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Influence of cadmium on the cellular part of the immune system of young cattle

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Contents

Abstract

The article presents the results of research on the effect of cadmium load on the body of young cattle. The negative effect of Cadmium on the liver causes a wide range of pathological changes at different levels of its organization. The impact of heavy metals on the immune system is particularly significant, because it performs a leading role in maintaining health and is recognized as one of the most sensitive to adverse factors, even in relatively low concentrations. The aim of the study was to investigate the influence of cadmium on the cellular part of the immune system of young cattle. The research was carried out on 10 bulls of six months of age, Ukrainian black-and-white dairy breed, which were formed into 2 groups of 5 animals each: control and experimental. The bulls of the control group were on a normal diet. Animals of the experimental group were administered cadmium chloride at a dose of 0.04 mg/kg body weight of the animal. It was found that feeding bulls with a diet of cadmium chloride, the number of B-lymphocytes on the 5th day of the experiment was 17.54 ± 0.95 %. The lowest number of B-lymphocytes was on the 20th day of testing – 15.12 ± 0.37 %. The study of the number of T-lymphocytes shows that at the beginning of analysis the number of T-lymphocytes in the blood of animals of the control and experimental groups ranged from 40.70 ± 3.62 and 40.85 ± 2.54 %. Subsequently, the number of T-lymphocytes in the blood of the experimental group began to decline. The lowest number of T-lymphocytes was in the experimental group of animals on the 20th day of the research, compared with the control group, this figure decreased by 3.63 %. The state of immunity of animals under cadmium load significantly depends on the ratio of T-helpers to T-suppressors. It was found that the immunoregulatory index of blood of bulls of the experimental group probably decreased from 10 days of the research. The number of T-helper lymphocytes in the blood of the experimental group of bulls under cadmium loading is probably reduced by 15, 20 and 30 days of testing. A probable increase in the number of T-suppressors was noted in the bull's blood of the experimental group on the 20th day of the research. Immunoglobulins of different classes are crucial among bull's serum proteins under cadmium loading. The concentration of immunoglobulins in the blood under cadmium load decreased by 15.9 % relative to the control group on the 20th day of analysis.

Key words: toxicology, heavy metals, cadmium, blood, immune system, lymphocytes.

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1. Introduction

Cadmium is one of the most toxic heavy metals. It belongs to the second class of danger – highly dangerous substances. Like many other heavy metals, cadmium has a pronounced tendency to accumulate in the body: its half-life is 10–35 years. Its total amount in the human body can reach 30–50 mg even up to 50 years. Cadmium in the body accumulates in the kidneys (30–60 % of the total) and liver (20–25 %). Cadmium is also found in the pancreas, spleen, tubular bones, other organs and tissues (Vorozhenko & Skalskyi, 2011; Gutyj et al., 2015).

Cadmium pollution is constantly increasing due to the intensive emissions of industrial enterprises. As a result, it also increases the contamination of soils and food products grown on them (Fregoneze et al., 1997). The body of animals is an important link in the food chain, where mainly heavy metals come from fodder, are absorbed and distributed to various organs and tissues (Ali et al., 1986; Salvatori et al., 2004; El-Shahat et al., 2009; Al-Azemi et al., 2010).

The results of many experimental research indicate that in mammals cadmium has a toxic effect on a number of organs and systems, including the cardiovascular, reproductive, excretory, respiratory, hematopoietic, musculoskeletal (Fregoneze et al., 1997; Rodríguez et al., 2001; Uetani et al., 2005; Gutyj et al., 2015). The most dangerous effects are carcinogenic and mutagenic effects of this element. It is known that under conditions of intoxication of animals with cadmium compounds, anemia occurs. Also suppression of the functional state of the immune system and other disorders of hematopoiesis develop (Honskyy et al., 2001; Gutyj et al., 2015; Gutyj et al., 2016).

The problem of the impact of heavy metals on the immune system is extremely important, as it plays a leading role in maintaining health and is recognized as one of the most sensitive to adverse effects, even in relatively low concentrations (Lu et al., 2005; Zinko, 2017).

