

Integral Intoxication Indices in Liver Diseases in Dogs: Clinical Characteristics and Relevance

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ABSTRACT

One of the indicators characterizing the severity of endogenous intoxication is considered the integral indices of intoxication, in which the indicators of the leukocyte formula are used. By changes in the leukocyte formula, taking into account other hematological parameters, one can judge the severity of the pathological process and the effectiveness of the therapy. As a result of the analysis of integral intoxication indices, it was found that on the arrival day, leukocyte intoxication index, which is used to assess the intoxication level, indicated the average degree of intoxication of animals with liver damage. On the 10th day of the study, the best result was observed in the 3rd group of animals. The value of leukocytal intoxication index in dogs of this group became 1.74 ± 0.07 , which indicates a decrease in the level of intoxication to normal. The Dashtayants nuclear index is

also used to assess the severity of intoxication of the animal. When comparing different treatment regimens, it was found that therapy using fresh frozen plasma allows to rid the body of intoxication and improve the condition of the animal.

Keywords: Dogs, Intoxication, Integral Intoxication Indices, Liver, Liver Damage.

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INTRODUCTION

The clinical significance of integral intoxication indices for liver lesions in dogs is of some relevance in light of the difficult diagnosis, verification of the diagnosis and targeted treatment of animals. They are used to assess the severity of diseases, to compare the effectiveness of the methods of therapy, since they can change already in the very early stages of the disease. A number of integral hematological indices are proposed to be used as candidate markers of the immunological reactivity of the body, indicating its violations.

Severe endogenous intoxication, as a rule, accompanies chronic diseases of the liver, kidneys, pancreas, burn toxicosis, peritonitis, acute intestinal obstruction, sepsis, extensive injuries, gynecological diseases [1, 2, 3]. Most of these conditions are characterized by: hyperbilirubinemia, hyperglobulinemia, impaired synthesis of proteins, amino acids due to impaired synthetic, detoxification function of the liver [4, 5].

The reasons for the development of the syndrome can conditionally be divided into two groups. First of all, these are destructive processes, as a result of which an excess amount of intermediate and final metabolic products accumulates in the body, which cause a toxic effect on the most important life support systems [6, 7, 8, 9]. The second group is a violation of the functional state of the physiological systems of the body responsible for the binding, inactivation and elimination of both natural metabolites and toxic products. Primary damage to these

systems or failure to adapt and compensate for any pathological process also leads to the occurrence of endogenous intoxication syndrome [1, 10, 11].

Hepatopathy is a toxic-inflammatory degenerative damage to the liver parenchyma cells that occurs under the influence of a number of factors. According to modern data, liver diseases in dogs make up 5% of non-communicable diseases registered in this animal species, of which about 70% are chronic diffuse liver diseases [5, 6, 12, 13]. High compensatory abilities of the liver cause insufficient information of clinical, laboratory and instrumental methods for the diagnosis of liver lesions [11, 14, 15, 16].

The filtration and adsorption processes are disturbed, which causes a change in the physicochemical state of the intercellular substance, an increase in the interstitial space, hypoxia and a violation of the humoral and nervous regulation of the cell. These changes further aggravate intracellular homeostasis disorders and are accompanied by the release of a large number of pathological metabolites. In this case, a violation of the relationship in the regulatory system is manifested by a mismatch between the rate of metabolite accumulation and the rate of transformation and excretion, which leads to the accumulation in the tissues and liquid sectors of cell decomposition products, pyrogens, neurotransmitters, free radicals, as well as other biologically active substances of various types. The active process of the humoral movement of toxic substances from the local focus with the flow of blood and lymph throughout the body and distance damage to organs and tissues depending on their

resistance and tropism to one or another metabolite begins [17, 18, 19, 20].

In scientific literature, the concept of endogenous intoxication syndrome was formulated, which includes manifestations of pathological conditions of different etiology and severity caused by excessive accumulation of endotoxic substances in tissues and biological fluids of the body [3, 21, 22]. A key link in the pathogenesis of chronic liver diseases is a change in the metabolism of hepatocytes and their destruction.

The aim of the study is to provide a comparative description of methods of control over intoxication in liver damage in dogs.

