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Bakhtiyor Burhanovich Hasanov
The Bukhara State Medical Institute
Reseacher

EXPERIMENTAL CHRONIC TOXIC HEPATITIS AND HEMATOLOGICAL FEATURES IN THE DYNAMICS OF LACTATION IN MOTHER AND PROPERTY

Abstract: *The purpose of the study was to study the occurrence of autoimmune processes in chronic heliotrin hepatitis and its effect on the hematological parameters of mother and offspring in the dynamics of lactation.*

The work was carried out on white outbred female rats, which were studied after heliotrin intoxication before pregnancy, the presence of antihepatic antibodies in female rats was carried out by passive hemagglutination by the Boyden method, as well as hematological parameters in mother and offspring in lactation dynamics by generally accepted methods.The presence of antihepatocytic autoantibodies during lactation, mainly in the blood serum, and in small quantities in the milk of female rats was established, therefore, antihepatic antibodies of the mother with toxic hepatitis are not a pathological agent for the offspring during breastfeeding. In the body of female rats and offspring anemia occurs, progressing until the second week of lactation, that is, the transition of the cubs to a mixed diet, therefore, it is more advisable to carry out therapeutic measures before this period.

Key words: *chronic hepatitis, lactation, mother, offspring, antihepatic antibodies, anemia.*

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Introduction

It is known that the normal development of the child depends on the process of conception, i.e. from the gene pool of X and Y chromosomes of both parents, it is then directly related to the state of the mother's body during pregnancy and breastfeeding. That is, the growth and development of the future newborn in the embryonic and fetal periods of development depends on the full functioning of the mother - placenta - fetus system, then after birth this scheme changes to mother - mammary gland - newborn. Consequently, the adaptation of developing offspring to environmental factors begins even in the embryonic period of development, where immunoglobulins, hormones and bioactive substances begin to flow through the placenta along with the necessary nutrients. And yet, man, like many types of mammals, brings unripe offspring, the formation and functioning of the life support systems of which occurs further during breastfeeding. However, this harmonious system of relations between the mother and the offspring is violated in case of illnesses of the mother.

It should be noted that the frequency of various extragenital pathologies in women of childbearing age is still significant. First of all, the risk of chronic damage to the hepatobiliary system increases as a result of transferred viral or toxic hepatitis, which under the influence of adverse environmental conditions often take a chronic, protracted form [3, 4]. It should also be noted that in multiparous women, there is also a high risk of hepatobiliary pathology. The possibility of transmission of hepatitis virus from HbsAg carriers to newborns, the development of persistence of HbsAg in some children, and the formation of primary chronic hepatitis is beyond doubt [5, 8]. In particular, experimental studies have established that chronic intoxication with heliotrin contributes to the onset of interstitial hepatitis, which subsequently progresses to liver cirrhosis [4]. Along with this, in recent years, with heliotrin intoxication, the presence of microcirculatory disorders was also

detected in other organs, which indicates the presence of interorgan and intersystem relationships in the body of experimental animals [1]. One of the liquid media that binds the body into a single system is blood, in which "its general condition is reflected in a mirror". At the same time, the importance of autoimmune processes unfolding in the mother's body with hepatitis, in the dynamics of lactation and their effect on the development of offspring during breastfeeding and how they affect the hematological parameters of the mother and offspring, are still poorly understood.

The aim of our study was to study the effect of chronic heliotrin intoxication of female rats before pregnancy on autoimmune processes in the mother's body and on the hematological parameters of mother and offspring and in the dynamics of lactation.

II.Literature review

For the experiment, 3-month-old sexually mature white outbred female rats (72) weighing 120-140 grams were used. The animals were kept on a normal laboratory diet and were quarantined for two weeks before the experiment. As a model of hepatitis, we used chronic heliotrin intoxication [1]. After quarantine, the females of the experimental group (O) were injected with heliotrin at a dose of 0.05 mg / gram body weight per 0.5 ml of physiological saline subcutaneously weekly for 6 weeks, the animals of the control group (K) were injected only with saline. 10 days after the last injection, males were planted in the females. For the study, females of the experimental (40) and control groups (32) on 1, 3, 7, 15, 21, and 30 days of lactation were selected. The determination of antihepatocytic antibodies was carried out by RPHA according to the Boyden method. To carry out serological reactions, we used blood serum (0.5 ml) and milk samples (0.2 ml) taken from female rats in the above study periods. The sheep erythrocytes were prepared according to the generally accepted method. A 2.0 g sample of the liver of an intact female rat was used as antigen, the preparation of which was carried out by water-chloroform extraction according to the method of T. A. Alekseeva [8]. The antigen content was controlled by the amount of protein, which was adjusted to 1%. For a more accurate calculation and convenience in comparison, the results were expressed in log2 [7]. For the study, the blood of females from the control and experimental groups was used, as well as their rat pups on days 1, 3, 7, 14, 21, and 30 of lactation. The following hematological parameters were studied in the work: the amount of hemoglobin (Hb in gram%) according to the generally accepted method using a Salihemometer, the total number of red blood cells (x1012 / l) and white blood cells (x109 / l) using a Goryaev's camera. The data obtained were processed according to Fisher-Student, reliable differences were considered reliable satisfying $P < 0.05$.

