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Research Article

Functional peculiarities of the hemostasis system in the relaxed newborn calves and pigs, getting gamavit

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ABSTRACT

Introduction: The optimal functioning of the mechanisms of hemostasis during the neonatal period substantially determines the state of the fluid parameters of the blood, and, consequently, the trophism of the organs of the animal. The newborn phase in calves and piglets is considered the most important stage of their ontogenesis and is characterized by the development of functioning, including hemostatic processes.
Objective: to assess the dynamics of the physiological parameters of hemostasis in weakened newborn calves and piglets against the background of the use of gamavit in them.
Material and methods: The study was taken 48 physically weakened newborn calves, which were examined and examined three times: on the 1st and 5th day of life. Also, the work was performed on 39 weakened newborn piglets, which were examined on the 1st and 5th day of life. All attenuated animals received gamavit in a dose of 0.03 ml/kg in the form of daily intramuscular injections once a day, in the morning for 5 days. The use of the drug in all cases began on the first day of life. The arithmetic mean values taken into account in the work of the parameters that were obtained from healthy newborn calves (42 heads) and healthy newborn piglets (35 heads) after their three-time examination during the neonatality phase were used as controls.In work hematologic and statistical methods of research are applied.
Results: It was found out that on the first or second day of life in weakened calves and piglets, a number of physiologically unfavorable changes in the parameters of the hemostatic parameters of platelets, blood vessels and plasma hemostasis are recorded. Coming violations can cause negative changes in all their organs and contribute to their general maladjustment to the conditions of their existence. In the case of the use of the biostimulatorgamavit in weakened newborn calves, a gradual physiologically acceptable reduction in the activity of the components of platelet and plasma hemostasis is achieved with a functionally balanced increase in the hemostatic properties of the vessel walls. The use of gamavit in physically weakened piglets leads to similar positive changes in these indicators, bringing them closer to the level of control.
Conclusion: The study showed that the use of Gamavit is able to eliminate the existing disorders in the hemostatic system in weakened calves and piglets during the newborn phase, thereby increasing their level of adaptation to the environment and providing conditions for their further growth and development.

Keywords: Piglets, Calves, Blood, Hemostasis, Neonatal phase, Gamavit.

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INTRODUCTION

The development of a living organism is determined by the precise work of all its internal organs and systems[1,2]. Of great importance in this is the functioning of the organism

integrating systems — the nervous system[3] and the blood[4,5]. Recently, researchers have paid particular attention to the dynamics of blood parameters, ensuring its internal constancy[6,7,8]. It is clear that the beginning of ontogenesis outside the maternal organism and the initial state of the mechanisms of adaptation to environmental conditions is functionally extremely important in calves and piglets and strongly depends on humoral regulation and trophism[9]. However, blood counts are strongly determined by the hemostatic properties of platelets, blood vessels and plasma hemostasis[10,11].

It is known that the functional properties of platelets, blood vessels and hemocoagulation significantly determine the state of microcirculation in young productive animals[12]. Violations of hemostatic mechanisms can have a very negative effect on the work of adaptation mechanisms and slow down the growth of animals, especially in the debut of their ontogenesis[13]. Especially vulnerable in this regard are young animals born for various reasons, weakened[14]. To overcome asthenia and various disorders, it seems promising to use various biological stimulants in such animals that can optimize metabolism and eliminate existing dysfunctions in the hemostasis system[13]. One of the very commonly used biostimulants is gamavit, but its ability to influence hemostasis is not sufficiently evaluated. In this regard, the goal was set in the work: to assess the dynamics of the physiological parameters of hemostasis in weakened newborn calves and piglets against the background of the use of gamavit in them.

MATERIALS AND METHODS

The studies were conducted in strict accordance with the ethical principles established by the European Convention for the Protection of Vertebrate Animals 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 physiologically mature weakened newborn calves and piglets, which were obtained from first-calf cows and sows after the first farrowing, which had a body mass slightly below the norm at the time of insemination.

