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The impact of motor activity level of newborn calves with dyspepsia on correction efficiency of hypercoagulation state in them with the help of gamavit

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Abstract

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While examining the newborn calves with noninfectious dyspepsia we noted strengthening of lipids' peroxidation in plasma, activation of blood coagulation, weakening of anticoagulation and fibrinolysis. Gamavit application (0.03 mg/kg) to the observed calves provided positive dynamics of accountable indices which was more evident at untethered (free) keeping of animals. In this case we noted maximal fall of plasma acylhydroperoxides' level (in 2.4 times) because of evident strengthening of its antioxidant activity (by 34.2%). The newborn calves with dyspepsia only at free keeping reached normalization of coagulation factors' activity, the time of common coagulation tests, activity of antithrombin III and protein C. It was also accompanied in calves at free keeping by level normalization of plasminogen, α_2-antiplasmin and the time of spontaneous euglobulin lysis. In calves which were kept tethered, positive dynamics of accountable indices was less evident what allowed normalizing none of them.

Keywords: dyspepsia; newborn calves; gamavit; blood coagulation

Introduction

Hemocoagulation is an important element of the system of homeostasis provision. Its activity has great significance at all the ontogenesis stages of living beings including cattle (Maksimov et al., 2017a). It's acknowledged that activity of coagulation system rather essentially determines fluid properties of blood thus providing necessary conditions for maximal development of animals' productive potential (Korepanova et al., 2015).

Notwithstanding the serious technological progress in cattle breeding the newborn calves still often have dyspepsia (Medvedev, 2017a). It can lead to significant weakening of their resistance, inhibition of their growth processes and often causes death of animals (Glagoleva and Zavalishina, 2017a; Zavalishina, 2017a). Being rather often present in newborn calves dyspepsia remains to be studied rather poorly in respect of the changes of blood parameters and especially blood coagulation system against its background (Zavalishina, 2017b). The impact of widely used in cattle breeding metabolism stimulator – gamavit – on hemocoagulation of calves with dyspepsia being kept in different conditions, is not clear yet.

Taking these facts into account we put the following aim in our work: to determine peculiarities of the dynamics of coagulation hemostasis parameters in newborn calves with

dyspepsia at tethered and untethered keeping against the background of gamavit application.

Materials and Methods

The study was 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, 18th, 1986, and confirmed in Strasbourg on June, 15th, 2006), approved by the local Ethics Committee of K.I. Skryabin Moscow State Academy of Veterinary Medicine and Biotechnology (record № 12, dated December, 3rd, 2015), the local Ethics Committee of the Kursk State University (record № 11, December, 4th, 2015), the local Ethics Committee of the Kursk State Medical University (record № 12, dated December, 3rd, 2015) and the local Ethics Committee of the Samara National Research University (record № 12, dated December, 3rd, 2015).

The study involved 75 newborn calves (1-2 days of life) with noninfectious dyspepsia including 36 newborn calves being at tethered keeping (experimental group №1) and 39 calves being at untethered keeping (experimental group №2). All the experimental calves were conducted state correction with the help of gamavit intramuscular introduction 0.03 mg/kg once a day in the morning in the course of 5 days. Estimation of the calves' state was conducted at the beginning and in 5 days after the end of correction. Control values in our work were presented by average values of indices received in 35 healthy calves at their daily examination in the course of the newborn phase.

In all the taken under observation calves we determined the activity of plasma lipids' peroxidation according to the quantity of acylhydroperoxides (AHP) (Csovari et al., 1991) and thiobarbituric acid (TBA)-active products in it using the kit of the firm "Agat-Med" (Russia). We also determined plasma antioxidant activity (Volchegorskij et al., 2000). Functional activity of hemocoagulation system was determined according to the state of common coagulation tests (activated partial thromboplastin time, prothrombin and thrombin time), and also according to the activity of some coagulation factors (I, II, V, VII, VIII, IX, X, XI, XII) (Barkagan and Momot, 1999). Plasma anticoagulation activity in calves was determined according to the level of antithrombin III and protein C in it (Barkagan and Momot, 1999). The state of fibrinolytic plasma activity in animals was determined according to the duration of spontaneous euglobulin lysis, the level of plasminogen and α_2-antiplasmin (Barkagan and Momot, 1999).

