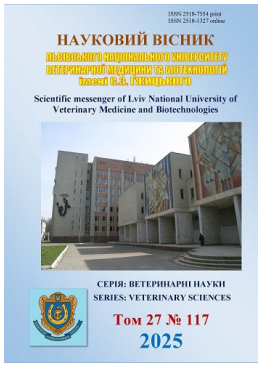

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The effect of fasciolosis invasion on the protein-synthesizing function of the liver in cows sensitized by atypical mycobacteria and the influence of corrective factors

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Among the most common parasitic pathologies in ruminants, trematode diseases, particularly fasciolіasis, occupy a leading position in terms of severity and the economic losses they cause. Both domestic and foreign literature also confirm that, alongside fascioliasis in cattle, mycobacteriosis has become widely spread. Therefore, the study aimed to determine the effect of Lipointersil and Cloverm A on the protein-synthesizing function of the liver in cows with experimental fascioliasis sensitized by atypical mycobacteria. Animals in the experimental groups were intramuscularly administered Cloverm A at 0.5 ml per 10 kg of body weight and Lipointersil at 10 ml per animal. The liposomal preparation "Lipointersil" contains interferon and the fruits of the milk thistle. It was established that in cows with fascioliasis, sensitized by mycobacteria, the protein-synthesizing function of the liver is suppressed, which is manifested by a 12.7% decrease in total protein levels, a 28.2 % decrease in albumin levels, and a 16.3 % increase in globulin levels in their blood. The preparations "Cloverm A" and "Lipointersil" contributed to the restoration of the liver's protein-synthesizing function, as Cloverm A causes the death of Fasciola. After the body is cleared of parasites, toxins no longer affect the liver, and inflammatory processes subside. Lipointersil, which contains milk thistle fruits, stimulates protein synthesis and normalizes liver function. Therefore, for effective treatment of cows with fascioliasis sensitized by atypical mycobacteria and to reduce side effects on the immune, antioxidant systems, and metabolism, it is recommended to use Cloverm A at a dose of 0.5 ml per 10 kg of body weight and Lipointersil at a dose of 10 ml per animal.

Key words: *fascioliasis, mycobacteriosis, milk thistle, interferon, clozaverm A, lipointersil.*

Introduction

Fasciolosis is a helminthiasis in domestic and wild animals caused by trematodes of the genus *Fasciola*, clinically and anatomically characterized by a predominantly chronic course and lesions of the hepatobiliary system (liver, bile ducts), sometimes affecting organs of other systems, causing anemia, hypoproteinemia, intoxication, reduced productivity, and a decline in product quality. The causative agents of the disease are two species of trematodes – *Fasciola hepatica* L., 1758 (common liver fluke) and *Fasciola gigantica* Cobbold, 1855 (giant liver fluke), from the family Fasciolidae Railliet, 1855 (Spithill et al., 1997; Kravchuk, 2014; Knubben-Schweizer & Torgerson, 2015; Mas-Coma et al., 2019).

The causative agents of fasciolosis are helminths, which develop using the organism of the final host (domestic and wild animals, sometimes humans), as well as intermediate hosts: the tiny pond snail (*Limnaea truncatula*) for *Fasciola hepatica*, and the ear-shaped pond snail (*Limnaea auricularia*) for *Fasciola gigantica* (Lalrinkima et al., 2021; Ponomarenko, 2023).

In Ukraine, this disease has been known for a long time. The first reports in the literature about fasciolosis in domestic animals appeared in the 19th century. A significant number of scientists have worked on the problem of studying the spread of fasciolosis in ruminants in Ukraine.

In particular, the specifics of the epizootology of helminthiasis in ruminants in Ukrainian farms are reflected in scientific papers (Sobolta & Hutyi, 2016; Avramenko et al., 2019).

