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Functional Activity Of The Blood Coagulation System Against The Background Of The Influence Of Krezacin And Gamavit In Newborn Piglets Who Underwent Acute Hypoxia.

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ABSTRACT

Until now, piglets at birth often have acute hypoxia, leading to a regular decrease in their resistance, inhibition of growth and increase in mortality. At the same time, the state of the coagulation system in newborn piglets after acute hypoxia has not been studied sufficiently. Also, the possibility of its normalization in these pigs has not been established with the help of a combination of metabolically active drugs currently used in pig production - krezacin and gamavit. During the survey of this category of newborn piglets, excessive thrombogenesis was detected, which is worse controlled by the weakening system of natural anticoagulants. The dystrophic phenomena in endothelium caused by hypoxia in these animals in many cases contribute to the disruption of the binding of activated antithrombin III to heparin sulfate and glucosaminoglycans lining the surface of the endothelium, which lowers the thrombore resistance of the vessels. The reliable decrease in the blood of newborn pigs diagnosed in the work after acute hypoxia of the amount of protein C indicated weakness in their inhibitory control over the activity of V and VIII factors. The use of a combination of kresazin and gamavit normalized the level of plasma lipid peroxidation in all the piglets observed, increasing the initially weakened antioxidant potential. The optimization of the activity of plasma hemostasis achieved at the same time was possible as a result of a reduction to the norm of all initially activated coagulation factors. The revealed dynamics of their activity against the background of krezacin and gamavit in the newborn piglets after acute hypoxia should be considered as a consequence of a positive reaction of hepatic metabolism to the administration of these drugs into the body. The functioning of hemocoagulation in these animals was facilitated by an increase in the anticoagulant properties of their plasma. Moreover, in observed newborn piglets against the background of krezacin and gamavit, it was possible to achieve a normalization of the intensity of plasminogen synthesis with suppression of excessive plasma antiplasmin activity, which normalized the fibrinolysis process. As a result of the study, we can assume that in the newborn piglets, who underwent acute hypoxia at birth and who received krezacin and gamavit, complete normalization of the initially enhanced coagulation activity of the plasma is possible, with restoration to the norm of its anticoagulant and fibrinolytic ability.

Keywords: acute hypoxia, piglets, newborn phase, krezacin, gamavit, blood coagulation.

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INTRODUCTION

Continuous functioning of the body requires optimal coordinated work of all blood systems [1,2], which are important for maintaining its liquid state [3,4]. Great role in this process of blood cells [5], capable of aggregation [6] and the allocation of a large number of physiologically significant substances [7]. Also of great importance is the plasma protein system [8,9], which can convert fibrinogen into fibrin and cause blood coagulation [10,11]. This system is very sensitive to environmental factors and changes in the functional state of the organism [12]. It has long been noted that in the conditions of dysfunctions and pathology [13,14] a very large number of blood parameters suffer, causing an aggravation of the state of the whole organism [15,16]. These physiological indices have tremendous economic importance in productive animals [17], since their state strongly influences their growth and development, and, consequently, the quantity of products obtained from them [18]. This is explained by the fact that the dynamics of activity of all components of hemostasis is an important physiological mechanism for the formation of the organism during early ontogeny in all productive animals, including piglets [19]. In this case, the coagulation system largely determines the fluid properties of the blood, to a large extent, providing optimal conditions for the realization of the pig's genetic development program after birth [20].

Until now, pigs in many pig farms at birth often develop acute hypoxia, leading to a regular decrease in their resistance, inhibition of growth and an increase in mortality [21]. At the same time, the state of the coagulation system in newborn piglets after acute hypoxia has not been studied sufficiently. Also, the possibility of its normalization in these pigs has not been established with the help of a combination of metabolically active drugs currently used in pig production - krezacin and gamavit.

In this connection, the goal is to determine the dynamics of coagulation hemostasis activity in newborn piglets, who underwent acute hypoxia at birth and received krezacin and gamavit.

MATERIALS AND METHODS

The research was conducted in strict accordance with ethical principles established by the European Convent on protection of the vertebrata used for experimental and other scientific purposes (adopted in Strasbourg in March, 18th, 1986, and confirmed in Strasbourg in June, 15th, 2006), approved by the Local Ethics Committee of K. I. Skryabin Moscow State Academy of Veterenary Medicine and Biotechnology (record №14, dated December, 1st, 2015), the Local Ethics Committee of Russian State Social University (record №11, dated December, 4th, 2015) and the Local Ethics Committee of All-Russian Scientific Research Institute of Physiology, Biochemistry and Animals' Nutrition (record №11, dated December, 4th, 2015).

The study included 28 newborn piglets, who underwent acute hypoxia during childbirth. Control in the work were the average values for the phase of neonatality of daily recorded indices in 36 healthy piglets.