MATERIALS AND METHODS

The studies were carried out on the basis of the Department of Veterinary Medicine of the Agrarian and Technological Institute of the Peoples' Friendship University of Russia (RUDN University). The research objects were 63 dogs of various breeds aged 3 to 14 years, in which, as a result of the examination, liver damage of various etiologies was detected. After conducting clinical and laboratory research methods, 42 patients were selected from all animals, taking into account the breed and age. Dogs of medium and large breeds aged 3-10 years were selected.

The selected animals were divided into 3 groups of 14 animals each. In addition, we formed the 4th control group, which included clinically healthy dogs in the amount of 6 animals at the age of 5-8 years, blood tests from which were taken during the medical examination. Animals of the 1st, 2nd and 3rd experimental groups were treated, for which three treatment regimens were used:

1 group. An intravenous isotonic sodium chloride solution at a dose of 20 ml / kg of weight 1 time per day, reopoliglyukin dropwise at a dose of 10 ml / kg 1 time per day, glucose of a 40% solution at a dose of 2 ml / kg weight 1 time per day, heptral 1 ml of solution per 10 kg of animal weight 5 days, every other day; intramuscularly amoxoyl retard in a dose of 1 ml per 10 kg of weight 1 time per day for 5 days. Vitamins B1 (10-20 µg / kg), B6 (50-250 mg / kg), B12 (10-20 µg / kg) subcutaneously 1 time per day, for 10 days; ascorbic acid 10 mg / kg body weight 1 time per day.

2 group. Ringer-Locke solution is administered intravenously at a dose of 20 ml / kg 1 time per day, reopoliglukin 10 ml / kg 1 time per day, a 20% glucose solution at a dose of 2 ml / kg / 1 time per day, heptral 1 ml of solution per 10 kg of dog weight once every other day; subcutaneously catazal 0.5-5 ml per animal; ascorbic acid 10 mg / kg once a day, intramuscularly amoxoyl retard at a dose of 1 ml per 10 kg of weight 1 time per day for 5 days; Vitamins B1 (10-20 µg / kg), B6 (50-250 mg / kg), B12 (10-20 µg / kg) subcutaneously 1 time per day, for 10 days. Inside lactulose stad in a dose of 5-10 ml 3 times a day daily for 10 days.

3rd group. Intravenously 10% glucose solution at a dose of 10 ml / kg / day., Reopoliglyukin 10 ml / kg / day, Ringer-Locke solution 40 ml / kg / day. Caninsulin with glucose 0.25 U / kg; Essential Forte N at a dose of 0.25 ml / kg / day for 7 days, intramuscularly 5% solution of ascorbic acid 3 ml / day., for 10-15 days. Vitamins B1 (10-20 µg / kg), B6 (50-

250 mg / kg), B12 (10-20 µg / kg) subcutaneously 1 time per day, for 10 days. intramuscularly amoxoyl retard in a dose of 1 ml per 10 kg of weight 1 time per day for 5 days. Fresh frozen plasma 10 ml / kg / day for 3 days. Heptral in a daily dose of 400 mg for 2 weeks, maintenance therapy - the next 2-4 weeks. Mexidol-Vet 10-15 mg / kg / day - 5 days, then up to 5.0-7.5 mg / kg of animal weight up to 30 days.

Venous blood was taken at the the initial visit, then on the 3rd, 7th and 10th day of the study from v. saphena. For a complete blood count (CBC), blood was collected in vacuum tubes with K3EDTA. Based on the results of the leukogram, intoxication indices were studied: leukocytal intoxication index (LII) according to Ostrovsky V.K. [14], the Dashtayants nuclear index (NI), white blood cell shift index (WBCS), leukocyte to blood sedimentation rate ratio (LTBS), lymphocytic granulocyte index (LGI), Krebs index (KI), neutrophil-monocyte index (NMI), lymphocyte-monocyte index (LMI) [8].

The data obtained were processed by the method of variation statistics using the Statistica software package for Windows.