In studying the epizootology of fasciolosis in ruminants, an important aspect is the investigation of the source and factors of transmission of the infection, as indicated by literature data (Berezovskyi & Koval, 2016; Berezovskyi & Hrytsyk, 2016). The primary source of the infection is a wide range of definitive hosts, namely carriers of mature Fasciola, which can contaminate the surrounding environment for up to 5 years. According to the authors, the infection of ruminants with Fasciola occurs when they consume grass from lowland and swampy pastures and meadows, fresh hay, and grass mown in such places (Roberts & Suhardono, 1996; Kuljaba et al., 2016). A rainy summer contributes to a sharp increase in the number of snails in the habitats of the tiny pond snail and the number of infected animals.

The preferred location of Fasciola is the bile ducts of the liver and the gallbladder. However, they can also be found in the lungs, heart, lymph nodes, and pancreas. Since fasciolas migrate within the infected animal's body, they can be found in many other organs during this period (Kravchuk, 2014; Dietrich et al., 2015).

The pathogenic effects of Fasciola on the animal's body consist of mechanical, inoculation, antigenic, toxic, and trophic effects. Through their movements and metabolic products, fasciolas irritate the lining of the bile ducts, initially causing acute and chronic inflammation. Such injuries are accompanied by bleeding, especially hepatic, and acute inflammation of the damaged organs. Due to acute hepatitis and progressing anemia caused by bleeding, infected animals may sometimes die (Chernushkin et al., 2020; Stybel et al., 2021).

The nature of liver damage in animals infected with fasciolosis was similar and depended on the stage of the disease. It was established that in the acute phase of the disease, the liver is significantly enlarged in volume, and the capsule is tense, shiny, and smooth. Under the capsule and within the liver, strands of dark red color are observed (Beesley et al., 2018; Gutyj et al., 2024). In the chronic phase of the disease, due to the proliferation of fibrous tissue in the interlobular connective tissue, the liver becomes dense in consistency. It was diffusely enlarged in some cases, while it had a lumpy surface in others. Due to the proliferation of fibrous connective tissue, the thickened walls of the bile ducts are visible. When cut, the parenchyma also had an uneven clay-brown color (Carmona & Tort, 2017).

Reports in both domestic and foreign literature also confirm that, alongside fasciolosis in cattle, mycobacteriosis has become widely spread (Kulyaba et al., 2017). The causative agents of mycobacteriosis in animals are so-called potentially pathogenic mycobacteria (atypical, anonymous, or unclassified), which are characterized by a broad spectrum of natural drug resistance (Baturo). Moreover, mycobacteriosis usually develops only in the weakened bodies of animals that have been subjected to unfavorable environmental conditions or the development of various diseases, including parasitic ones (Kuljaba et al., 2022). Despite the large number of studies dedicated to fasciolosis in cattle, issues such as the pathogenesis of fasciolosis in cows sensitized by atypical mycobacteria, their adequate therapy, and disease prevention require more in-depth scientific approaches.

The aim of the study

Our work aimed to determine the effect of lipointersil and clozaverm A on the protein synthesis function of the liver of cows with experimental fasciolosis sensitized with atypical mycobacteria.

Material and methods

For the experiments, 15 Holstein cows were selected and divided into 3 groups with five animals in each. During the research, the rules required for performing zootechnical experiments were followed, particularly regarding the selection and housing of analogous animals in groups and the technology of feed preparation, utilization, and accounting for the consumed feed. The animals' diet was balanced for nutrients and minerals, ensuring their need for essential elements of nutrition.

The control group (C) animals were infected with mycobacteriosis and fasciolosis. For the first experimental group (E_1), cows with experimental fasciolosis, sensitized by atypical mycobacteria, were intramuscularly administered Cloverm A at 0.5 ml per 10 kg of body weight. Cows in the second experimental group (E_2), sensitized by atypical mycobacteria with experimental fasciolosis, were intramuscularly administered Cloverm A at the same dose (0.5 ml per 10 kg of body weight) and Lipointersil at a dose of 10 ml per animal.

