

Research Article**Correction of the functional state of hemostasis in piglets who have undergone prolonged transportation****L. P. Solovyova^{1*}, T.V.Kalysh¹, A. L. Kryazhev²,****Yu. A.Voevodina² and V. I. Zamuravkin¹**¹Kostroma State Agricultural Academy, Kostroma, Russia²Vologda State Dairy Farming Academy named after N.V. Vereshchagin,
Vologda, Russia

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ABSTRACT**Objective:** to determine the dynamics of platelet activity, hemocoagulation and fibrinolysis in piglets who have undergone prolonged transportation during the use of fumaric acid in them.**Material and methods:** The work was performed on healthy piglets of the large white breed at the age of 2 months. The experimental group was made up of 56 animals that transferred long-term transportation in a closed van from the breeding pig farm of the Kostroma State Agricultural Academy to the farms of the Kostroma region of Russia after they were sold for further cultivation. The control group consisted of 27 healthy piglets of 2 months of age, a large white breed contained in the standard conditions of the breeding pig farm of the Kostroma State Agricultural Academy and did not tolerate transportation. In work hematologic and statistical methods of research are applied.**Results:** Adverse environmental effects are often able to disrupt the overall functional state of the body of piglets and reduce their viability. Markers of these disorders are changes in the activity of the components of hemostasis. Platelet activity and coagulation hemostasis are very sensitive to the negative effects of the environment, responding to the development of hemostasis. This leads to worsening of hemocirculation in small vessels and weakening of tissue trophism. These changes lead to inhibition of growth and weakening of pigs, thereby causing serious economic damage. The study found that transport stress in piglets is accompanied by excessive platelet aggregation in response to adenosine diphosphate, increased hemocoagulation, and weakening of fibrinolysis. Given that this situation is quite common, it was decided to explore the possibility of correcting these violations. Fumaric acid at 0.1 g/kg was used in the work as an additive to the feed for 20 days in piglets who have undergone prolonged transportation.**Conclusion:** As a result of the exposure, platelet activity and hemocoagulation decreased, and the fibrinolysis process in them increased to the level of control. As a result of the study, it became clear that the use of fumaric acid in piglets who had undergone environmental effects of excessive intensity can restore the functional state of their hemostasis. This returns them to a minimum risk of micro-formation and disruption of tissue trophism.**Key words:** Platelets, Hemocoagulation, Anticoagulation, Fibrinolysis, Piglets, Transport stress, Fumaric acid.***Corresponding author:** SolovyovaLyubovPavlovna, Tel +79102732263,
E-mail: ilmedv1@yandex.ru**INTRODUCTION**

The viability of the body and the weakening of its various functional indicators at any stage of ontogenesis depends on a variety of external and internal factors acting on it.^{1,2} Sometimes the

body is affected by very strong factors that can cause serious disruption to its functioning.^{3,4} The development of such situations is of great interest among physicians^{5,6} and practical

biologists.^{7,8} In the first case, the study of this issue on a person has great social significance and ultimately aims to increase the average duration of human life.^{9,10} In the second case, this is connected with the achievement of the highest possible level of development of economically useful traits in productive animals in the process of their rearing^{11,12} and is of great economic importance.¹³

Normal optimal functioning of the body of young productive animals is possible in the case of a balanced diet, optimal microclimate and the absence of stressful situations.¹⁴ Despite the prominence of the importance of these conditions during early ontogenesis in productive animals, it is not always possible to strictly observe them.^{15,16} As a result, there is a high risk of developing various dysfunctions, which can lead to a deterioration of the general condition and a decrease in the level of gains.¹⁷ It becomes clear that the basis for reducing the viability of a living organism is often a violation of the optimum microcirculation in the organs that cause deterioration of the processes of tissue metabolism.^{18,19,20} In view of the fact that microcirculation largely depends on the state of blood cells²¹, including platelets²², as well as on the activity of other components of the hemostasis system²³, it is of great interest to restore the functional properties of platelets, coagulation hemostasis and fibrinolysis after negative environmental influences.²⁴ Of great practical importance is the continuation of the search for options for the correction of hemostasis in piglets, which improve their blood flow in small vessels and stimulate the trophism of their tissues. The solution to the question of the possibility of the restoration of normal hemostasis activity in these productive animals can be of great economic importance, since it can eliminate the economic damage due to the inhibition of their growth after many adverse effects. In this regard, of great interest is the reaction of hemostasis of piglets who have suffered a very frequent unfavorable environmental factor - the transport stress of an available biostimulator, fumaric acid. In this regard, the goal of the study: to determine the dynamics of platelet activity, hemocoagulation

and fibrinolysis in piglets who have undergone prolonged transportation during the use of fumaric acid in them.