RESULTS AND DISCUSSION

The reasons for the development of the syndrome can conditionally be divided into two groups. First of all, these are destructive processes, as a result of which an excess amount of intermediate and final metabolic products accumulates in the body, which cause a toxic effect on the most important life support systems [6, 7, 8, 9, 44]. The second group is a violation of the functional state of the physiological systems of the body responsible for the binding, inactivation and elimination of both natural metabolites and toxic products. Primary damage to these systems or failure to adapt and compensate for any pathological process also leads to the occurrence of endogenous intoxication syndrome [1, 10, 11, 23]. The primary processes of damage in the cell are associated with a change in the properties of its membranes, which leads to a violation of intracellular homeostasis. As liver disease progresses, gradual destruction occurs liver parenchyma is gradually destroyed, hepatocyte metabolism changes and their destruction, resulting in the formation of endogenous intoxication syndrome.

When evaluating the results of the leukocyte formula, a nonspecific picture is observed. On the day of admission, mild leukocytosis ($25.3 \pm 0.8 \times 10^9 / l$) is detected in dogs, which is interpreted in the scientific literature as a response of the body to stress [1, 4, 5, 7, 50-55]. In addition, in all groups, even on the 3rd day of treatment, monocytosis is observed. In the 1st group, it was $15.3 \pm 1.9\%$, in the 2nd - $14.7 \pm 1.2\%$, in the 3rd - $12.8 \pm 1.1\%$, unlike the 4th the control group, where the number of monocytes was only $2.6 \pm 1.2\%$ (Table 1).

By the 10th day of therapy, improvements are noticeable, which, when counting leukogram, were expressed in a decrease in the number of monocytes and an increase in the number of lymphocytes. In the 1st group, the values of monocytes amounted to $11.1 \pm 1.1\%$, lymphocytes - $10.7 \pm 2.3\%$, which is outside the range of reference values. A similar picture is observed in the 2nd group of dogs, where

the number of monocytes was $9.8 \pm 1.1\%$, and lymphocytes - $11.2 \pm 0.7\%$. In the 3rd group, the number of monocytes was $6.3 \pm 1.3\%$, lymphocytes - 20.5 ± 1.5 , which is included in the range of reference values. From this we can conclude that

the therapy given to these animals leads to an improvement in performance, however, the use of fresh frozen plasma in the treatment regimen allows one to achieve a better effect.

Table 1: The leukogram in complete blood count in dogs with liver disease

Indicators	PD	First visit day	Study days	Groups			
				1st	2nd	3rd	4th
Leukocytes $\times 10^9/l$	6-16	25,3 \pm 0,8	3	22,1 \pm 1,9	20,7 \pm 2,1	21,9 \pm 2,3	6,8 \pm 0,9
			7	20,6 \pm 0,8	17,8 \pm 1,4	15,4 \pm 2,2	7,1 \pm 1,2
			10	18,2 \pm 0,6	15,9 \pm 1,6	10,6 \pm 1,1	7,2 \pm 1,6
Band neutrophils, %	0-3	3,5 \pm 1,2	3	3,1 \pm 0,8	3,4 \pm 1,1	3,9 \pm 0,5	0,3 \pm 0,3
			7	3,1 \pm 0,6	3,8 \pm 1,6	3,2 \pm 0,7	0,5 \pm 0,1
			10	2,9 \pm 1,1	2,9 \pm 0,9	2,7 \pm 0,3	1,2 \pm 0,1
Segmented neutrophils, %	60-70	73,3 \pm 2,3	3	72,4 \pm 2,8	73,3 \pm 1,8	73,4 \pm 1,4	68,8 \pm 1,0
			7	70,2 \pm 2,4	73,3 \pm 0,6	70,7 \pm 1,9	70,0 \pm 0,8
			10	72,6 \pm 1,6	71,6 \pm 2,4	69,3 \pm 2,1	71,4 \pm 1,3
Eosinophils, %	0-5	2,6 \pm 1,7	3	2,4 \pm 0,8	3,1 \pm 0,5	2,9 \pm 0,3	4,4 \pm 0,7
			7	3,7 \pm 1,4	2,5 \pm 0,7	2,4 \pm 0,1	3,8 \pm 0,3
			10	3,1 \pm 0,3	3,7 \pm 0,4	1,1 \pm 0,1	4,1 \pm 0,6
Monocytes, %	2-7	15,6 \pm 0,8	3	15,3 \pm 1,9	14,7 \pm 1,2	12,8 \pm 1,1	2,6 \pm 1,2
			7	13,6 \pm 0,8	10,5 \pm 2,5	8,7 \pm 0,7	2,9 \pm 0,8
			10	11,1 \pm 1,1	9,8 \pm 1,1	6,3 \pm 1,3	3,4 \pm 0,3
Basophils, %	0-1	0,7 \pm 0,1	3	0,9 \pm 0,3	0,4 \pm 0,1	0,7 \pm 0,6	0,3 \pm 0,4
			7	0,8 \pm 0,5	0,5 \pm 0,3	0,4 \pm 0,5	0,5 \pm 0,5
			10	0,6 \pm 0,7	0,8 \pm 0,4	0,1 \pm 0,1	0,1 \pm 0,1
Lymphocytes, %	12-30	4,3 \pm 1,1	3	5,9 \pm 1,2	5,1 \pm 1,4	6,3 \pm 0,3	23,6 \pm 1,1
			7	8,6 \pm 1,0	9,4 \pm 0,6	14,6 \pm 1,2	22,3 \pm 2,3
			10	10,7 \pm 2,3	11,2 \pm 0,7	20,5 \pm 1,5	19,8 \pm 2,4
Sedimentation rate of erythrocytes, mm/h	0-6	21 \pm 1,9	3	15 \pm 2,3	14 \pm 1,0	16 \pm 1,3	3 \pm 0,6
			7	11 \pm 1,5	12 \pm 1,3	10 \pm 0,7	2 \pm 0,8
			10	7 \pm 2,1	8 \pm 1,5	4 \pm 0,6	2 \pm 0,7