III.Analysis

As a result of our study, a certain dynamics of changes in the titer of antihepatocytic antibodies of blood and milk of rats with toxic hepatitis in the dynamics of lactation was established. Autoantibodies reaching a titer of 1: 128 are found in the blood serum of females of the experimental group immediately after birth, this trend persists up to 3 days of lactation, while in the control group of animals the titer of autoantibodies is 1: 8 and 1: 4 for 1 and 3 days after childbirth, respectively. In the subsequent periods of lactation, serum in a dilution of 1:64 was found to be seropositive until the end of the lactation period.In contrast, in the control group, antibodies were detected in females only up to 7 days of breastfeeding, not exceeding a titer of 1: 4, in the subsequent periods of lactation only traces were observed.

In contrast to blood serum, in a serological study of milk samples of females of the experimental group on days 1-7 after delivery, autoantibodies were determined in a 1: 8 dilution. In subsequent periods, antihepatic antibodies were not always detected even at a 1: 4 dilution. In the control group, the indicators of serological studies of milk during breastfeeding did not reveal significant differences from the experimental group.

To conduct more accurate studies and the possibility of comparing changes in the titer of antihepatocytic antibodies in the blood serum and milk of female rats during lactation, the results of serological studies were expressed in log2 (see Table). According to these data, with toxic heliotrin hepatitis, the appearance of autoantibodies against the liver is characteristic only of blood serum, which are present until the end of the period of breastfeeding. While in milk samples obtained from females with toxic hepatitis, an insignificant titer of autoantibodies was not significantly different from those in females of the control group.

Table 1. Changes in the activity of antihepatic antibodies in the blood and milk of female rats with chronic heliotrin intoxication in the dynamics of lactation

(data expressed in log2, M ± m)

Researched Material	**Gr. wx**	**Duration of lactation (in days)**				
		1	3	7	14	21
Blood	K	1,68±0,158	0,75±0,161	0,68±0,149	0,48±0,142	0,33±0,104
	O	6,03±0,089*	5,45±0,127*	5,10± 0,114*	4,90±0,120*	4,73±0,114*

Milk	K	1,60±0,206	1,48±0,089	1,30±0,082	0,83±0,196	0,78±0,164
	O	3,75±0,133	3,45±0,158	3,43±0,212	2,00±0,199	1,95±0,225

Note: ** - differences are significant relative to control at P <0.05*

Chronic heliotrin hepatitis also contributes to the occurrence of certain changes in hematological parameters, both in the females themselves and in their offspring (see Tables 2 and 3). In female rats, a significant decrease in the amount of hemoglobin is observed starting from the first week after childbirth and up to 14 days of lactation. Although from the first days of lactation there is a relative decrease in the number of red blood cells of females of the experimental group than in the control, a significant decrease in the number of red blood cells becomes only on the 14th day of lactation.

Table 2. The effect of toxic hepatitis on the hematological parameters of female rats in the dynamics of lactation (M ± m, n = 10)

The investigated parameters	**Gr. wx**	**Duration of lactation (in days)**					
		1	**3**	**7**	**14**	**21**	**30**
Hbingram%	K	11,2± 0,02	11,2± 0,03	11,1± 0,09	11,0± 0,01	11,2± 0,17	11,8±0,05
	O	10,8± 0,29	10,8± 0,25	10,7±0,12*	10,6±0,22*	10,9± 0,25	11,4±0,33
Red blood cells x10^9 / l	K	5,28± 0,11	5,21± 0,05	5,20± 0,08	5,13± 0,06	5,23± 0,11	5,41±0,08
	O	5,00± 0,12	4,90± 0,15	4,85± 0,20	4,78±0,09*	5,15± 0,17	5,3±0,14
White blood cells x10^6 / l	K	9,21± 0,17	9,06± 0,05	9,44± 0,21	9,60± 0,24	9,61± 0,16	9,72±0,15
	O	8,42±0,28*	8,21±0,18*	8,43±0,26*	8,71±0,29*	9,11±0,36	9,20±0,38

Table 3. The effect of toxic hepatitis in female rats on the change in hematological parameters of the offspring in the dynamics of early postnatal ontogenesis (M ± m, n = 10)

