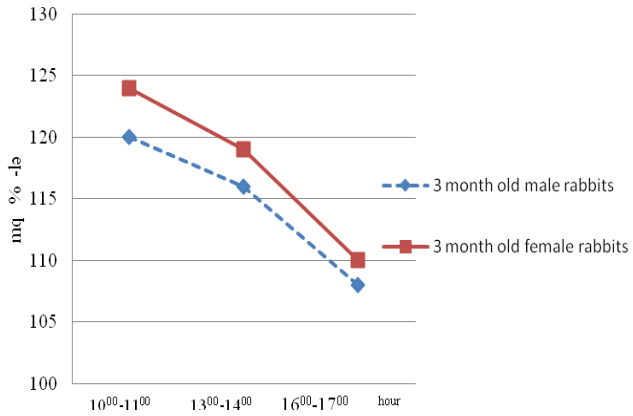
98-113 mg% in 2-month-old males, 96-115 mg% in females, 107-116 mg% in 3-month-old males, and 110-121 mg% in females. This means that glucose homeostasis in a relatively young animal can cause certain changes in a mild form of hypoxia. It is also noticeable here that in the first moments of the effect, that is, at the beginning of hypoxia, the level of glucose in the blood rises significantly above the norm, and then gradually decreases, falling to the normative limits. After hypoxia in 3-month-old animals, the change in the amount of glucose in the blood has a somewhat different dynamic. Thus, during the entire experience, cases of its statistically reliable increase over the norm are recorded. Differences observed between male and female glycemic responses are less pronounced during mild hypoxia.

In the second experimental variant, animals were subjected to 20 minutes of severe hypoxia (maintenance in an environment of 95% nitrogen and 5% oxygen). Our results 3.2.3. given in table no. Experience has shown that in this case, the level of glucose in the blood fluctuates between 97-118 mg% (in 2-month-old males) and 102-117 mg% (in 2-month-old females) during the day. In 3-month-old rabbits, due to the effect of severe hypoxia, the level of glucose in the blood increases significantly in the first hours, reaches 120 ± 4.6 mg% (in males) and 124 ± 2.4 mg% (in females), and then decreases. This trend is reflected in fig.1.

Figure 1. *Curves of blood glucose levels in 3-month-old male and female rabbits after severe hypoxia.*



We do not know exactly the reason for such a sharp increase in blood glucose in the first moments of severe hypoxia. It can be assumed that due to severe oxygen deficiency in tissues and cells in severe hypoxia, oxidation (decomposition) of glucose in mitochondria, i.e. processes of consumption of ATF synthesis, is sharply reduced, as a result, glucose in the blood is high. Or, during hypoxia, additional glucose resources enter the blood as an adaptive response. Hypoxia, and even more so its severe forms, according to many researchers, for the human and animal organisms are both extreme, stressful and pathogenic factors of multilateral and long-term action [8–11].

Considering the data available in the literature [12, 13], it can be assumed that the occurrence of hyperglycemia in this case is probably due to two reasons. In severe hypoxia, when the oxygen concentration in the tissues decreases sharply, the rate of glucose oxidation in cells decreases, so its content in the blood at an early stage is increased. However, during hypoxia, an urgent mobilization of glucose into the blood from peripheral metabolic funds can occur as an adaptive-compensatory reaction in case of a shortage of glucose for the brain, heart, and other organs that are severely affected by hypoxia.

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