MATERIAL AND METHODS

The study was conducted in strict accordance with the ethical principles established by the European Convention for the Protection of Vertebrates, used for experimental and other scientific purposes (adopted in Strasbourg on March 18, 1986 and confirmed in Strasbourg on June 15, 2006).

The work was performed on healthy piglets of the large white breed at the age of 2 months. The experimental group was made up of 56 animals that transferred long-term transportation in a closed van from the breeding pig farm of the Kostroma State Agricultural Academy to the farms of the Kostroma region of Russia after they were sold for further cultivation. For the subsequent correction of the functional state of the animals, they were added to the feed fumaric acid at a dose of 0.1 g / kg per day for 20 days. The control group consisted of 27 healthy piglets of 2 months of age, a large white breed contained in the standard conditions of the breeding pig farm of the Kostroma State Agricultural Academy and did not tolerate transportation.

In the work with the help of a micromethod, platelet aggregation was evaluated in response to ADP in the standard dose. An assessment of the coagulation level of hemostasis was also carried out using a number of indicators. The activated partial thromboplastin time was recorded, the concentration of fibrinogen in the plasma was estimated, the level of soluble fibrin-monomer complexes was determined using the orthophenanthroline method.²⁵ In the plasma of animals, the level of a type 1 plasminogen activator inhibitor was recorded using a specific chromogenic substrate and the Coatest PAI-1 test system manufactured by Chromogenix. Fibrinolytic properties of blood were found using the traditional method²⁵. Statistical processing of the obtained digital results was carried out using the standard software package. Differences were considered significant at $p < 0.05$.

RESULTS AND DISCUSSION

In animals that have just undergone transportation, marked violations of a number of hematological parameters were noted. In the experimental group there were no differences with the control of the number of platelets in the blood. Moreover, their aggregation activity in piglets of the experimental group in response to the introduction of ADP into plasma was accelerated by 33.9%. In experimental animals, this was accompanied by a shortening (by 29.3%) of the activated partial thromboplastin time, an increase in the amount of fibrinogen in the blood by 77.3% and a decrease in the fibrinolytic capacity of their blood by 38.2%. This was accompanied by an increase in the blood of piglets from the experimental group of the amount of soluble fibrin-monomer complexes by 41.5% and a significant increase in it (by 87.3%) in the level of type 1 plasminogen activator inhibitor.

As a result of the use of fumaric acid in animals undergoing transport stress, recovery of

impaired hematological parameters was observed. In piglets of the experimental group, platelet blood levels did not significantly change. However, their aggregation in response to ADP weakened by 31.5%, reaching the level of control. In these animals, activated partial thromboplastin time (by 28.1%) significantly lengthened against the background of fumaric acid. By the end of the observation, in these piglets, plasma fibrinogen level decreased by 69.4%, and their blood age fibrinolytic activity by 36.4%, reaching the level of control. At the same time, the amount of soluble fibrin-monomeric complexes in the blood of these animals by the end of the observation also corresponded to the control level, having decreased from the outcome by 38.1%. In addition, the use of fumaric acid caused a decrease in the level of tissue plasminogen activator inhibitor type 1 by 86.0% in these piglets, which ensured that it reached the level of animals of the control group.

Table. Considered indicators in the examined piglets

Registered Indicators	Core group, M±m, n=27	Experienced group, M±m, n=56	
		at the beginning of the observation	in the end observations
Platelet count, 10 ⁹ /l	196.5±1.33	210.1±1.62	200.1±1.27
Platelet aggregation with ADP, s	49.7±0.34	37.1±0.29 p<0.01	48.8±0.26
The value of activated partial thromboplastin time, s	40.1±0.53	31.0±0.43 p<0.01	39.7±0.34
Fibrinogen, g/l	2.2±0.34	3.9±0.19 p<0.01	2.3±0.25
Plasma fibrinolytic activity, min	7.6±0.47	5.5±0.27 p<0.01	7.5±0.20
Soluble fibrin monomeric complexes, mg%	4.1±0.34	5.8±0.42 p<0.01	4.2±0.36
The amount of inhibitor of tissue activator plasminogen type 1, ng/ml	29.2±0.48	54.7±0.75 p<0.01	29.4±0.69

Note: p - reliability of differences in the experimental group from the values in the control group.