The investigated parameters	**Gr. wx**	**Dates of postnatal development (in days)**					
		1	**3**	**7**	**14**	**21**	**30**
Hbingram%	K	10,2±0,08	9,5±0,06	9,5±0,03	9,3±0,05	9,1±0,07	8,9±0,12
	O	9,1±0,10*	9,1±0,07*	9,0±0,06*	8,9±0,08*	8,8±0,18	8,8±0,17
Redbloodcells x10^9 / l	K	3,65±0,05	3,25±0,05	3,30±0,04	3,35± 0,05	3,56±0,05	3,82±0,06
	O	3,25±0,14*	3,02±0,05*	3,01±0,03*	2,90±0,07*	3,16±0,22	3,60±0,18
White blood cells x10 / l	K	12,62±0,16	9,96±0.03	9,70±0,08	9,29±0,10	9,10±0,15	9,02±0.08
	O	11,02±0,08*	8,76±0,13*	8,61±0,08*	8,91±0,16	8,80±0,64	8,92±0,46

In the study of the total number of leukocytes, leukopenia was established, which stably lasts up to 14 days of lactation. In the subsequent periods of lactation, a relative normalization of hematological parameters is noted.

The study of blood parameters of rat pups in the dynamics of early postnatal ontogenesis revealed that in the body of newborns of the experimental group there is a decrease in the amount of hemoglobin and erythropenia, which lasts up to 14 days after birth. A decrease in the total number of leukocytes noted in rat pups on the 1st day after birth remains up to 7 days of development. On days 21 and 30, blood indices are approaching the lower boundary of the data of the rat pups in the control group.

IV.Discussion

It is known that chronic heliotrin intoxication leads to the onset of toxic hepatitis, which generally tends to progress, i.e. is a model of aggressive chronic hepatitis [1]. With active forms of hepatitis, changes in the immune status occur, in particular, profound changes in the T- and B-systems of immunity are noted and an increase in the titer of immunoglobulins of various classes, an increase in the gamma fraction of globulins, are the criteria for assessing the activity of a developing pathological process. In cases of the transition of the process to a chronic form against the background of a slight decrease in T-helpers, the number of T-suppressors (killers) is significantly reduced, which contributes to the formation of antihepatic antibodies and activation of the pathological process [3,9]. Along with this, we believe that a violation of the detoxification function of the mother's liver is of great importance. The fetal liver is not yet ready for sufficient detoxification of metabolic products. It is clear that, in this case, the accumulation in tissues, including the liver, of substances that have

a cytotoxic effect is possible. Another cause of pathological changes in the offspring, apparently, is certain immunopathological changes in the body, since the protein products of decaying hepatocytes cause an autoallergic reaction. In particular, the results of our study once again showed that heliotrinal intoxication of female rats before pregnancy is a trigger for an auto-allergic process that progresses over time. Along with this, the relatively low titers of antihepatic antibodies in the blood serum are apparently associated with changes in the mother's body in the dynamics of pregnancy and lactation, stimulating regeneration processes. The almost double excess of the titer of autoantibodies immediately after birth, relative to the further period of lactation (1: 128 on 1 day and 1:64 in the subsequent periods of lactation), is possibly due to the effect of the fetus, which is alien to the mother's body and, of course, the loss of the immunosuppressive effects of placental hormones during pregnancy, which ceased to act after childbirth.

When comparing the results of hematological studies of the blood of females with chronic heliotrin intoxication and their offspring with the literature data, we can assume that the deep metabolic changes that occur in the mother's body with toxic hepatitis, in particular, impaired protein-vitamin metabolism, as well as liver detoxification function [1,4] contribute to the occurrence of anemia, not only in the mother, but also in the offspring. The progression of anemia in the female's body on the 14th day of lactation is apparently associated with the growth of rat pups and an increase in the need for milk, and consequently, the stress of the mother's body. The immunodeficiency state of the mother with hepatitis leads to the fact that her milk does not completely eliminate the immunodeficiency in the body of the offspring [2], which is probably due to leukopenia in rat pups. The transition of calves to mixed nutrition, on the one hand, helps to reduce the burden on the mother's body, and on the other hand, reduces the intake of hepatotoxins [3] and antihepatic antibodies [5] in the rat pups, and as a result, the blood parameters of the mother and offspring are relatively normal at the end of the period of breastfeeding.

Thus, antihepatic antibodies are determined in the blood of female rats with toxic hepatitis after childbirth and in the dynamics of lactation, but during breastfeeding, they are transmitted to rat pups through milk in small quantities and, most likely, are not the main cause of the lag of the formation of the digestive and immune systems offspring. Along with this, with chronic heliotrin hepatitis, both in the mother's body and in the offspring, anemia is detected that progresses before the rat pups switch to a mixed diet, therefore, therapeutic measures would be more effective until this period of development.

V.Conclusion

1. In chronic toxic hepatitis, autoimmune hepatitis occurs in the body of a lactating female, as evidenced by the presence of antihepatocytic antibodies in the blood serum. Minor amounts of antibodies in milk indicate that they are not the main pathological factor for the baby.

2. In chronic hepatitis, anemia occurs, both in the body of female rats and in offspring, which progresses before the rats switch to a mixed diet.

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