Animal examination included an evaluation of the lipid peroxidation (LPO) activity of plasma by the number of acyl hydroperoxides and thiobarbituric acid-active products with the Agat-Med kit. In all piglets, the antioxidant activity of plasma was recorded [16]. The functional possibilities of the blood coagulation system were determined for each piglet under the control of a number of clotting factors (I, II, V, VII, VIII, IX, X, XI, XII), duration of activated partial thromboplastin time, prothrombin and thrombin time [22].

The condition of the anticoagulant capacity of blood plasma in the examined animals was established according to the level of antithrombin III and protein C in it [22].

The level of the fibrinolytic blood plasma system in animals was estimated from the time of spontaneous euglobulinlysis, the activity of plasminogen, α2-antiplasmin, and the amount of fibrin degradation products in it by the phenanthroline method [22].

All the piglets that had undergone acute hypoxia at birth were corrected by applying kresazin 4 mg/kg/day, precipitated in the morning for five days and gavavit 0,03 mg/kg intramuscularly once a day, in the morning for five days, starting simultaneously with krezatsinom. Assessment of the state of animals was carried out after the end of the corrective action. The statistical processing of the results was carried out by Student's t-test.

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RESULTS

In newborn piglets, who had experienced acute hypoxia at birth, an increase in the level of thiobarbituric acid-active products was observed in plasma by 1.58 times in comparison with the control. At the same time, the amount of acyl hydroperoxides in it exceeded the level of healthy animals by 2.26 times. The revealed enhancement of LPO in the liquid part of the blood in the experimental piglets was possible as a result of weakening of the antioxidant potential of the plasma by 1.34 times (Table).

Table: Dynamics of biochemical and coagulation indices in acute neonatal pigs who received acute krezacin and gamavit

Indicators	Experienced group, n=28 exodus	after correction	Control,n=36
Acylhydroperoxide plasma, D_{233}/1 ml	2.99±0.09 p_1<0.01	1.34±0.14 p<0.01	1.32±0.11
Thiobarbituric acid-active plasma products, µmol/l	4.86±0.06 p_1<0.01	3.08±0.02 p<0.01	3.06±0.12
Antioxidant plasma potential, %	27.9±0.08	38.0±0.24 p_1<0.01	37.3±0.13 p<0.01
clotting factor I, g/l	2.0±0.19	1.5±0.17	1.5±0.05 p<0.05
clotting factor II, %	68.4±0.27	64.4±0.24	64.3±0.16 p<0.05
clotting factor V, %	117.9±0.26	90.0±0.48 p_1<0.05	89.9±0.13 p<0.01
clotting factor VII, %	79.3±0.38	72.6±0.29	72.7±0.07 p<0.05
clotting factor VIII, %	134.6±0.45	98.4±0.32 p_1<0.05	98.2±0.10 p<0.01
clotting factor IX, %	97.3±0.29	88.5±0.19	88.3±0.13 p<0.01
clotting factor X, %	65.3±0.26	61.7±0.14	61.7±0.13 p<0.05
clottingfactorXI, %	94.2±0.32	91.0±0.16	90.8±0.14 p<0.05
clottingfactorXII, %	90.3±0.16	90.1±0.19	90.0±0.12
Activated partial thromboplastin time, s	27.5±0.30 p_1<0.05	35.9±0.15 p<0.01	36.3±0.26
Prothrombintime, s	12.6±0.25	16.0±0.24 p_1<0.05	16.1±0.16 p<0.01
Thrombintime, s	15.9±0.29	17.9±0.18	17.8±0.16 p<0.05
Antithrombin activityIII in plasma,%	82.3±0.12	91.3±0.26 p_1<0.05	91.5±0.12 p<0.01
ProteinC, %	42.4±0.22	50.4±0.23 p_1<0.05	50.6±0.16 p<0.01
Time of spontaneous euglobulinlysis, min.	232.8±0.46	188.1±0.24 p_1<0.01	186.6±0.35 p<0.01
Plasminogen, %	85.7±0.29	111.9±0.37 p_1<0.01	112.5±0.19 p<0.01
$\alpha_2$antiplasmin, %	142.4±0.23	127.0±0.14 p_1<0.01	127.2±0.24 p<0.01
Degradation products fibrin, µg/ml	29.1±0.16	28.9±0.12	28.8±0.19

Legend: p - reliability of differences in indicators in outcome and control, p_1 - reliability of the dynamics of indicators against the background of correction.

In the study, a significant increase in plasma activity levels of I, II, V, VII, VIII, IX, X and XI at a normal XII factor was found in newborn piglets that experienced acute hypoxia. In these animals, the duration of activated partial thromboplastin time was accelerated by 32.0%, prothrombin time by 27.8%, thrombin time by 11.9%.

The activity of antithrombin III in newborn piglets that underwent acute hypoxia in labor was reduced by 11.2% in comparison with healthy animals, which was accompanied by a decrease in the level of protein C by 19.3% ($p < 0.01$) with significant inhibition of spontaneous euglobulinlysis by 24.7%, a decrease in the level of plasminogen by 31.3%, and an increase in the activity of $\alpha_2$antiplasmin by 11.9% (Table).