Note. $P < 0,05$; PD - physiological data

As hepatopathy progresses, the liver parenchyma gradually degrades with the gradual convergence of neighboring extended portal fields and small groups of preserved hepatocytes that fall into the expanded portal zones. There is necrobiosis of the liver cells and the formation of endogenous intoxication syndrome [4, 24, 25].

The concept of endogenous intoxication syndrome, which includes manifestations of pathological conditions of various etiologies and severity caused by excessive accumulation of endotoxic substances in tissues and biological fluids of the body [1, 5, 38-43]. To characterize the severity of endogenous intoxication of the body, leukocyte indices can be used. According to the scientific literature, these indices make it possible to evaluate the functioning of the effector mechanisms of the immune system, as well as the level of immunological reactivity that determine the process of formation of non-specific adaptive reactions [8, 26].

Violation of the relationship between monooxygenase and immune systems determines the mismatch in the rate of formation and elimination of both pathological and physiological metabolic products in the fluid sectors and tissues. Consequently, endogenous intoxication develops either as a result of the imbalance of the components of the

detoxification system, or with the failure of one of the links, or all of its components at the same time [21, 27, 28].

Massive damage to the liver parenchyma in severe poisoning by hepatotoxic poisons, infections, sepsis, despite the significant compensatory capabilities of this organ, are accompanied by deep violations of its numerous and extremely important functions for organs. Standard biochemical and hematological studies for liver lesions are often not able to reflect the severity of endogenous intoxication. In the development of endogenous intoxication in sick animals, along with metabolic disorders caused by an acute infectious process, the initial failure of the detoxification systems of the body plays a significant role. Clarification of these circumstances, as well as the nature of the violation of the reactivity of the body can serve as a study of the quality and relation [6, 18, 21]

With endogenous intoxication, the functional activity of all hematopoietic lineages changes. Among the hematological syndromes, anemia comes to the fore. The development of anemia is associated with a toxic effect on red blood cells and a deficiency of plastic substrate, primarily protein deficiency. In addition, the development of anemia is due to excessive destruction of red blood cells in the spleen and microhemolysis in the vascular bed. Red blood cells actively sort endotoxic substances on their surface, the fixation of

which leads to a violation of the deformability of the erythrocyte membrane [4, 5, 29, 30].

The leading function of the liver is detoxification, it is natural to assume that the development of the pathology of the organ leads to the accumulation of endotoxins in the body, helping to trigger the mechanisms of endotoxin aggression. In addition, toxins that enter the bloodstream from any source of inflammation can have a damaging effect on liver tissue. A key link in the pathogenesis of chronic liver diseases is a change in the metabolism of hepatocytes and their destruction [3, 20, 26].