The study was taken 48 physically weakened newborn calves, which were examined and examined three times: on the 1st and 5th day of life. Also, the work was performed on 39 weakened newborn piglets, which were examined on the 1st and 5th day of life. All attenuated animals received gamavit in a dose of 0.03 ml/kg in the form of daily intramuscular injections once a day, in the morning for 5 days. The use of the drug in all cases began on the first day of life. The arithmetic mean values taken into account in the work of the parameters that were obtained from healthy newborn calves (42 heads) and healthy newborn piglets (35 heads) after their three-time examination during the neonatality phase were used as controls.

The level of activity of platelet aggregation (AP) was estimated by the time of its occurrence in response to the use of ADP (0.5×10^{-4} M), collagen (1: 2 dilution from the main suspension) and adrenaline (5.0×10^{-6} M)[15].

The intensity of the transformation of platelet arachidonic acid into thromboxane and the enzymatic activity of the cyclooxygenases and thromboxane synthetase that provide this were determined by using three transfer tests on a photoelectrocolorimeter[16]. In the platelets, the quantitative content of ATP and ADP was evaluated and the severity of their secretion in response to collagen was determined[16]. The basal levels of actin and myosin were assessed and their content changed in the case of platelet activation by collagen[16].

The work determined the level of vascular control over platelet aggregation, hemocoagulation and fibrinolysis. The antiaggregatory properties of the vessels were assessed by registering AP with all inductors before and after temporary venous occlusion and the subsequent calculation of the value of the antiaggregatory index of the vessel wall. Its value was established during the division of the duration of AP in plasma obtained against the background of temporary venous stagnation by the value of the time of occurrence of AP in plasma obtained from blood taken from the cuff without imposing[15]. Vascular control of

hemocoagulation was assessed by detecting the activity of antithrombin III in plasma taken without placing the cuff on the vessel and in the plasma after temporary venous occlusion[17]. Subsequently, the index value of the anticoagulant activity of the vascular wall was calculated. This was done by dividing the level of antithrombin III activity in plasma taken with venous occlusion by its activity in plasma taken without it. The level of vascular control over fibrinolysis was assessed by reducing the duration of spontaneous euglobulinlysis in intact plasma and in plasma obtained after temporary venous occlusion[17]. The index value of the fibrinolytic activity of the vascular wall was calculated by dividing the time of development of euglobulinlysis in plasma, taken without venous occlusion by the time value of euglobulinlysis in plasma taken on its background.

The activity of coagulation hemostasis was assessed by the level of activity of some coagulation factors (I, II, VII, VIII, X, XII), time of hemocoagulation in the test of activated partial thromboplastin time, prothrombin time and duration of the onset of thrombin time using standard methods[17]. Results were processed using Student's td test.

RESULTS

In the outcome in the blood of weakened newborn calves, a normal platelet count was noted. In calves, when taking a study, the time of AP development in response to collagen was 21.3±0.19 s, yielding 46.5% of control. Similarly, they had accelerated AP in response to ADP (by 51.5%) and adrenaline (by 35.3%). Initially, in the blood of weakened newborn piglets, normal platelet count was also noted. The development time of AP under the influence of collagen was also accelerated compared to the control by 52.4%. In response to ADP and adrenaline AP, they developed faster than in the comparison group by 43.7% and 29.9%, respectively (table).

Table. Dynamics of hemostasis parameters in weakened newborn calves and piglets fed gamavit