With many dysfunctions and diseases, hemostasis activation may develop.^{26,27} Its formation is associated with the action of

excessive environmental adverse factors through a number of mechanisms.^{28,29} Hemostasiopathy is very dangerous in terms of vascular spasm and

deterioration of blood rheology, in small arterioles and capillaries, especially during the period of active growth.^{30,31} It is almost always manifested by the activation of platelets and coagulation hemostasis, which was followed in a study conducted on piglets that underwent prolonged transportation. Increased platelet aggregation inevitably worsened their microcirculation in the capillaries and was a serious threat to the inhibition of growth due to a weakening of the metabolism. The observed increase in plasma hemostasis activity in the observed piglets apparently occurred as a result of an increase in the activity of most blood coagulation factors³², which ensured a significant increase in hemocoagulation along the external coagulation pathway revealed in the work.

The found weakening in the blood of piglets of the experimental group of fibrinolytic mechanisms additionally increased their risk of microthrombus formation. Under these conditions, an increase in fibrinogen level was an important mechanism for the simultaneous enhancement of platelet aggregation and the process of hemocoagulation. This was due to the fact that it was a molecule that binds platelets to each other, as well as a substrate for the effects of thrombin during the formation of a blood clot.^{33,34}

An important mechanism of this disorder in the observed piglets apparently is the activation of plasma lipid peroxidation, which is able to stimulate the synthesis of α_2 -antiplasmin and weaken blood fibrinolysis. The imbalance of the components of hemostasis that is formed at the same time ensured its constant activation, leading to a deterioration of the microcirculation in the whole organism.³⁵

The use of fumaric acid in piglets of the experimental group led to the elimination of dysfunctions of hemostasis and the elimination on this background of the risk of developing pathology. Hemostasiopathy, which had arisen before them, was eliminated, which minimized the risk of vasospasm and deterioration of blood rheology. In piglets treated with fumaric acid, platelet activity and coagulation hemostasis decreased to the norm. The weakening of

platelet aggregation worsened microcirculation in their capillaries, leveling the risk of inhibition of growth. The achieved weakening of plasma hemostasis activity apparently occurred as a result of a decrease in the number of all initially activated coagulation factors, which ensured the normalization of procoagulative phenomena along both ways of coagulation.^{36,37}

Increased activity and fibrinolytic mechanisms in piglets treated with fumaric acid minimized the risk of microthrombus formation. Reducing the amount of fibrinogen in the blood can be considered an important mechanism for the simultaneous weakening of their platelet activity and hemocoagulation. Firstly, it weakened the binding of platelets to each other during aggregation, and, secondly, the amount of substrate for the action of thrombin decreased, which hampered the development of a thrombus.³⁸ The use of fumaric acid in the observed piglets apparently weakened plasma lipid peroxidation, which inevitably slowed down the synthesis of α_2 -antiplasmin and enhanced plasma fibrinolytic activity.^{39,40} Thus, the imbalance of hemostatically important substances, eliminated against the background of fumaric acid in piglets that have undergone long-term transportation, ensured the normalization of the mechanisms of hemostasis important for microcirculation, which contributed to the optimum of their gains.

CONCLUSION

The normal functioning of the body of a piglet is significantly determined by the nature of the environmental factors affecting it and the severity of the response to them of its hemostatic system. In the case of long-term transportation, piglets develop hemostatic disorders in the form of increased platelet activity and hemocoagulation, while simultaneously weakening fibrinolysis. The resulting hemostasis can be stopped by using fumaric acid mixed with feed in these animals for 20 days. The achieved results indicate the fundamental possibility of overcoming the dysfunction of hemostasis in piglets caught in adverse environmental conditions with the help of a metabolite that stimulates energy exchange.

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