As the disease progresses, a gradual destruction of the liver parenchyma occurs with a gradual convergence of neighboring extended portal fields and small groups of preserved hepatocytes that fall into the expanded portal zones [1, 18, 31]. The concept of endogenous intoxication syndrome, which includes manifestations of pathological conditions of different etiology and severity, due to excessive accumulation of endotoxic substances in tissues and biological fluids of the body [4, 24]. To characterize the severity of endogenous intoxication of the body, leukocyte indices can be used. According to the scientific literature, these indices make it possible to evaluate the functioning of the effector mechanisms of the immune system, as well as the level of immunological reactivity that determine the

process of formation of non-specific adaptive reactions [6, 25].

As a result of the analysis of integral intoxication indices, it was found that on the day of receipt of LII, which is used to assess the level of intoxication, indicated the average degree of intoxication of animals with liver damage (Table 2). At a physiological index of 1.10-2.10 in sick dogs, the LII value was 3.69 ± 0.87 . Already on the 7th day of treatment, positive dynamics were noted: in the 1st group of dogs, the LII was 3.05 ± 0.14 , in the 2nd - 2.74 ± 0.21 , and in the 3rd - 2.66 ± 0.31 . On the 10th day of the study, the best result was observed in the 3rd group of animals. The value of LII in dogs of this group became 1.74 ± 0.07 , which indicates a decrease in the level of intoxication to normal. In the 1st (2.76 ± 0.11) and 2nd (2.15 ± 0.13) groups, mild intoxication was still observed on the 10th day of treatment.

NI is also used to assess the severity of intoxication of the animal. When calculating NI on the day of animal intake, it was equal to 0.34 ± 0.14 , that is, it can be said that the condition of sick animals of moderate severity, which is LII. When applying treatment regimens on the 10th day of the study in dogs of the 1st group, the UI decreased to 0.23 ± 0.04 , in the 2nd group it decreased to 0.12 ± 0.05 , and in the 3rd group to 0.10 ± 0.04 , which indicates a satisfactory condition of the animals.