Registered Indicators	**Calves, M±m**			**Piglets, M±m**		
	at the beginning of the observation, n=48	at the end of the observation, n=48	control, n=42	at the beginning of the observation, n=39	at the end of the observation, n=39	control, n=35
Platelet aggregation with ADP, s	26.8±0.12	38.6±0.16 p_1<0.01	40.6±0.10 p<0.01	27.2±0.14	37.6±0.10 p_1<0.01	39.1±0.16 p<0.01
Platelet aggregation with collagen,s	21.3±0.19	30.1±0.22 p_1<0.01	31.2±0.14 p<0.01	20.2±0.24	29.6±0.17 p_1<0.01	30.8±0.09 p<0.01
Platelet aggregation with adrenaline,s	72.8±0.10	97.7±0.09 p_1<0.01	98.5±0.18 p<0.01	74.8±0.16	94.8±0.12 p_1<0.01	97.2±0.15 p<0.01
The index of antiaggregatory activity of the vascular wall with ADP	1.42±0.17	1.60±0.10 p_1<0.01	1.68±0.13 p<0.01	1.48±0.19	1.63±0.16 p_1<0.01	1.66±0.17 p<0.01
The index of antiaggregatory activity of the vascular wall with collagen	1.32±0.07	1.56±0.09 p_1<0.01	1.60±0.08 p<0.01	1.34±0.11	1.52±0.08 p_1<0.01	1.58±0.10 p<0.01
The index of antiaggregatory activity of the vascular wall with adrenaline	1.50±0.09	1.62±0.13 p_1<0.01	1.65±0.09 p<0.01	1.46±0.15	1.60±0.08 p_1<0.01	1.63±0.13 p<0.01
AT-III activity, %	86.7±0.14	95.8±0.18 p_1<0.01	99.8±0.17 p<0.01	85.6±0.10	96.2±0.14 p_1<0.01	98.6±0.21 p<0.01
Anticoagulant Index vascular wall activity	1.16±0.06	1.30±0.05 p_1<0.01	1.33±0.07 p<0.01	1.15±0.09	1.29±0.04 p_1<0.01	1.30±0.05 p<0.01
Spontaneous time	236.0±0.42	197.2±0.37	186.1±0.41	227.5±0.54	189.7±0.32	183.1±0.32

euglobulinlysis, min		p_1<0.01	p<0.01		p_1<0.01	p<0.01
Fibrinolytic index vascular wall activity	1.25±0.06	1.39±0.11 p_1<0.01	1.42±0.16 p<0.01	1.23±0.09	1.37±0.07 p_1<0.01	1.39±0.12 p<0.01
Coagulation factor I, g / l	2.4±0.12	1.7±0.13 p_1<0.01	1.8±0.13 p<0.01	2.2±0.14	1.6±0.15 p_1<0.01	1.7±0.09 p<0.01
Coagulation factorII, %	78.8±0.39	74.1±0.25 p_1<0.05	74.2±0.23 p<0.05	79.7±0.36	75.0±0.24 p_1<0.05	74.0±0.18 p<0.05
Coagulation factorVII, %	71.2±0.19	71.6±0.23	70.6±0.10	72.8±0.24	71.9±0.16	71.2±0.16
Coagulation factorVIII, %	142.6±0.10	96.6±0.14 p_1<0.01	94.,0±0.12 p<0.01	156.2±0.09	97.3±0.13 p_1<0.01	93.2±0.18 p<0.01
Coagulation factorX, %	62.7±0.09	61.7±0.12	62.1±0.14	62.5±0.14	61.3±0.17	61.8±0.19
Coagulation factorXII, %	90.8±0.22	90.2±0.16	90.3±0.24	91.4±0.21	90.0±0.19	89.7±0.15
Activated partial thromboplastin time, s	31.6±0.16	38.2±0.21 p_1<0.01	40.2±0.30 p<0.01	32.0±0.28	38.8±0.19 p_1<0.01	39.2±0.24 p<0.01
Prothrombin time, s	14.1±0.19	17.2±0.20 p_1<0.01	17.9±0.18 p<0.01	14.3±0.15	17.0±0.24 p_1<0.01	17.6±0.16 p<0.01
Thrombin time, s	16.2±0.29	18.2±0.21 p_1<0.01	18.6±0.20 p<0.01	16.1±0.31	17.5±0.18 p_1<0.01	18.0±0.25 p<0.01

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

When taking in a study of weakened newborn calves, there was a decrease in vascular wall control over the AP process: in relation to ADP, the antiaggregation activity index of the vessel wall was reduced by 18.3%, in relation to collagen and adrenaline, its value was lower than the control level by 21.2% and 10.0%, respectively. In weakened newborn piglets, a decrease in the degree of influence of the vascular wall on AP was also found in the outcome: in relation to ADP, the value of the antiaggregatory activity index of the vessel wall was lower than control by 12.2%, in relation to collagen and adrenaline, its level was lower than in the control group by 17.9% and 11.6%, respectively.