The immune system is one of the most important homeostatic systems in the body, which determines the degree of the animals health, their adaptive capacity (Hariv et al., 2016; Khariv et al., 2017; Martyshuk et al., 2019). It is an indicator of the physiological state of the body, and clearly responds to changes in environmental conditions, the entry into the body of heavy metals, including cadmium (Liu et al., 2003; Lavryshyn et al., 2018; Ostapyuk & Gutyj, 2020). Violation of its function is considered as one of the pathogenetic mechanisms of the pathological process (Gajduk et al., 2016; Gutyj et al., 2017; Khariv et al., 2017). Immunotoxicity is defined as the property of a toxicant to cause dysfunction of the immune system, manifested by inadequate immune responses (Stojanovskyj et al., 2016; Slobodian et al., 2020). Immunotoxicity of heavy metals is considered in two aspects: the direct damaging effect of the substance on the immune system and the participation of the immune system in the implementation of the mechanisms of their toxic action (Lavryshyn et al., 2019; Ostapiuk & Hutyi, 2020).

The reaction of the immune system may be to the substance itself, its metabolites, complex antigens formed in the body during intoxication. The toxic effect of cadmium on the immune system is different in intensity and is aimed at different stages of immunogenesis (Ali et al., 1986; Uetani et al., 2005; Peng et al., 2015; Lavryshyn & Gutyj, 2019).

The aim of the study was to investigate the effect of cadmium on the cellular part of the immune system of young cattle.

2. Materials and methods

The research was conducted on the basis of a farm in the village of Ivanivtsi, Zhydachiv district, Lviv region on 10 bulls of six months of age, Ukrainian black-spotted dairy breed. two groups of animals were formed, five in each: control and experimental. The bulls of the control group were on a normal diet. The bulls of the experimental group were fed cadmium chloride at a dose of 0.04 mg/kg body weight of the animal.

To conduct research, the rules required for zootechnical experiments on the selection and maintenance of analogue animals in groups, technologies of harvesting, use and accounting of consumed fodder were followed. The diet of the animals was balanced in terms of nutrients and minerals, which provided their need for basic nutrients.

All animal manipulations were carried out following the European Convention on the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes (Strasbourg, 1986). and the “General Ethical Principles of Animal Experimentation,” adopted by the First National Congress on Bioethics (Kyiv, 2001). The experiments were carried out in accordance with the principles of humanity set out in the European Community Directive.

The experiment lasted for 30 days. Blood for analysis was taken from the jugular vein on the 5th, 10th, 15th, 20th and 30th day of the experiment.

Determination of the number of T-lymphocytes was carried out in the reaction of spontaneous rosette formation with sheep erythrocytes according to the method described below. Active rosette-forming lymphocytes with receptors capable of attaching sheep erythrocytes without incubation, theophylline-resistant (TGF) helper lymphocytes, which form rosettes after incubation with theophylline, were isolated. To determine B-lymphocytes, an EAC system (erythrocytes sensitized with antibodies and complement) was prepared by adding hemolytic serum to sheep erythrocytes (Vlizlo, 2012).

The Statistica 6.0 software package was performed for analysis of the research. The reliability of the difference between the groups was assessed by Student's t-test. The results were considered plausible at * – $P < 0.05$, **– $P < 0.001$ (ANOVA).

3. Results and discussion

In the research of the body's immune response under cadmium loading, it is important to examine the quantitative composition of leukocytes, and in particular T- and B-lymphocytes. They are the leading immunocompetent blood cells, as they characterize the level of the body's defenses and the state of specific immunity.

It was found that during feeding bulls with cadmium chloride fodder, the number of B-lymphocytes on the 5th day of testing was 17.54 ± 0.95 %. On the 10th day of the determination, the number of B-lymphocytes in the blood of animals of the experimental group decreased by 0.72 % relative to the values of the control group. It should be noted that the number of B-lymphocytes in the blood of the experimental group probably decreased from the 15th day of tasting, where compared with the control it fell to 1.19%, respectively. The lowest number of the studied indicator was on the 20th day of the experiment, where, respectively, was 15.12 ± 0.37 % (table 1).

