

# Molecules of Medium Mass as an Integral Indicator of Endogenous Intoxication in the Diagnosis of Hepatopathy and its Effect on Improving the Economic Efficiency of Veterinary Measures in the Field of Dairy Farming

M.P. Semenenko<sup>1</sup>, E.V. Kuzminova<sup>1</sup>, E.V. Tyapkina<sup>1</sup>, A.A. Abramov<sup>1\*</sup>, K.A. Semenenko<sup>2</sup>

<sup>1</sup>Federal State Budget Scientific Institution "Krasnodar Scientific Research Veterinary Institute", Krasnodar, Russia

<sup>2</sup>Kuban State Agrarian University named after I.T. Trubilin, Krasnodar, Russia

## Abstract

The article represents results of studies of the concentration of medium-mass molecules (MMM) in the blood serum of cattle in healthy animals and in various pathological conditions of hepatobiliary system. As a result the decrease rate in MMM can serve as a prognostic criterion for assessing the severity of the pathological process in liver of animals and can be a marker of effectiveness of the treatment and disease prognosis, that allows to increase significantly the economic efficiency of veterinary measures in the dairy industry.

**Key words:** medium-mass molecules (MMM), cattle, hepatopathies, endotoxiosis

## INTRODUCTION

Today one of the serious problems of animal breeding is the growth of the number of hepatopathies. Liver, as the central organ of metabolic processes, organ of exchange of a number of hormones, vitamins, enzymes and trace elements and organ of neutralization of endogenous and exogenous toxins, often does not withstand the functional load, that results in the development of hepatodystrophic processes. Livestock farming suffers tremendous economic damage from hepatopathy due to a loss of animals, decrease in productivity, reproductive capacity, resistance, development of many infectious and non-communicable diseases against this background, as well as an increase in the direct material costs of conducting therapeutic and prophylactic measures [1].

Hepatopathy affects all farm animals, fur-bearing ones, dogs, and poultry. This disease affects animals with high productivity more often than the others, which is associated with a greater intensity of metabolic processes in their body [2].

Clinical features of hepatopathies are not pronounced in nature but manifested in decrease in appetite, rare and lethargic cud, hypotension of fore-stomachs, and in increase in the percutaneous boundaries of liver, some pain during palpation, obesity (in some cases, thinning), demineralization of bone tissue followed by softening of the last caudal vertebrae and transverse processes of the lumbar vertebrae, dullness and fragility of hair. The weight of liver increases to 22 kg, when normal rate is 9-10 kg. The task is complicated by the fact that liver plays a multifaceted role in metabolic processes, intermediate metabolism, biosynthesis and disintegration of a huge amount of substances, as a result of which symptoms of the liver disease do not allow to make an accurate diagnosis caused by hepatopathy [3].

Early and accurate diagnosis of liver disease is an important criterion for assessing the functional state of this organ in farm animals [4].

That is why one of the new diagnostic methods for assessing the development of the pathological process in liver hepatocytes in highly productive animals can be the determination of the level of endogenous intoxication in an organism [5].

In recent years, the study of the syndrome of endogenous intoxication (EI) plays an important role. Endotoxemia develops in all pathological conditions associated with increased catabolism or blockade of the body's detoxication systems. As a substrate, that is responsible for the occurrence of pathological effects of endogenous intoxication in renal and hepatic insufficiency, are considered to be protein toxins - medium molecular peptides (MMPs) or medium-mass molecules (MMM). The chemical composition of MMM is very heterogeneous and includes peptides, glycopeptides, nucleopeptides, endorphins, amino sugars, polyamines, polyhydric alcohols, some humoral regulators - insulin, glucagon, some vitamins, nucleotides, oligosaccharides, glucuronic acid derivatives and others that are endopathogenes and have a damaging effect on various structures of a living organism.

An important feature of MMM is their distinctly expressed high biological activity. Accumulation of MMM is not only a marker of endointoxication, they further aggravate the course of the pathological process, acquiring the role of secondary toxins, affecting the vital activity of all systems and organs of the body.

Nowadays the biological effect of MMM has been studied in sufficient detail. Many of them possess neurotoxic activity, inhibit the processes of protein biosynthesis, inhibit the activity of a number of enzymes, disentangle the processes of oxidation and phosphorylation, disrupt the regulation of the synthesis of adenylyl nucleotides, alter the transport of ions through membranes, erythropoiesis, phagocytosis, microcirculation, lymphodynamics, induce a state of secondary immunodepression [6].

MMPs are able to connect and block receptors of any cell, not adequately affecting its metabolism and function. They

can penetrate through the placental barrier, having a direct toxic effect on the fetus, causing polyorganic disturbances of a different nature [7].

Endotoxemia in medicine is recognized as a fundamental factor in the development of multi-organ and multisystem insufficiency, determining height and outcome of the disease, and occupies one of the leading positions in the structure of the study of pathological conditions. However, in veterinary science such studies are scarce and only recently the term "endogenous intoxication" begins to penetrate from human to veterinary medicine. For this reason, there are still no established norms for the types of animals and age groups, as well as scientific data on the diagnosis of endotoxemia in various pathological conditions (including hepatopathies) and the possible application of these tests in veterinary medicine in order to improve the economic methods of organizing of veterinary services. Economic analysis of the effectiveness of veterinary measures in modern conditions becomes important, since it characterizes the end result of the work of veterinary medicine specialists. Applying the system of economic indicators, it is possible to develop more effective measures to prevent damage from hepatopathology in animals and to solve problems related to providing the population with food.