At the time of taking under observation in weakened newborn calves, there was a weakening in the production of endotheliocytes by antithrombin III. This was judged by lowering its blood level in these animals by 15.1% and by decreasing the anti-coagulation index value of the vascular wall by 14.6%. Also in the calves, an increase in the spontaneous euglobulinlysis time by 26.8% was found, which was combined with a decrease in the vascular fibrinolytic activity index by 13.6%. In the study of weakened newborn piglets, the first examination also found a low level of antithrombin III activity and a reduced value of the index of anticoagulant activity of the vascular wall (by 13.0%). Also in piglets, the duration of spontaneous euglobulinlysis was increased by 24.2%, and the index of fibrinolytic activity of the vascular wall was reduced by 13.0%.

In weakened newborn calves, an increase in the activity of a number of coagulation factors was noted: factors I, II, and VIII, with normal activity of factors VII, X, and XII. The weakened piglets at the time of taking in the study also increased the activity of factors I, II and VIII and noted the normal level of activity of the rest of the coagulation factors determined in the work - VII, X and XII.

The time of onset of coagulation in general coagulation tests in weakened calves was regularly accelerated, reflecting changes in the activity of individual coagulation factors in their plasma. So, they found a shortened activated partial thromboplastin time by 27.2%,

prothrombin time by 26.9% and thrombin time by 14.8%. A similar decrease in time in coagulation tests was observed in weakened newborn piglets. They have an acceleration of activated partial thromboplastin time by 22.5%, prothrombin time by 23.1% and thrombin time, by 11.8%.

As a result of the use of gamavit in the blood of weakened newborn calves, the normal number of platelets was maintained. As a result of the correction in calves, the time of AP development under the influence of collagen increased to 30.1±0.22 s, in response to ADP to 38.6±0.16 s, and with the use of adrenaline to 97.7±0.09 s, coming out during all cases on the level of control. In the blood of weakened newborn piglets treated with gamavit, the preservation of a normal number of platelets was also noted. They also achieved the achievement of the level of control indicators of the development of AP under the influence of collagen, ADP and adrenalin.

The use of gamovit provided in weakened newborn calves a gradual increase in control of the vascular wall over AP. This was indicated by their increase to the level of control of the values of the indexes of antiaggregatory activity of the vessel wall with respect to all the inductors tested. In weakened newborn piglets treated with gamavit, normalization of the values of the antiaggregation indexes of the vascular wall was also noted. This became possible as a result of their increase in relation to ADP by 10.1%, in relation to collagen by 13.4% and in respect of adrenaline by 9.6%.

In weakened newborn calves treated with gamavit, an increase in the production of antithrombin III by endotheliocytes was established, as judged by an increase in its blood level by 10.5% and by an increase in the value of the anticoagulant activity index of the vascular wall to 1.30±0.05. This was accompanied by their increased synthesis in the vessels of the tissue activator plasminogen, which was indicated by a reduction in the time of spontaneous euglobulinlysis by 19.7%, and an increase in the fibrinolytic activity index of the vessels by 11.2%. The observed weakened newborn piglets on the background of gamavit also found an increase in blood level of antithrombin III by 12.4% with an increase in the index of anticoagulant activity of the vascular wall by 12.2%. At the same time, the treated vascular control of the fibrinolysis process increased to the level of control in the treated weakened piglets. This was indicated by a decrease in the time of spontaneous euglobulinlysis by 19.9% and an increase in the value of the fibrinolytic activity index of the vascular wall by 11.4%.

In weakened newborn calves, as a result of the application of gamavit, normalization of the activity of the initially activated coagulation factors was achieved while maintaining the normal activity of the original undisturbed activity of factors VII, X and XII. Similar dynamics of the activity of hemocoagulation factors was observed in weakened piglets during the use of gamavit in them.