Table 1
The number of B-lymphocytes in the blood of bulls under the influence of chronic cadmium toxicosis (M ± m, n = 5)

Blood test time (days)	B-lymphocytes (%)	
	Groups of animals	
	Control	Experimental
Initial values	17.06 ± 0.80	17.10 ± 0.65
5th day	17.11 ± 0.74	17.54 ± 0.95
10th day	17.07 ± 0.61	16.35 ± 0.47
15th day	17.06 ± 0.48	15.87 ± 0.40*
20th day	17.15 ± 0.50	15.12 ± 0.37*
30th day	17.13 ± 0.75	16.20 ± 0.95

Note: the degree of probability compared with the control group – $P < 0.05$ – *, $P < 0.001$ – **

It is important in the research of the cellular part of the immune system of animals to determine the number of T-lymphocytes. It was found that at the beginning of the analysis the number of T-lymphocytes in the blood of animals of the control and experimental groups ranged from 40.70 ± 3.62 and 40.85 ± 2.54 %. Subsequently, the number of T-lymphocytes in the blood of the experimental group compared with the control increased by 0.31 %. The lowest number of T-lymphocytes was in the experimental group of animals on the 20th day of the experiment, where compared with the control group, this figure decreased by 3.63 % (table 2).

The results of studies of the number of T-active lymphocytes in the blood of bulls of the experimental group indicate that the feeding of animals with cadmium chloride in a toxic dose reduces the amount of this indicator from 10 days of the research. It should be noted that the lowest number of T-active lymphocytes in the blood of bulls of the experimental group was on the 20th day of testing, where compared with the control group it fell to 4.39 % (table 3). On the 30th testing day, the number of T-active lymphocytes in the blood of the experimental group increased to 33.22 ± 1.10 % compared to the previous day.

Table 2
The number of T-lymphocytes in the blood of bulls under the influence of chronic cadmium toxicosis (M ± m, n = 5)

Blood test time (days)	T-lymphocytes (%)	
	Groups of animals	
	Control	Experimental
Initial values	40.70 ± 3.62	40.85 ± 2.54
5th day	41.25 ± 2.59	41.56 ± 3.25
10th day	40.94 ± 2.71	39.42 ± 4.11
15th day	40.85 ± 1.10	38,16 ± 1.85
20th day	41.10 ± 1.34	37.47 ± 1.65
30th day	41.14 ± 1.98	39.12 ± 2.88

Table 3
The number of T-active lymphocytes in the blood of bulls under the influence of chronic cadmium toxicosis (M ± m, n = 5)

Blood test time (days)	T-active (%)	
	Groups of animals	
	Control	Experimental
Initial values	35.15 ± 0.95	35.33 ± 0.86
5th day	35.23 ± 1.08	34.54 ± 1.00
10th day	34.95 ± 0.87	33.75 ± 0.95
15th day	34.74 ± 0.97	32.35 ± 0.85
20th day	35.21 ± 1.00	30.82 ± 1.05*
30th day	35.05 ± 0.99	33.22 ± 1.10

T-helpers are inducers of the immune response, they regulate its strength to a foreign antigen and control the stability of the body's internal environment. They also increase the production of antibodies.

It was found that the number of T-helper lymphocytes in the blood of the experimental group of bulls probably decreases by 15, 20 and 30 days of the research. Respectively, on the 15th testing day the number of the studied indicator in the blood of bulls of the experimental group fell to 1.73 %, on the 20th day – by 4.19 % and on the 30th day of the experiment – by 3.53 % compared to the control group (table 4).

Thus, a decrease in T-helper lymphocytes indicates an immune deficiency that develops in bulls under cadmium loading.

Table 4
The number of T-helpers in the blood of bulls under the influence of chronic cadmium toxicosis (M ± m, n = 5)

Blood test time (days)	T-helpers (%)	
	Groups of animals	
	Control	Experimental
Initial values	32.46 ± 0.84	32.39 ± 0.57
5th day	32.13 ± 0.95	31.47 ± 0.74
10th day	32.90 ± 0.75	30.81 ± 0.65
15th day	32.54 ± 0.90	29.67 ± 0.75*
20th day	32.30 ± 1.00	28.11 ± 0.56*
30th day	32.84 ± 0.76	29.31 ± 0.60*

Also important in the study of the cellular part of the immune system are T-suppressors, which are the most important mechanism for internal self-regulation of the immune system. Suppressor cells on the one hand limit the immune response to the antigen, thereby preventing the development of an allergic reaction, and on the other hand, prevent the possibility of autoimmune reactions.

Based on the studies, it was found that the number of T-suppressors in the blood of bulls with chronic cadmium toxicosis on the 5th day of the experiment increased by 0.58 %, and on the 10th day of the experiment – by 1.01 % relative to control values. A probable increase in the number of T-suppressors in the blood of bulls of the experimental group was noted on the 20th day of the research, where, respectively, they were 21.58 ± 0.35 %, while in the control this figure was 19.10 ± 0.49 % (table 5).