Table 2: Calculation of integral intoxication indices in dogs with liver damage

Intoxicati on indices	PD	First visit day	Study days	Groups			
				1st	2nd	3rd	4th
LII	1,10-2,10	$3,69 \pm 0,87$	3	$3,49 \pm 0,12$	$3,52 \pm 0,42$	$3,59 \pm 0,24$	$1,41 \pm 0,08$
			7	$3,05 \pm 0,14$	$2,74 \pm 0,21$	$2,66 \pm 0,31$	$1,45 \pm 0,12$
			10	$2,76 \pm 0,11$	$2,15 \pm 0,13$	$1,74 \pm 0,07$	$1,62 \pm 0,17$
NI	0,05-1,00	$0,34 \pm 0,14$	3	$0,26 \pm 0,05$	$0,25 \pm 0,17$	$0,41 \pm 0,03$	$0,07 \pm 0,03$
			7	$0,24 \pm 0,16$	$0,19 \pm 0,08$	$0,22 \pm 0,15$	$0,13 \pm 0,09$
			10	$0,23 \pm 0,04$	$0,12 \pm 0,05$	$0,10 \pm 0,04$	$0,11 \pm 0,05$
WBCS	1,40-2,52	$4,03 \pm 0,53$	3	$3,89 \pm 0,11$	$3,82 \pm 0,73$	$3,62 \pm 0,21$	$1,81 \pm 0,11$
			7	$3,31 \pm 0,08$	$3,27 \pm 0,24$	$3,09 \pm 0,18$	$1,89 \pm 0,07$
			10	$2,96 \pm 0,11$	$2,64 \pm 0,31$	$2,16 \pm 0,13$	$2,03 \pm 0,13$
LBSR	0,29-0,39	$2,47 \pm 0,81$	3	$2,29 \pm 0,61$	$2,36 \pm 0,43$	$2,43 \pm 0,18$	$0,35 \pm 0,04$
			7	$1,97 \pm 0,04$	$2,01 \pm 0,08$	$1,38 \pm 0,04$	$0,31 \pm 0,15$
			10	$0,97 \pm 0,06$	$0,43 \pm 0,04$	$0,35 \pm 0,05$	$0,36 \pm 0,04$
LGI	4,19-4,93	$1,61 \pm 0,46$	3	$1,92 \pm 0,05$	$1,83 \pm 0,14$	$1,85 \pm 0,11$	$4,48 \pm 0,21$
			7	$2,41 \pm 0,09$	$2,88 \pm 0,07$	$3,17 \pm 0,08$	$4,22 \pm 0,26$
			10	$3,88 \pm 0,01$	$4,06 \pm 0,11$	$4,21 \pm 0,26$	$4,35 \pm 0,14$
KI	1,34-2,26	$5,18 \pm 0,77$	3	$4,43 \pm 0,21$	$3,84 \pm 0,18$	$4,19 \pm 0,18$	$1,83 \pm 0,15$
			7	$3,87 \pm 0,15$	$3,31 \pm 0,21$	$2,26 \pm 0,23$	$1,94 \pm 0,08$
			10	$2,47 \pm 0,17$	$2,21 \pm 0,19$	$2,03 \pm 0,14$	$1,79 \pm 0,11$
LI	0,38-0,44	$0,19 \pm 0,11$	3	$0,27 \pm 0,12$	$0,21 \pm 0,03$	$0,19 \pm 0,07$	$0,43 \pm 0,01$
			7	$0,30 \pm 0,13$	$0,27 \pm 0,08$	$0,33 \pm 0,02$	$0,41 \pm 0,06$
			10	$0,33 \pm 0,09$	$0,36 \pm 0,03$	$0,40 \pm 0,05$	$0,42 \pm 0,04$
NMI	10,52-13,14	$6,11 \pm 0,25$	3	$6,63 \pm 0,48$	$7,41 \pm 0,37$	$7,08 \pm 0,31$	$11,65 \pm 1,14$
			7	$8,15 \pm 0,21$	$8,62 \pm 0,57$	$9,46 \pm 0,48$	$11,93 \pm 0,45$
			10	$9,97 \pm 0,17$	$10,07 \pm 0,16$	$11,51 \pm 0,36$	$12,41 \pm 0,38$
LMI	5,80-7,20	$1,47 \pm 0,64$	3	$1,94 \pm 0,15$	$2,03 \pm 0,17$	$2,88 \pm 0,12$	$7,15 \pm 1,32$
			7	$3,49 \pm 0,72$	$4,57 \pm 0,84$	$4,89 \pm 0,45$	$6,82 \pm 0,51$
			10	$5,03 \pm 0,58$	$5,21 \pm 0,34$	$6,23 \pm 0,69$	$6,61 \pm 0,74$

Note. $P \leq 0,05$; PD - physiological data

NI: 0,05-0,1 – satisfactory condition, 0,1-1,0 – intermediate severity, more than 1,0 – critical condition.

LII - Leukocytal intoxication index; NI - Dashtayants nuclear index; WBCS - White blood cell shift index; LBSR - Leukocyte to blood sedimentation rate ratio; LGI - Lymphocytic granulocyte index; KI - Krebs index; LI - Leukocyte index; NMI - Neutrophil-monocyte index; LMI - Lymphocyte-monocyte index

The WBCS increase indicates an active inflammatory process, intoxication and impaired immunological reactivity. On the 3rd day of the study, WBCS was 3.89 ± 0.11 in the 1st group, 3.82 ± 0.73 in the 2nd and 3.62 ± 0.21 in the 3rd with physiological index 1, 40-2.52. On the 10th, improvements occurred in all groups of sick dogs. However, only in the 3rd group did the indicators reach the range of reference values. In the 1st group, WBCS became equal to 2.96 ± 0.11 , in the second - 2.64 ± 0.31 , in the third - 2.16 ± 0.13 .

The LBSR indicators can also be judged on the presence of intoxication. On the 3rd day of the study, in clinically healthy animals from the 4th group, LBSR was 0.35 ± 0.04 , and in patients 2.29 ± 0.61 , 2.36 ± 0.43 , and 2.43 ± 0.18 in the 1st group, in the 2nd and 3rd group, respectively, with normal values of 0.29-0.39. On the 10th day of treatment with values of 0.97 ± 0.06 , 0.43 ± 0.04 and 0.35 ± 0.05 in the 1st, 2nd and 3rd group of animals, an improvement in LBSR to the norm is only for dogs from the 3rd group, which speaks in favor of the applied treatment regimen.