The results were processed by Student's criterion (t). Statistical processing of received information was made with the help of the program package "Statistics for Windows v. 6.0", "MicrosoftExcel". Differences in data were considered reliable in case of $p<0.05$.

Results

The experimental newborn calves with noninfectious dyspepsia were found to have quantity increase of TBA-active products in plasma in more than 1.6 times. At the same time, the quantity of AHP in plasma of both experimental groups surpassed the level of healthy animals in nearly 2.4 times. Activation of lipids' peroxidation in plasma of all the experimental calves developed owing to comparable decrease of the level of their plasma antioxidant activity by more than 30% (Table 1).

In both groups of experimental animals the time of common coagulation tests turned out to be rather short-cut. The value of activated partial thromboplastin time in them was lowered, on the average, by 30.1%; prothrombin time - by 20.0%; thrombin time - by 11.0%. In all the experimental calves it was accompanied by activity rise of I, II, V, VII, VIII, IX, X and XI plasma coagulation factors at normal activity of XII factor.

The activity of antithrombin III and protein C in both experimental groups of animals was lowered in comparison with the control group, on the average, by 13.0% and 17.0% respectively. At the same time, the time of spontaneous euglobulin lysis in calves with dyspepsia was increased, on the average, by 27.2%, the activity of plasminogen turned out to be lowered, on the average, by 30.9% and the activity of α_2-antiplasmin rose, on the average, by 12.0% (Table 1).

Gamavit application to newborn calves with dyspepsia caused positive dynamics of animals' common state and all the accountable indices. It was more evident in the 2nd group. By the end of observation the signs of dyspepsia were stopped in both groups. All the animals remained alive. At the same time, the 2nd group of calves was noted to have quicker elimination of dyspepsia manifestations, more evident appetite and higher activity. All that pointed at fuller restoration of their common state.

At untethered (free) keeping the levels of AHP and TBA-active compounds in plasma were maximally low by the end of observation ($p<0.01$) and reached the control level in the result of state normalization of plasma antioxidant protection of these animals (Table 1).

The time of coagulation tests in kept freely newborn calves from the 2nd experimental group reached the level of control values in the result of correction: activated partial thromboplastin time increased in them by 30.2% ($p<0.05$),

Table 1. Dynamics of hematological parameters in newborn calves with dyspepsia who received gamavit