Housing, feeding, care, and all procedures involving the animals were carried out in accordance with the European Convention “On the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes” (Strasbourg, 1986) and the “General Ethical Principles of Animal Experiments”, adopted at the First National Congress on Bioethics (Kyiv, 2001). The experiments were conducted following the humane principles outlined in the European Community Directive.

The protein-synthesizing function of the liver was determined by the level of total protein (biuret reaction) and protein fractions (electrophoresis method in polyacrylamide gel) in the blood serum (Vlizlo, 2012). Blood samples were taken from the jugular vein before infection and on the study's 7th, 14th, 21st, and 28th days.

Data analysis was performed using the Statistica 6.0 software package. The significance of differences was evaluated using Student's t-test. The results of the mean values were considered statistically significant at *– $P < 0.05$ (ANOVA).

Results and discussion

The condition of the protein-synthesizing function of the liver was studied based on the level of total protein, which reflects protein metabolism and the overall protein content in the blood serum. Plasma proteins are divided into groups with different structures and functions, known as protein fractions. Among these, albumins, alpha, beta,

and gamma-globulins are distinguished. Determining and evaluating their ratios allows a more accurate assessment of the dysfunctions in internal organs.

Measuring total protein in blood is one way to evaluate the physical state of animals. The total protein test shows the amount of protein in the blood serum. Generally, the level of total protein or changes in certain types of globulins is assessed, as these are associated with the development of various diseases. This helps diagnose the disease, monitor changes in health status, and indicate the need for further tests.

Our experiments (Table 1) established that in cows with experimental fasciolosis sensitized by atypical mycobacteria, the level of total protein in the blood serum decreased. On the 14th and 21st days of the experiment, the level of total protein decreased by 9 % and 12.7 %, respectively, compared to the initial values.

The presence of two main protein groups, albumins and globulins, was quantitatively assessed. The study of protein fractions revealed that the albumin level in the blood of cows from the control group on the 21st day of the study decreased to 31.15 ± 1.28 g/L, while the globulin level increased to 31.07 ± 1.09 g/L.

Thus, in cows with experimental fasciolosis sensitized by atypical mycobacteria, the synthesis of albumins in the liver is suppressed due to the toxins released by the Fasciola and mycobacteria.

In the first experimental group (E_1), treated with the drug “Clozaverm A”, a gradual increase in total protein levels in their blood was observed throughout the experiment. On the 14th day of the study, the total protein level in the blood of the first experimental group increased by 5.5 %, and on the 21st day, it increased by 7.3 % compared to the control group.

When using the liposomal drug “Lipointersil”, a significant increase in the total protein level was observed. Specifically, on the 14th day, the total protein level in the blood of the second experimental group of cows significantly increased to 69.17 ± 1.46 g/L, while in the control group, this figure was 63.72 ± 1.32 g/L. The highest level of total protein was recorded on the 21st and 28th days of the study, where, compared to the control group, it increased by 14.5 % and 11.8 %, respectively.

The insufficient recovery of the total protein level in cows treated only with Clozaverm A is due to the low level of albumins in their blood. Their levels on the 14th and 21st days of the study ranged from 39.23 ± 1.01 to 38.26 ± 1.22 g/L. However, compared to the control group, the albumin level in the first experimental group was higher by 13.8 % and 22.8 % on these days, respectively. On the 28th day, the albumin level in the blood of cows in the first experimental group was 39.14 ± 1.15 g/L, while in the control group, it was significantly lower at 33.66 ± 1.09 g/L.

With the combined use of Clozaverm A and the liposomal drug “Lipointersil”, a slightly higher albumin level was found. On the 14th and 21st days of the study, the albumin level in the second experimental group increased by 21.7 % and 38.6 %, respectively, compared to the control group. On the 28th day of the study, the albumin level reached physiological values, with a final level of 43.48 ± 1.35 g/L.