LGI makes it possible to differentiate autointoxication and infectious intoxication. In the 1st group of animals on the 3rd day of the study, the LGI value is 1.92 ± 0.05 , in the 2nd group - 1.83 ± 0.14 , in the 3rd - 1.85 ± 0.11 , which is 2.2, 2.3 and 2.3 times lower than normal, respectively. According to published sources, with endogenous intoxication, the number of neutrophils with endogenous intoxication increases, and lymphocytes decreases, which proves the results and its low information content in the diagnosis of liver lesions [7, 31, 47]. Similar results were obtained when calculating the NMI, which allows us to judge the ratio of the components of the microphage-macrophage system. At normal values of 10.52-13.14 in the 1st group on the 3rd day of the study, it was 6.63 ± 0.48 , in the 2nd - 7.41 ± 0.37 , in the 3rd - 7.08 ± 0.31 . On the 10th day, the NMI indices returned to normal in accordance with the normalization of the values of the leukocyte formula, on the basis of which the intoxication indices are calculated. In the 1st group, the NMI value was 9.97 ± 0.17 , in the 2nd group - 10.07 ± 0.16 , in the 3rd - 11.51 ± 0.36 .

LMI reflects the balance between lymphocytes and monocytes and indicates the level of cell-phagocytic defense. On the 3rd day of treatment in the 4th group of clinically healthy animals, it was 7.15 ± 1.32 , and in the group of sick animals - 1.94 ± 0.15 , 2.03 ± 0.17 and 2.88 ± 0.12 in the 1st, 2nd and 3rd groups, respectively, at normal values of 5.80-7.20, which indicates pronounced monocytosis and lymphopenia with liver damage. On the 10th day, the indicators increased, but in the 1st and 2nd groups were outside the reference values (5.03 ± 0.58 and 5.21 ± 0.34 , respectively), and in the 3rd group they became within the physiological index (6.23 ± 0.69).

The primary processes of damage in the cell are associated with a change in the properties of its membranes, which leads to disruption of intracellular homeostasis. The result is the isolation of metabolic products (primary toxins) and the

onset of local damage processes. Filtration and adsorption processes are disrupted, which causes a change in the physicochemical state of the intercellular substance, an increase in the interstitial space, hypoxia and a violation of the humoral and nervous regulation of the cell. These changes further aggravate the disorders of intracellular homeostasis and are accompanied by the release of a large number of pathological metabolites [5, 7, 8, 48-52].

The value of such indices as LI and KI on the day of admission also indicates the presence of moderate intoxication in sick dogs, as well as a decrease in humoral immunity and an increase in the role of the cellular component of immunity. LI was equal to 0.19 ± 0.11 with a norm of 0.38-0.44, KI - 5.18 ± 0.77 with a norm of 1.34-2.26. On the 10th day of the study, the LI indicators increased and amounted to 0.33 ± 0.09 in the 1st group, 0.36 ± 0.03 in the 2nd, and 0.40 ± 0.05 in the 3rd. In turn, the KI indicators decreased in the 1st group by 2.1 times, in the 2nd group - by 2.3 times, and in the 3rd group - by 2.5 times.

CONCLUSION

Thus, as a result of our research, it was found that the determination of integral intoxication indices allows us to assess the general condition of the body without the use of special research methods. The calculation of such integral intoxication indices that based on a general blood test such as the Krebs index, leukocyte intoxication index, WBCS and LBSR in dogs with liver damage indicate the presence of endogenous intoxication. As a result of this, according to changes in the leukogram and taking into account other hematological parameters, one can judge the severity of the pathological process, especially during periods of exacerbation. In this case, the relief of the negative impact of intoxication as a pathognomonic symptom in hepatopathy, as well as the possibility of constant monitoring of therapeutic measures, will allow for full monitoring of the condition of sick animals. When comparing different treatment regimens, it was found that therapy using freshly frozen plasma allows you to quickly rid the body of intoxication and improve the condition of the animal. So, in the 3rd group, already on the 7th day, recovery to the reference values of NI (0.22 ± 0.15), LGI (3.17 ± 0.08), KI (2.26 ± 0.23) was observed. On the 10th day in the 3rd group of dogs, such indicators as LII, WBCS, LBSR, NMI, LMI returned to normal, while in other groups the values of these indices were outside the reference values.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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