The main aim of the study was to assess the level of medium-mass molecules in the blood of healthy animals (dairy cows) and animals with pathology of liver of various genesis.

#### METHODOLOGY OF RESEARCH

For the diagnosis we used the method proposed by N.I. Gabrielyan, V.I. Lipatova (1984). The principle of the method is based on the change in the optical density of blood serum released from coarsely dispersed proteins in proportion to the number of molecules of medium weight, and consists in the precipitation of proteins with a solution of trichloroacetic acid, followed by the determination of MMM by direct spectrophotometry of deproteinized supernatant, at wavelengths of 254 nm and 280 nm. The D254 indicator is considered as an integral criterion for the content of UV absorbing substances of low and medium molecular weight from 500 to 5000 D, to which in addition to peptides about 200 compounds of normal and abnormal metabolism are classified.

To study the average molecules 1,0 ml of blood serum was placed in a centrifuge tube, a 10% TCA solution of 0,5 ml was added, thoroughly mixed and after 5 minutes centrifuged for 30 minutes at 3000 rpm. Then 0,5 ml of the supernatant was transferred to a tube with 4,5 ml of distilled water and spectrophotometric measurements were carried out at a wavelength of 254 and 280 nm in a 1 cm cuvette against distilled water after mixing.

#### RESULTS

The results of studies of blood serum of large horn-cattle (n = 100) allowed to establish the following levels of values of medium-molecular peptides:

In healthy animals, the level of MMM did not exceed 0,185 AU (the limits of variation were from 0,010 to 0,185 AU),

and their concentration above this indicator showed the presence of signs of endogenous intoxication in animals.

The most marked changes in the concentration of blood MMM occurred in diseased animals with hepatocellular integrity disorder and inflammatory syndrome (the concentration of MMM increased in several times from 0,284 to 0,963 AU).

In cows with hepatic-cellular insufficiency syndrome the level of MMM increased insignificantly (up to 0,270 AU).

A similar picture was observed with cholestatic syndrome. In some cases the MMM indices did not practically exceed the upper limits of the conditional norm, there were approximately 0,195-0,260 AU.

However, there was a direct relationship between the concentration of MMM in blood and the severity of the pathological process. The persistent increase of MMM level in liver pathology, despite the improvement of a number of biochemical indicators, may be a sign of an unfavorable outcome of the disease.

#### DISCUSSION

We have encountered only a single publication on the use of the determination of medium-mass molecules as a marker of endogenous intoxication in gastrointestinal pathology [8]. Although the value of determining the content of MMM is an inexpensive and informative method for assessing the health status of animals, it was strongly correlated with other laboratory tests [9]. At the same time, the rate of decrease in MMM can serve as a prognostic criterion for assessing the severity of the pathological process in the liver of animals and be a marker of the effectiveness of the treatment and the prognosis of the disease. In animals with diagnosed chronic liver pathology the regular determination of the level of medium molecules during the remission period will allow foreseeing the development of relapse and conduct a preventive therapy.

#### CONCLUSION

In the conditions of market relations, the veterinary measures to be carried out should not only be expedient, effective, but also cost-effective, financially viable and profitable for the owners of animals, and also profitable for the veterinary service.

In this case, the definition of the level of MMM, along with the generally accepted laboratory tests, will allow not only to evaluate the rationality of the treatment, to predict its duration and intensity and to monitor its success in the treatment process, but also to ensure a high payback of therapeutic measures.

#### REFERENCES

- [1] Semenenko, M.P., Kuzminova, E.V., Onishchuk, F.D., Tyapkina E.V. Etiopathogenesis and features of hepatotropic therapy of cows in hepatitis. *Veterinary Medicine*. 2016, 4, 42-46.
- [2] Antipov, V.A., Semenenko, M.P., Basova, N.Yu., Turchenko, A.N., Sapunov, A.Ya., Kuzminova, E.V. et al. Increasing safety and productivity of imported dairy cattle. Krasnodar, 2009.
- [3] Semenenko, M.P., Kuzminova, E.V., Fomin, O.A. New approaches to laboratory diagnostics of liver diseases in highly productive dairy cattle. *Kuban Veterinary Medicine*. 2014, 3, 11-13.
- [4] Kuzminova, E.V., Semenenko, M.P., Starikova, E.A., Mikhalev, T.V. Diagnostic value of biochemical blood indices in hepatopathology. *Kuban Veterinary Medicine*. 2013, 5, 11-13.

- [5] Chernitsky, A.E., Sidelnikova, V.I., Retskiy, M.I. Modified method for the determination of medium molecular peptides in biological fluids. *Veterinary Medicine*. 2014, 4, 56-58.
- [6] Matveev, S.B., Fedorova, N.V., Godkov, M.A. Integral assessment of endogenous intoxication in emergency conditions. *Medicine of Critical States*, 2009, 6, 26-31
- [7] Dzhurtubaeva, D.I. The state of medium-molecular peptides of blood plasma in acute, chronic viral hepatitis and cirrhosis of the liver: the dissertation author's abstract on the scientific degree of candidate of medical sciences. Nalchik, 2003, 23.
- [8] Borchenko, R.V, Kiseleva, R.E., Makogon, I.P. The binding capacity of albumin and the concentration of medium-mass molecules in the calf blood serum in diarrhea. *Agricultural Biology*, 2007, 2, 82-86.
- [9] Gidulyanov, A.A. Molecules of medium mass as biomarkers for the estimation of anthropogenic pollution of the environment. *Ecosystems, their optimization and protection*. 2014, 10, 186-188.