Table 1

The effect of Lipointersil and Clozaverm A on the protein-synthesizing function of the liver in cows with experimental fasciolosis sensitized by atypical mycobacteria (M ± m; n = 5)

Indicator	Animal groups	Before infection	Research period (days)			
			7	14	21	28
Total protein, g/L	C	70.12 ± 1.55	68.04 ± 1.29	63.72 ± 1.32	61.22 ± 1.49	62.93 ± 1.43
	E_1	70.21 ± 1.47	69.38 ± 1.57	67.24 ± 1.53	65.68 ± 1.49	67.18 ± 1.54
	E_2	70.28 ± 1.32	70.13 ± 1.53	69.17 ± 1.46*	70.11 ± 1.37**	70.34 ± 1.51*
Albumin, g/L	C	43.40 ± 1.27	38.16 ± 1.32	34.47 ± 1.24	31.15 ± 1.28	33.66 ± 1.09
	E_1	43.48 ± 1.19	41.33 ± 1.25	39.23 ± 1.01*	38.26 ± 1.22**	39.14 ± 1.15**
	E_2	43.43 ± 1.12	42.14 ± 1.17	41.96 ± 1.28**	43.17 ± 1.31***	43.48 ± 1.35***
Globulin, g/L	C	26.72 ± 1.05	29.88 ± 1.00	29.25 ± 1.14	31.07 ± 1.09	30.27 ± 1.17
	E_1	26.73 ± 0.99	28.05 ± 1.13	28.01 ± 1.18	27.42 ± 1.11*	28.04 ± 1.20
	E_2	26.82 ± 1.07	27.99 ± 1.21	27.21 ± 1.07	26.94 ± 1.10*	26.86 ± 1.14*
A/G ratio	C	1.62	1.27	1.18	1.00	1.11
	E_1	1.63	1.44	1.40	1.40	1.40
	E_2	1.62	1.51	1.54	1.60	1.62

As seen from the data in Table 1, in cows with experimental fasciolosis sensitized by atypical mycobacteria, the use of experimental drugs contributed to a decrease in the level of globulins in the blood of both experimental groups. Thus, in the first experimental group's blood, the globulins level on the 14th day of the study was 28.01 ± 1.18 g/L, while in the control group, this value was 29.25 ± 1.14 g/L. On the 28th day of the study, the globulin level was the lowest, but it did not reach the physiological range.

The level of globulins in the blood of the second experimental group fluctuated between 27.99 ± 1.21 and 26.86 ± 1.14 g/L from the 7th to the 28th day of the study. Starting from the 21st day of the study, the level of globulins was within the physiological range. On the 28th day of the study, the globulin level in the blood of the second experimental group of animals treated with Clozaverm A and Lipointersil was 11.3 % lower compared to the control group at this study stage.

An important indicator of liver functional status is the albumin-to-globulin (A/G) ratio. The smaller it is com-

pared to the optimal value, the more significant the reduction in the protein-synthesizing function of the liver in animals. As shown in the data from Table 1, in cows treated with the drug “Clozaverm A”, the A/G ratio gradually normalized. However, by the 28th day of the study, it remained 14.4 % lower than the initial values measured before the invasion. The use of Clozaverm A and Lipointersil in the second experimental group of animals contributed to an increase in the A/G ratio, so on the 21st and 28th days of the study, it was 60 % and 45.9 % higher, respectively, compared to the control group of cows.

Conclusions

In cows with fasciolosis and sensitized by mycobacteria, the liver's protein-synthesizing function is suppressed, manifested by a decrease in the total blood protein, a reduction in albumin levels, and an increase in globulin levels.

The drugs “Clozaverm A” and “Lipointersil” contributed to the restoration of the liver's protein-synthesizing function because Clozaverm A causes the death of Fasciola. After the body is freed from the parasites, their toxic effects on the liver cease, and the inflammatory processes disappear. Lipointersil, which contains milk thistle fruit, stimulates protein synthesis and normalizes liver function.

Conflict of interest

The authors declare that there is no conflict of interest.

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