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EFFICACY OF THIONONTRITE-S FOR PREVENTION OF METABOLIC LIVER DISEASE IN CATTLE

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SUMMARY

The data of the efficacy study of Thionontrite-S-complex preparation in the prevention of metabolic liver disease in cattle are presented. Use of the preparation in 6–7-month-old cows in dry period for two weeks at the dose of 0.3 g/kg body weight corrects biochemical homeostasis and prevents the development of pathogenetic shifts resulting from metabolic liver disorders. The symptoms faded on Day 12–14, preventive efficacy was 90%. In the control group 55% of cows demonstrated the disease symptoms. The use of Thionontrite-S promoted an increase in liver protein-synthesizing function; in particular, an increase in total protein level was 8.8% against the baseline values in the experimental group. The increase in glucose level compared to baseline values in the experimental group was 26.6%, in the control group this parameter decreased by 6.7%. The preparation restored liver functional and barrier properties, normalized the enzyme production. At the end of the experiment the level of alanine aminotransferase in the first group was 1.8 times lower than the control levels, the level of aspartate aminotransferase was 1.6 times lower than the negative control levels. The positive effect of Thionontrite-S was also observed with regard to pigment metabolism; the concentration of total bilirubin in the experimental group was within physiological limits (4.28 ± 0.55 μM/l), whereas in the control group hyperbilirubinemia was 1.6 times higher than the upper normal limits. Improvement of biochemical parameters in the experimental group correlated with the decrease in the level of medium-mass molecules and peroxidation products of unsaturated fatty acids. The decrease in the level of medium weight molecules in experimental cows at λ = 254 nm wavelength was 8.3% and at λ = 280 nm wavelength nm was 10%. In the experimental group, the level of conjugated dienes decreased by 14.3% with regard to baseline values, of ketodienes – by 26.3%, of malondialdehyde – by 8.9% and of fluorescent Schiff bases – by 18.2%.

Key words: cattle, Thionontrite-S, prevention, liver.

INTRODUCTION

To achieve sustainability in modern livestock production intensive, high-concentrate diet is fed. Due to this fact, the organism synthesizes proteins intensely and the liver is stressed greatly. Moreover, lack of mineral substances, unsystematic use of antibiotics and other chemical medicinal products as well as feeding with low quality feeds containing mycotoxins, xenobiotics and other toxicants lead to hepatocyte functional disorders. Degenerative changes start developing in the liver, its barrier function decreases, metabolic process totally fails ultimately leading to decrease in natural resistance, high morbidity, diminished performance and animal cull. Profound metabolic disorders facilitate accumulation of toxic metabolites in the organism causing significant changes in homeostasis biochemical values [3, 4, 6].

Clinical signs of metabolic liver disease in cattle are observed during enhanced stress period for the organ, that is starting from Month 6–7 of the dry period up to the calving as well as during maximum gluconeogenesis (maximum lactation). If high-concentrate diet is continued and management conditions are violated, the liver, most important organ for the elimination of toxins and metabolites thereof, ceases to cope with an enhanced stress, contributing to the occurrence of severe diseases like hepatopathy, fatty liver disease, cirrhosis, etc. [1, 3].

Massive culling (30% and more) of 1–3-lactation cows are reported due to metabolic diseases (ketosis, rumen acidosis, fatty liver disease, etc.). The death rate or the percentage of emergently killed cows is about 40% from the total death rate [1, 2].

As it is almost impossible to avoid the effects of stress on animal organisms, the only way out here is to influence on it during the period of enhanced stress in order to keep the organism at the adaptation stage and prevent emaciation. In this context, it is feasible to use pathogenetic complex absorbing and detoxicating preparations, which

enable to lower the damaging effect on liver and activate reparation processes in hepatocytes [5, 7].

Up to date wide experiments in use of natural stratified-structured aluminosilicates (montmorillonites) to normalize metabolic processes in animals, have been carried out [2, 4, 5]. In the course of the abovementioned experiments, it was established that montmorillonites possess several unique properties, including adsorbing, buffer, ion-exchanging and catalytic ones, and contain almost all mineral macro- and microelements, necessary for birds and animals [5].

In order to potentiate sorbate and detoxicating properties of nontronite-based natural aluminosilicate (iron montmorillonite) a new preparation, Thionontrite-S, was developed and tested for its efficacy in prevention of bovine metabolic liver disorders by the Pharmacology Department of the Krasnodar Scientific and Research Veterinary Institute.

MATERIALS AND METHODS

Thionontrite-S preventive efficacy against metabolic liver disorders was studied in comparison to a positive (analogous preparation) and a negative controls in three cow groups ($n = 20$) being in the dry period for 6–7 months, selected based on their body weight and performance.

