



# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Functional Properties Of Fibrinolysis In Calves Of The First Year Of Life.

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### ABSTRACT

The dynamics of the activity of the fibrinolysis system in relativeogenesis is one of the most important physiological elements of providing a homeostasis in a living organism in the process of its growth and development. The optimality of the functional activity of the fibrinolytic system largely ensures adaptation to the external environment of the whole organism, maintaining the level of fluidity of the blood along the vessels, contributing to the optimal development of the genetic program of calf development. At the same time, the ontogenetic dynamics of activity of the fibrinolytic system in healthy calves during a change in diet during early ontogeny has not been studied enough. In the study, it was confirmed that the physiological dynamics of fibrinolysis activity largely ensures during the early ontogenesis in calves the necessary level of liquid blood properties and the optimal degree of perfusion of their internal organs. This greatly contributes to the metabolism in the calf's tissues, contributing to its further growth and development, being an indispensable element of the final functional maturation of the calf's organism in the changing nature of nutrition.

**Keywords:** the phase of milk supply, the phase of milk nutrition, the phase of milk and vegetable nutrition, the phase of plant nutrition, the system of fibrinolysis of blood, calves, lipid peroxidation.

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## INTRODUCTION

Further progressive development of the society is possible in the presence of a sufficient number of quality food products [1,2,3]. An important source is livestock, which gives milk and a large volume of meat products [4,5]. It is possible to intensify animal husbandry by actively using physiological knowledge about cattle in practice, especially during its growth and development.

A functionally important body system of the calf is blood, which ensures metabolism in tissues [7,8]. Optimum of its fluid properties provides fibrinolysis, which in calves during early ontogeny has not yet been fully studied [9,10].

The ontogeny of the activity of the fibrinolysis system is one of the most important physiological elements of providing homeostasis in the process of growth and development [11, 12]. The optimality of the functional activity of the fibrinolytic system largely provides adaptation to the external environment of the whole organism, maintaining its fluidity level in the vessels, promoting the optimal development of the genetic development program calf [13,14]. At the same time, the ontogenetic dynamics of activity of the fibrinolytic system in healthy calves during a regular diet change during early ontogeny has not been studied enough.

In this regard, the goal of the study was formulated: to elucidate the ontogenetic dynamics of the physiological activity of the fibrinolytic blood system in healthy calves in the phase of newborn, milk, dairy, plant and plant nutrition.

## MATERIALS AND METHODS

Research was conducted in strict accordance with ethical principles established by the European Convention on protection of the vertebrata used for experimental and other scientific purposes (adopted in Strasbourg March 18, 1986, and confirmed in Strasbourg June 15, 2006) and approved by the local ethic committee of Russian State Social University (Record №12 dated December 3, 2015).

The study included 29 physiologically mature, healthy new-born calves of black and motley breed for 1-2 days of life, 32 healthy calf of dairy nutrition for 11 days of life, 36 healthy calves of dairy and vegetable nutrition taken for 31 days of life, 39 healthy calves of plant nutrition, taken under observation for 91 days of life with normal indices of laboratory and instrumental studies and subsequently not having deviations in the state of health. The complex of examinations consisted of the determination of the activity of peroxide oxidation of plasma lipids by the content of acyl hydroperoxides and thiobarbituric acid-active products by the Agat-Med company (Russia) with an evaluation of the antioxidant activity of the liquid part of the blood.

To determine the activity of fibrinolytic ability of blood plasma in calves, a method for determining the time of spontaneous euglobulin lysis, the level of plasminogen,  $\alpha_2$  antiplasmin, and the content of fibrin degradation products with the phenanthroline method was used.

The calves included in the study were inspected and examined for the phase of milk supply: on 1-2 days, 3-4 days, 5-6 days, 7-8 days and 9-10 days. The observed calves of dairy nutrition were examined: on 11, 15, 20, 25 and 30 days of life. The indicators taken into account in healthy calves of milk and vegetable nutrition were determined: at 31, 45, 60, 75 and 90 days of life. During the phase of plant feeding calves were examined 4 times: 91 days, 6 months, 9 months and 12 months of life.