The use of a combination of krezacin and gamavit in the examined animals as a corrective effect ensured a pronounced positive dynamics of all indicators taken into account.

Initially activated in animals, LPO plasma as a result of the use of kresazin and gamavit decreased to normal values - the levels of acyl hydroperoxides and thiobarbituric acid-active compounds in it decreased 2.23 times and 57.8%, respectively, due to the increase in antioxidant activity of plasma 36.2%) to the level of the norm.

Against the background of the correction in the newborn piglets who underwent acute hypoxia, it was possible to completely normalize all the initially activated coagulation factors of the enzymatic (I, II, VII, IX, X and IX) and non-enzymatic nature (V and VIII) while maintaining the XII factor (Table).

The activity of coagulation tests in the observed newborn piglets against the background of correction completely reflected the achieved normalization of the plasma content of the individual clotting factors. Thus, in pigs, upon completion of correction, a significant increase in activated partial thromboplastin time was established by 30.5%. Shortened before the beginning of correction, the duration of prothrombin time in patients with acute hypoxia of pigs against the background of krezacin and gamavit significantly increased by 26.9%. At the same time, the thrombin time, reflecting the intensity of the transformation of fibrinogen into fibrin as a result of the applied effect, was braked by 12.6%, reaching control values.

As a result of the correction, the activity of antithrombin III and protein C in the observed pigs increased in comparison with the outcome by 10.9% and 18.8%, respectively. A pronounced decrease in the time of spontaneous euglobulinlysis found in this case indicated a normalization in animals of the activity of the fibrinolysis system. This was largely achieved as a result of weakening against the background of correction of the excess activity of α2-antiplasmin (127.0±0.14%) and the increase in the content of plasminogen (111.9±0.37%) in their blood.

DISCUSSION

Piglets at birth still often have a state of acute hypoxia, causing severe damage to pigs, weakening livestock and contributing to the case of young animals [23]. In the work carried out in newborn piglets, who underwent acute hypoxia, weakened antioxidant protection of the plasma with an increase in the level of the primary products of LPO-acyl hydroperoxides and secondary-tiobarbituric acid-active compounds, which inevitably caused the alteration of endotheliocytes and liver structures, disrupting the balance of procoagulants and anticoagulants in blood plasma [22]. This led them to stimulate plasma hemostasis, ensuring that they accelerate coagulation along both ways of coagulation and increase the risk of intraorganic thrombosis [24,25].

The excessive thrombin formation that occurs as a result of acute hypoxia in newborn piglets is worse controlled by the weakening system of natural anticoagulants, the most significant of which are antithrombin III and protein C. In addition, the dystrophic phenomena in the endothelium caused by hypoxia greatly contribute to the disruption of the binding of activated antithrombin III to heparin -sulfate and glucosaminoglycans lining the surface of the endothelium, which significantly decreases the thrombose-resistance of the vessels [26]. A reliable decrease in the blood of newborn piglets diagnosed in the work after

acute hypoxia of the amount of protein C indicated a weakness in these animals for inhibitory control over the activity of V and VIII factors [27]. The increase in the amount of α2-antiplasmin detected in animals with decreasing plasminogen caused a decrease in the fibrinolytic activity of the liquid part of their blood [28].

Diagnosed coagulopathy required rapid adequate correction aimed at eliminating metabolic imbalance and optimizing the functioning of the blood clotting system [29].

The applied metabolically significant correction normalized the level of plasma lipid peroxidation in all observed pigs, increasing the initially weakened antioxidant potential [30]. The optimization of the activity of plasma hemostasis achieved at the same time was possible as a result of a reduction to the norm of all initially activated coagulation factors. The revealed dynamics of their activity against the background of krezacin and gamavit in the newborn piglets after acute hypoxia is undoubtedly a consequence of the positive reaction of hepatic metabolism in response to the administration of these drugs into the body [31]. In this case, a significant increase in the anticoagulant ability of plasma was achieved in animals. Increasing to the level of the initially low level of antithrombin III provided optimization of thrombin generation and other initially activated protein coagulation factors (I, II, VII, IX, X and XI). The applied correction normalized in the blood of newborn piglets, who underwent acute hypoxia, the activity of protein C, providing in these animals the optimal inhibitory control of plasma over V and VIII coagulation factors. Moreover, in observed newborn piglets against the background of kresazin and gamavit it was possible to achieve a significant increase in the intensity of plasminogen synthesis with suppression of excessive plasma antiplasmin activity, normalizing fibrinolysis.

CONCLUSION

In newborn piglets, who underwent sharp hypoxia at birth and received krezacin and gamavit, complete normalization of the initially enhanced coagulation activity of the plasma is possible, with restoration to the norm of its anticoagulant and fibrinolytic ability.

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