Group 1 of experiment cows received Thionontrite-S for two weeks at the dose of 0.3 g/kg of boody weight, Group 2 (positive control) was given bentonite at the same dose and Group 3 (control group) animals were not treated at all. Management conditions (standard buildings, free ranging) and diets of all cows (mixed feeds, haylage, silage, hay, water from automated drinking bowls) were analogous and the farm was free from any infectious and invasive diseases.

Daily clinical examination was performed in the course of the experiment, paying attention to the disease symptoms; physiological condition based on biochemical blood parameters was assessed in the beginning and in the end of the study. Changes in biochemical parameters, in particular in liver pathology markers – transaminases (alanine aminotransferase, aspartate aminotransferase, bilirubin and thymol test) are more typical for metabolic liver disorders, than such clinical signs as depression, low appetite, rare and slow chewing, hypotonia, dyspeptic signs, liver painfulness during percussion and palpation, dingy and brittle hair), which can be slight or not manifested at all.

One of the effect factors of different endo- and exotoxins on liver cells is the increase in medium mass molecules (MMM) level in blood, which reaches its maximum during the peak intoxication. Analysis of MMM levels contributes a lot to understanding of processes occurring in the body due to different metabolic changes resulted from metabolism failure.

Taking into account that MMM level is considered an intoxication universal marker and is one of the most informative and easiest ways to assess the intoxication level and treatment efficacy for many metabolic body conditions, the level of medium molecular peptides in sera of test animals at different wave lengths was determined. Endogenous intoxication level was determined using the technique by N. I. Gabrielyan and B. I. Lipatova.

The genesis of many body conditions involves an universal non-specific element, which is the damage of cell membranes due to lipid peroxidation; that's why the peroxidation product concentration is one of the most important criteria, indicative of the homeostasis in all body systems. In this light unsaturated fatty acid peroxidation products were studied in bovine blood: primary – conjugated dienes (CD) and ketodienes (KD); secondary – malondialdehyde (MDA); and final – fluorescent Schiff bases (FSB).

The values of lipid peroxidation - antioxidant defense system were assessed in accordance with Methodical Guidance on Lipid Peroxidation and Antioxidant Defense System Analysis in Animals (VNIVIPFiT, 1997).

Laboratory biochemical tests were carried out using VitalabFlexor automated biochemical analyzer (the Netherlands).

RESULTS AND DISCUSSION

In the course of the experiment, the efficacy of Thionontrite-S against metabolic liver disorders in cows was established. The use of the preparation adjusted the homeostasis to a certain extent and prevented the development of pathogenetic shifts caused by metabolic liver disease; and this was expressed as a decrease in toxic manifestations and improvement of clinical conditions of test cows.

Two cows in Test Group 1 showed clinical signs on Day 6–8 and symptoms faded on Day 12–14, whereas in Test Group 2, in which an analogous drug was given to the animals, symptoms in diseased cows (four animals) faded on Day 16–18. Herewith the prevention efficacy in Group 1 was 90% and in Group 2 – 80% to the end of the experiment.

In control group symptoms were registered in 11 cows (55%); animals were depressed, had a lower appetite, some cows demonstrated hypotonia signs (less than 3 rumen contractions per 5 minutes), diarrhea.

Thionontrite-S administration normalized metabolic liver processes thus facilitating protein synthesis function improvement and enzymatic transamination system transformation. Increase in total protein level in test group animals compared to baseline values was 8.8%, which was 5.1% higher than a positive control. It should be noted that the increase in this value in cows of Groups 1 and 2 was within reference values, whereas control group cows showed dysproteinemia, expressed as hypoproteinemia (in 40% animals) and hyperproteinemia (in 45% animals), which correlated with the increase in gamma globulin fraction (by16.6%) and decrease in albumens (by 11%).

The development of mesenchymal inflammatory syndrome in control animals leading to enhanced gamma globulin fraction synthesis was confirmed by thymol turbidity test (test, which enables to detect changes in serum protein spectrum). Such deviations in serum protein spectrum of control cows are typical for liver failure.

Thyonontrite-S-caused reparative effect on liver metabolic functions manifested as a decreased level of indicator enzymes compared to the controls. At the end of the study alanine aminotransferase level in Group 1, in which cows were treated with Thyonontrite-S, was statistically ($p \leq 0{,}01$) the lowest: 31.4 ± 4.11 U/l, 12.3% lower than Group 2 values and 1.8 times lower than in controls. Drug normalizing effect on enzyme production by liver in test cows was also confirmed by statistically lower values of aspartate transaminase: 86.2–101.3 U/l, that is 36.9% lower compared to control analogues and 1.6 times lower than negative control.