Statistical processing of the results was carried out using Student's t-test.

## RESULTS OF THE STUDY

In healthy babies during the neonatal phase, the activity of the peroxide oxidation of plasma lipids was found to be constant (Table 1): the concentration of thiobarbituric acid-active products and the level of acyl hydroperoxides in their blood plasma did not experience significant dynamics throughout the neonatal phase. The stability of lipid peroxidation was ensured by the constancy of the calves during the milk supply phase of the level of antioxidant protection of the body - the antioxidant potential of the plasma in them on the average was  $33.7 \pm 0.14\%$  for the newborn. During the phase of milk nutrition in healthy calves, the stability of the level

of antioxidant activity of the plasma (on average  $32.6 \pm 0.21\%$ ) and the activity of blood lipid peroxidation remained - the level of acyl hydroperoxides averaged  $1.48 \pm 0.02$  D<sub>233</sub>/1 ml with a low content thiobarbituric acid-active compounds (average  $3.29 \pm 0.02$   $\mu\text{mol/l}$ ). In the phase of milk and vegetable nutrition in healthy calves, a significant decrease in the level of antioxidant activity of plasma ( $27.4 \pm 0.15\%$ ) was registered by the 45 days of life, with its subsequent increase to  $33.9 \pm 0.24\%$  by 90 days of life, which determined the regular dynamics of the level of the primary products of lipid peroxidation-acyl hydroperoxides: by 45 days, its peak ( $1.80 \pm 0.14$  D<sub>233</sub>/1 ml) was observed with a subsequent decrease ( $1.41 \pm 0.11$  D<sub>233</sub>/1 ml) to values lower than at the beginning of the phase. With a similar dynamics of the content of secondary products of free radical lipid oxidation, thiobarbituric acid-active compounds (at 45 day  $3.77 \pm 0.16$   $\mu\text{mol/l}$ , at 90 day  $3.45 \pm 0.19$   $\mu\text{mol/l}$ ), returning to the values characteristic for thiobarbituric acid-products at the beginning of the phase of dairy-plant nutrition. In the early stages of the phase of plant nutrition in healthy calves, there was a gradual increase in the level of antioxidant activity of the plasma to  $34.7 \pm 0.07\%$  by 6 months with the subsequent its additional increase to  $36.5 \pm 0.10\%$  to 12 months life. This led to a decrease in the level of acyl hydroperoxides: by 6 months up to  $1.33 \pm 0.07$  D<sub>233</sub>/1 ml and up to  $1.21 \pm 0.14$  D<sub>233</sub>/1 ml to 12 months life with a decrease in the content of thiobarbituric acid-active compounds by 6 months.  $3.36 \pm 0.12$   $\mu\text{mol/l}$ , by 12 months  $3.18 \pm 0.12$   $\mu\text{mol/l}$ , totaling for the phase of 7.9%.

During the neonatal phase, a small tendency of the plasminogen level to increase with a significant decrease in the inhibitor of its active form -  $\alpha_2$  antiplasmin by 27.5% was noted in healthy calves, which tended to slow the spontaneous euglobulin lysis time, the level of fibrin degradation products during the mammary feeding phase experienced the tendency to increase and being a marker of the optimal adaptation of the organism to the external environment by maintaining the activity of fibrinolysis at the required level (Table 1).

During the phase of milk and vegetable nutrition in healthy calves, a similar dynamics of the level of plasminogen was observed with a marked decrease in the inhibitor of its active form- $\alpha_2$  antiplasmin by 5.1% to 45 days of life, followed by their restoration and a smooth dynamics of their activity. This provided a sharp acceleration at 45 days of life with a subsequent return to values close to the baseline and a peak at this age, and subsequently a constant level of fibrin degradation products during the phase of milk and vegetable nutrition.