As a result of the correction, observed calves showed a reduction to the control level of clotting time in general coagulation tests. This reflected changes in the content of individual coagulation factors in their plasma. Thus, the activated partial thromboplastin time increased in them by 20.9%, the prothrombin time increased by 21.9% and the thrombin time slowed down by 12.3%. Similar changes in the time of onset of coagulation in general coagulation tests occurred in weakened newborn piglets fed gamavit. The time of hemocoagulation in them was normalized due to an increase in the rate, activated partial thromboplastin time by 21.2%, prothrombin time by 18.9% and thrombin time by 8.7%.

DISCUSSION

The physiologically extremely significant blood system in mammals is the hemostatic system[18,19]. The rheological parameters of blood, and, consequently, the maintenance of homeostasis in their body, depend largely on the optimum of its work throughout their life[20,21]. A decrease in the level of tension in the functioning of the mechanisms of platelet, vascular and coagulation hemostasis in weakened newborn calves and piglets can

significantly facilitate the adaptation of these animals to extrauterine life.

The above assessment of the dynamics of the ability of platelets to aggregate in response to all tested inductors gave reason to believe that, against the background of the use of gamavit, in weakened calves and piglets there is a decrease in the excessively elevated level of sensitivity to them platelets[22,23]. This provided in young animals of both species of productive animals rapid inhibition of antibodies to the optimum level[24].

At the basis of the revealed changes in calves and piglets, who received a course of correction with gamavit, a decrease in the sensitivity of platelets to the applied platelet aggregation agonists was noted. This contributed to its release in both species of animals to the level characteristic of the control. Apparently, this was largely based on the development of the normalization of the degree of expression of fibrinogen receptors (GPII-IIIa)[25,26], the level of activation of phospholipases A_2 and C[27,28], and the intensity of thromboxane formation in platelets[29,30], enhanced in these animals at the time of birth.

The increased anti-aggregation properties of the vascular wall in both groups of young animals achieved during the use of gamavit can be explained by the intensification of prostacyclin generation[31,32] and nitric oxide[33,34,35] in their vessels and limiting the activity of platelets and ensuring the physiological level of microcirculation in the internal organs[36,37].

A major role in the realization of the atrombogenic properties of the vascular wall in calves and piglets weakened at the time of birth is undoubtedly played by the state of its anticoagulant[38,39]and fibrinolytic parameters[40,41]. The first is associated with increased synthesis in the vascular endothelium and subendothelium of the strongest physiological anticoagulant, antithrombin III[42,43]. The second antithrombogenic mechanism of the vascular wall is associated with an increase in the production of plasminogen activators in calves and in piglets[44,45]. The use of gamavit was able to significantly optimize the work of these two mechanisms of hemostasis in young animals of both species of observed animals[46,47]. There is reason to believe that the restoration of the physiological optimum in the body is associated with the optimization of anabolic processes[48,49], the weakening of lipid peroxidation processes[50,51], the elimination of possible intoxication episodes[52,53] and foci of infection[54]. A very important point in optimizing hemostatic processes is the restoration of metabolism in blood cells[55], blood vessels[56] and liver[57], with the anabolism and catabolism processes[58] balanced in them.

The weakening of plasma coagulation activity enhanced at the moment of birth in weakened calves and piglets receiving gamavit was associated with a reduction to plasma level I, II, and VIII of plasma factors[59,60] involved in the implementation of both hemocoagulation pathways[61,62]. This was confirmed by the inhibition in all animals of the indicators of total coagulation tests: activated partial thromboplastin time, prothrombin time and thrombin time[63].

CONCLUSION

The changes in the activity of platelet, vascular and plasma hemostasis found in the observed individuals of both species of productive animals found during the course of the work while using gamavit were mildly physiological in nature, which ensured in all cases their exit to the normal level. The achieved optimization of the activity of the components of the hemostasis system in weakened newborn calves and newborn piglets while using gamavit in them indicated the possibility of normalizing with it the processes of microcirculation and trophism in the locomotor system and in the internal organs of weakened animals.

CONFLICT OF INTEREST: The author declares no conflict of interest.

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