In control group in addition to decrease in hepatocyte activity, transferase (indicator enzyme) level grew sig-

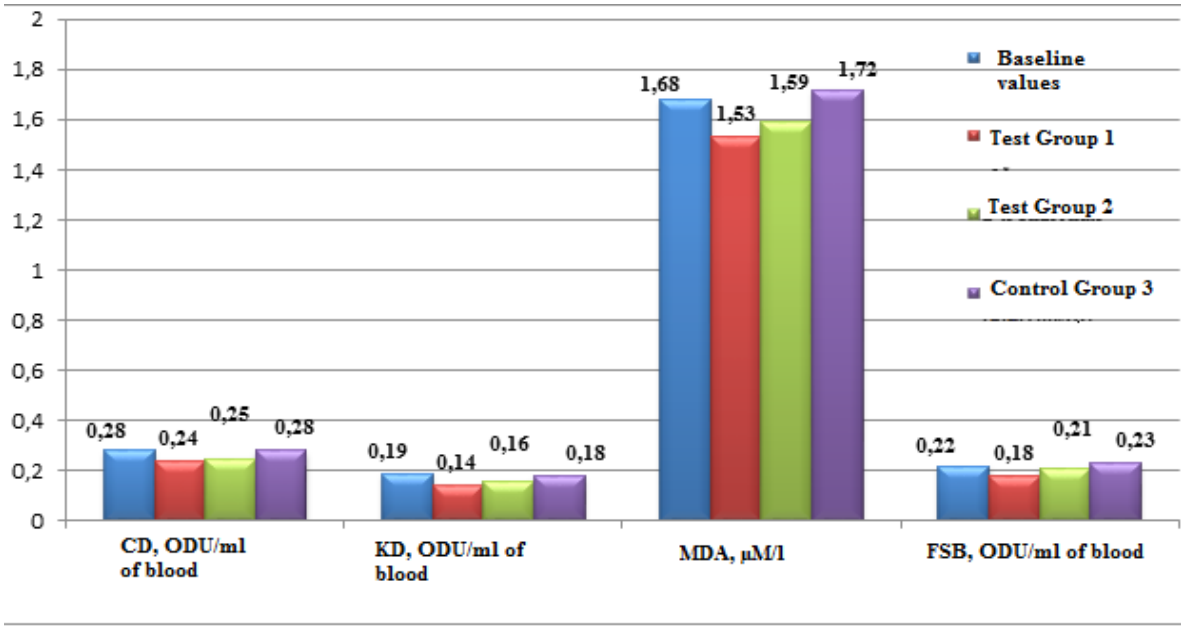

Fig. Lipid peroxidation product dynamics when using Thionontrite-S and Bentonite in cows for metabolic liver disease prevention (n = 20)

nificantly: 1.9 times for alanine aminotransferase and by 11.6% for aspartate transaminase.

Thyonontrite-S had a positive effect on pigmentary exchange too; when using the drug bilirubin concentration was within physiological limits (4.28 ± 0.55 μM/l), whereas hyperbilirubinemia was registered in control group, which was 1.6 times higher than upper normal limits.

The preparation also stabilized carbohydrate and lipid metabolism. Increase in glucose level against baseline values was equal to 26.6%, which was 11.8% more than positive control value. In negative control this value lowered by 6.7% due to intoxication. Thionitrite-S and Bentonite preventive administration optimized cholesterol and triacylglycerol content with better parameters shown by group 1 cows, 17.1 and 24% increase correspondingly, 7.9 and 3.3% higher than analogous values in group 2 animals.

The drug under study corrected calcium - phosphorus metabolism in test cows, manifested by 9.1% decrease in inorganic phosphorus level in sera and increase in total calcium by 23.8%, whereas calcium to phosphorus ratio in test cows was lower than species norm.

The decrease in hepatocyte activity of test cows also led to reduction in urea production: urea level at the end of the study was 1.5 times lower than baseline values. Urea levels in the test group and positive control group varied within physiological limits (5.0–5.4 mM/l).

Improvement of biochemical parameters in the test group correlated with the decrease in MMM level (indicators of pathological process severity) which serves as a prognostic criterion of metabolism failure. It was equal to 8.3% at λ = 254 nm wave length and 10% at λ = 280 nm wave length, which was lower than in animals treated with an analogous preparation by 12 and 14.3%. In the control group the development of pathological changes in parallel to a biochemical status breakdown was confirmed by MMM concentration enhancement (by 20.8% at λ = 254 nm, by 25% at λ = 280 nm).

The most well pronounced positive effect on parameters, indicating lipid peroxidation intensity was noted in cows after Thionitrite-S treatment. It was manifested by decrease in all lipid peroxidation product concentration (see Figure below).

Specifically CD level was by 14.3%, KD by 26.3%, MDA by 8.9% and FSB by 18.2% lower compared to baseline values and by 14.3; 22.2; 11.0 and 21.7% correspondingly lower compared to controls. In Bentonite-treated group, the decrease in unsaturated fatty acid peroxidation product level was less pronounced in dynamics: CD by 14.3%, KD by 15.8%, MDA by 5.4% and FSB by 4.5%.

CONCLUSION

Thus, the results of tests showed that use of Thionontrite-S for metabolic liver disorder prevention in cows contributes to animal health status improvement, blood biochemical picture normalization and liver function recovery.

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