Registered parameters	Experienced group 1, M±m		Experienced group 2, M±m		Control, M±m, n=35
	initial values, n=36	at the end of observation, n=36	initial values, n=39	at the end of observation, n=39	
acyl hydroperoxides, D_{233}/1ml	3.11±0.17 p<0.01	1.66±0.12 p_1<0.01	3.14±0.16 p<0.01	1.32±0.12 p_1<0.01	1.33±0.14
TBA-active products, umol/l	4.99±0.09 p<0.01	3.55±0.08 p_1<0.01	4.95±0.11 p<0.01	3.03±0.09 p_1<0.01	3.02±0.16
plasma antioxidant activity, %	28.3±0.08 p<0.01	34.0±0.14 p_1<0.01	27.5±0.18 p<0.01	36.9±0.19 p_1<0.01	37.0±0.10
activated partial tromboplastin time, s	27.4±0.25 p<0.05	32.0±0.20 p_1<0.05	27.8±0.16 p<0.05	36.2±0.12 p_1<0.05	36.1±0.18
prothrombin time, s	13.4±0.21 p<0.05	15.0±0.25 p_1<0.05	13.5±0.22 p<0.05	16.1±0.38 p_1<0.05	16.0±0.15
thrombin time, s	15.6±0.26 p<0.05	16.8±0.15	15.4±0.18 p<0.05	17.4±0.29 p_1<0.05	17.3±0.12
factor I, g/l	2.1±0.15 p<0.01	1.7±0.17 p_1<0.01	2.0±0.08 p<0.01	1.4±0.18 p_1<0.01	1.4±0.08
factor II, %	67.4±0.20 p<0.05	65.2±0.26 p_1<0.05	67.2±0.25 p<0.05	64.2±0.32 p_1<0.05	64.1±0.15
factor V, %	120.1±0.29 p<0.01	99.2±0.45 p_1<0.01	119.6±0.38 p<0.01	89.4±0.42 p_1<0.01	89.2±0.12
factor VII, %	78.7±0.32 p<0.05	78.3±0.26 p_1<0.05	78.9±0.37 p<0.05	72.4±0.46 p_1<0.05	72.3±0.08
factor VIII, %	132.8±0.40 p<0.01	111.2±0.33 p_1<0.01	133.2±0.25 p<0.01	97.7±0.37 p_1<0.01	97.6±0.12
factor IX, %	97.6±0.41 p<0.05	92.4±0.29 p_1<0.05	96.9±0.38 p<0.05	88.8±0.30 p_1<0.05	88.7±0.15
factor X, %	65.5±0.35 p<0.05	63.0±0.18 p_1<0.05	65.8±0.26 p<0.05	61.2±0.28 p_1<0.05	62.1±0.14
factor XI, %	94.7±0.30 p<0.05	92.1±0.25 p_1<0.05	95.2±0.28 p<0.05	89.9±0.36 p_1<0.05	90.2±0.12
factor XII, %	91.0±0.32	90.9±0.16	90.1±0.25	91.2±0.17	91.3±0.20
activity of antithrombin III in plasma, %	81.2±0.12 p<0.05	88.7±0.21 p_1<0.05	81.6±0.23 p<0.05	92.3±0.30 p_1<0.05	92.0±0.16
protein C, %	42.7±0.09 p<0.05	47.2±0.14 p_1<0.05	43.1±0.12 p<0.05	50.1±0.22 p_1<0.01	50.3±0.18
time of spontaneous euglobulin lysis, min.	242.6±0.52 p<0.01	201.2±0.34 p_1<0.01	239.8±0.42 p<0.01	188.4±0.46 p_1<0.01	188.5±0.38
plasminogen, %	84.0±0.26 p<0.01	101.3±0.37 p_1<0.01	84.4±0.32 p<0.01	110.5±0.27 p_1<0.01	110.2±0.24
α_2-antiplasmin, %	143.4±0.33 p<0.01	132.1±0.21 p_1<0.05	143.9±0.15 p<0.01	128.2±0.24 p_1<0.01	128.1±0.29

Note: p - reliability of differences in the initial indicators in the experimental groups and control, p_1 - reliability of the dynamics of the indicators in the experimental groups

the duration of prothrombin time increased by 19.2% (p<0.05) and thrombin time increased by 12.9% (p<0.05).

Full normalization of th e activity of all the excessively strengthened coagulation factors in newborn calves from the 2nd group (I, II, V, VII, VIII, IX, X and XI) at preservation of the optimal activity of XII factor (Table 1) lay in the basis of the received results.

In the result of correction the activity of antithrombin III and protein C in calves from the 2nd experimental group increased till the normal level by 13.1% (p<0.05) and by 16.2% (p<0.01) respectively. Besides, in the result of correction the activity of α_2-antiplasmin lowered in them by 12.2% (p<0.01) and the activity of plasminogen rose by 30.9% (p<0.01). It provided the achievement of the control values

by these indices. It was accompanied in them by duration shortening of spontaneous euglobulin lysis till the control level.

Gamavit application to newborn calves with dyspepsia which were kept freely (untethered) (the 1st experimental group) wasn't so effective as in the 2nd experimental group and didn't allow reaching normalization of all the accountable indices.

Discussion

Shortly after birth calves can develop various disorders in the body. As before, they often have non-infectious dyspepsia. Its presence can greatly weaken the body and often leads the body to death (Medvedev and Amelina, 2010; Glagoleva and Zavalishina, 2017b). In the study, a significant weakening of the antioxidant protection of plasma was recorded with an increase in the level of AHP and TBA-active compounds in it. The emerging situation naturally causes them to increase the aggregation of blood cells (Glagoleva and Zavalishina, 2017c; Zavalishina et al., 2017), damage to the walls of blood vessels and liver cells (Vorobyeva, 2017). All this greatly violates the balance between pro- and anticoagulants in their plasma (Skoryatina and Zavalishina, 2017a). In all experimental animals this was manifested by the acceleration of coagulation processes along the external and internal coagulation pathways. Developed disorders increased calf hypoxia in experimental calves and formed the risk of microcirculation disorders (Bikbulatova et al., 2017; Medvedev, 2017b).