Table 5
The number of T-suppressors in the blood of bulls under the influence of chronic cadmium toxicosis (M ± m, n = 5)

Blood test time (days)	T-suppressors (%)	
	Groups of animals	
	Control	Experimental
Initial values	19.12 ± 0.52	19.10 ± 0.54
5th day	18.95 ± 0.60	19.53 ± 0.42
10th day	19.20 ± 0.51	20.21 ± 0.39
15th day	19.05 ± 0.59	20.86 ± 0.50
20th day	19.10 ± 0.49	21.58 ± 0.35*
30th day	19.15 ± 0.54	20.11 ± 0.50

The state of immunity of animals under cadmium loading significantly depends on the ratio of T-helpers and T-suppressors. It was found that the immunoregulatory index of the blood of bulls of the experimental group probably decreased from the 10th day of the experiment, and accordingly it was 1.52 ± 0.039 against 1.71 ± 0.080. At 15 and 20 days of the research, this indicator decreased, respectively, in the animals of the experimental group by 17.0 and 23.1 % compared with the control group (table 6).

Immunoregulatory blood index of bulls in the experimental group remained lower than in the control on the 30th testing day of. This decrease in the immunoregulatory index is characteristic of immunodeficiency states.

Table 6
Immunoregulatory index of blood of bulls under the influence of chronic cadmium toxicosis (M ± m, n = 5)

Blood test time (days)	Immunoregulatory index	
	Groups of animals	
	Control	Experimental
Initial values	1.70 ± 0.085	1.70 ± 0.075
5th day	1.70 ± 0.069	1.61 ± 0.046
10th day	1.71 ± 0.080	1.52 ± 0.039*
15th day	1.71 ± 0.075	1.42 ± 0.050*
20th day	1.69 ± 0.064	1.30 ± 0.060*
30th day	1.71 ± 0.070	1.46 ± 0.049*

Table 7
The concentration of immunoglobulins in the blood of bulls under the influence of chronic cadmium toxicosis (M ± m, n = 5)

Blood test time (days)	Immunoglobulins (g / l)	
	Groups of animals	
	Control	Experimental
Initial values	22.4 ± 0.65	22.3 ± 0.61
5th day	22.1 ± 0.64	21.4 ± 0.35
10th day	22.3 ± 0.59	20.3 ± 0.51*
15th day	22.4 ± 0.70	19.1 ± 0.57*
20th day	22.0 ± 0.64	18.5 ± 0.50*
30th day	22.2 ± 0.62	19.2 ± 0.49*

Immunoglobulins of different classes are crucial among the serum proteins of bulls under cadmium load. The special value of determining immunoglobulins in the blood of animals is that they are the end products of the B-system of immunity, and their concentration correlates with their resistance to diseases of various etiologies, including cadmium toxicosis.

The results of studies (table 7) showed that in bulls with cadmium toxicosis, the concentration of immunoglobulins probably decreases starting from the 10th day of the experiment, and compared with the control, this figure reduced by 9.0 %. The concentration of immunoglobulins in the blood of the experimental group was 19.1 ± 0.57 g/l, while in the control group – respectively 22.4 ± 0.70 g/l on the 15th day of the experiment

On the 20th day of the experiment, the concentration of immunoglobulins in the blood of bulls treated with cadmium decreased by 15.9 % relative to the control group.

The decrease in the concentration of immunoglobulins in the blood of bulls of the experimental group may be due to their intensive use in the neutralization of toxins that enter the body of animals.

Therefore, feeding cadmium chloride to bulls of the experimental group contributes to the suppression of the cellular part of the immune system.

4. Conclusions

Suppression of the cellular part of the immune system of young cattle during a 30-day load of cadmium. Suppression of the cellular part of the immune system of bulls is manifested by a decrease in the number of T- and B-lymphocytes in their blood. The state of immunity of animals under cadmium load significantly depends on the ratio of T-helpers to T-suppressors. It was found that the immunoregulatory index of the blood of bulls in the experimental group probably decreased throughout the experiment. In bulls with cadmium toxicosis, the concentration of immunoglobulins probably decreased from 10 days of the experiment, this is due to their intensive use in neutralizing toxins that enter the body of experimental animals.

Our studies have more deeply revealed the pathogenesis of the toxic effects of cadmium on the body of bulls and use these data to develop an antidote for cadmium intoxication.

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Conflict of interest

The authors declare that there is no conflict of interest.

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