Excessive thrombin formation, developing in calves with non-infectious dyspepsia, was less inhibited by weakened by their natural anticoagulants - antithrombin III and protein C (Zavalishina, 2017c; Skoryatina and Zavalishina, 2017b). At the same time, enhanced lipid peroxidation processes that damaged the endothelium significantly contributed to the disruption of binding of antithrombin III to heparin sulfate and glucosaminoglycans on its surface, which greatly reduced the level of vascular thrombore resistance (Kutafina, 2017; Oshurkova et al., 2017). Calves found in newborn calves with dyspepsia weakened the plasma activity of protein C, indicating a depression in their inhibitory control over the activity of V and VIII factors (Sizov and Zavalishina, 2015). This was accompanied in all experienced calves by the excess activity of α_2-antiplasmin and a decrease in the functionality of plasminogen, leading to a decrease in the fibrinolytic capacity of their blood.

Diagnosed in experimental calves coagulopathy required an effective correction, which can eliminate violations of hemocoagulation mechanisms (Maksimov et al., 2017b; Maksimov et al., 2017c). To this end, gamavit was used, which enhances the metabolic processes against the background of different motor activity in newborn calves when tethered and unbonded.

The use of gamavit maximally positively influenced the observed calves on the level of plasma lipid peroxidation, metabolism in the liver and bone marrow only with loose-fitting content. Apparently, motor activity, which stimulates metabolic and enzymatic processes, is able to potentiate the effect of glycopin, providing the maximum possible activation of the antioxidant protection of the calves. The normalization of hemocoagulation results achieved at the same time was due to a reduction in the level of activity norm of all clotting factors. The registered dynamics of their activity against the background of gamavit in calves with dyspepsia, located on loose-fitting content, can be considered a consequence of the increase in the background of correction of hepatic metabolism (Medvedev and Skoryatina, 2010). The use of the drug was accompanied in both experimental groups of calves by increased anticoagulant plasma activity. The highest expression was in the second group of animals. Apparently, only in the case of free-bound content, the most pronounced increase in the initially lowered activity of antithrombin III is possible. It was as a result of this that it was possible to control the level of activation of calf factor II, VII, IX, X, XI and XII in calves (Medvedev and Danilenko, 2010; Medvedev, 2017c). In addition, free muscle activity in the conditions of application of gamavit led to a normalization in the blood of calves of the activity of protein C, thereby inhibiting the generation of V and VIII clotting factors in their plasma (Medvedev and Gromnatskii, 2005; Maksimov et al., 2017d). In newborn calves with dyspepsia, who received gamavit, the intensity of synthesis of plasminogen was increased to normal (Simonenko et al., 2008) only in the second experimental group, which was accompanied by suppression of excess level of antiplasmin in their plasma (Medvedev et al., 2006; Medvedev, 2007). The obtained results are confirmed by the literature data on the possibility of potentiating the effect of medications with moderate muscle activity with respect to components of the hemostasis system. The obtained results confirm the point of view on the high stimulating activity of muscular activity on the mammalian organism. In particular, loose bonding enhances life processes in cattle and increases its productivity (Zaitsev et al., 2017). The study showed that free muscle activity in new-born calves with dyspepsia increases the effect of gamavit, which leads to complete normalization of the hemocoagulation system, optimizing the fluid properties of their blood and thereby creating functionally beneficial conditions for maximizing the calves' recovery (Medvedev, 2016).

Conclusion

For newborn calves with dyspepsia, it is common for plasma coagulation activity to be enhanced and its anticoagulant and fibrinolytic mechanisms weakened. With the use of gamavit in these newborn calves, normalization of the coagulation activity of plasma and its mechanisms of anticoagulation and fibrinolysis in the case of their free content is achieved. In newborn calves with dyspepsia that are on adherent maintenance, the use of gamavit in the same dose and with the same mode of administration does not allow us to normalize the indicators taken into account.

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