In the dynamics of fibrinolytic ability of blood of calves aged between 3 and 12 months a statistically significant regularity was found. The switch to vegetable nutrition in healthy calves contributed to a reliable dynamics of plasminogen levels with a significant decrease in the inhibitor of its active form -  $\alpha_2$  antiplasmin by 4.9% to 6 months life with the subsequent additional similar dynamics of their activity, which ensured the acceleration of the process of fibrinolysis, estimated from the time of spontaneous euglobulin lysis from 3 to 12 months by 11.4%. In the estimated age period, the invariability of the concentration of fibrin degradation products in the blood was recorded, which indicated an optimal level of adaptation of the organism to the external environment due to the maintenance of fibrinolysis activity at the required level.

Thus, during the change in dietary habits in early ontogenesis, the calves showed a regular dynamics of fibrinolysis activity associated with a gradual and reliable increase in plasma levels of plasminogen and a decrease in  $\alpha_2$  antiplasmin with a jump in their activity by 45 days, followed by recovery at a level close to the values at the beginning of the phase milk and vegetable nutrition with further strengthening of fibrinolysis on plant nutrition.

**Table 1. Dynamics of taken into account indicators in calves in early ontogeny**

Registered parameters	Newborn phase, n=29, M±m		Milk phase, n=32, M±m		Milk and vegetable nutrition phase, n=36, M±m					Phase of plant nutrition, n=39, M±m			
	1-2 day of life	9-10 day of life	11 day of life	30 day of life	31 day of life	45 day of life	60 day of life	75 day of life	90 day of life	91 day of life	6 months of life	9 months of life	12 months of life
Acid hydroperoxide of plasma, $D_{233}/1\text{ ml}$	1.49±0.10	1.44±0.12	1.46±0.07	1.53±0.20	1.54±0.08	1.80±0.14 p<0.01	1.66±0.12 p<0.01	1.42±0.15 p<0.01	1.41±0.11	1.40±0.09	1.33±0.07 p<0.05	1.28±0.17 p<0.05	1.21±0.14 p<0.05
Thiobarbituric acid products, $\mu\text{mol/l}$	3.49±0.11	3.47±0.11	3.51±0.14	3.55±0.16	3.59±0.22	3.77±0.16 p<0.01	3.67±0.14 p<0.01	3.51±0.23 p<0.01	3.45±0.19	3.43±0.25	3.36±0.12 p<0.05	3.27±0.16 p<0.05	3.18±0.12 p<0.05
Antioxidant plasma potential, %	34.2±0.16	33.5±0.09	32.8±0.23	32.8±0.15	29.3±0.17	27.4±0.15 p<0.05	30.6±0.14 p<0.01	32.8±0.12 p<0.01	33.9±0.24	33.9±0.09	34.7±0.07 p<0.05	35.4±0.08 p<0.05	36.5±0.10 p<0.05
Time of spontaneous euglobulin lysis, minutes	186.3±0.52	178.9±0.42	178.2±0.34	170.3±0.15 p<0.05	170.0±0.26	152.3±0.10 p<0.01	167.7±0.14 p<0.01	165.0±0.13 p<0.05	162.1±0.09 p<0.05	161.7±0.20	155.1±0.14 p<0.05	150.7±0.16 p<0.05	145.1±0.10 p<0.05
Plasminogen, %	115.2±0.17	120.1±0.45	122.0±0.05	128.6±0.10 p<0.05	128.9±0.02	138.8±0.07 p<0.01	130.2±0.09 p<0.01	132.6±0.08 p<0.05	134.5±0.08 p<0.05	132.8±0.10	135.2±0.06 p<0.05	138.7±0.13 p<0.05	142.5±0.07 p<0.05
$\alpha_2$ antiplasmin, %	130.4±0.32	102.3±0.28 p<0.05	101.3±0.19	96.4±0.09 p<0.05	96.1±0.15	80.4±0.17 p<0.01	93.6±0.05 p<0.01	90.4±0.08 p<0.05	89.0±0.03 p<0.05	89.2±0.10	93.6±0.12 p<0.05	96.7±0.06 p<0.05	99.6±0.09 p<0.05
Products degradation of fibrin, $\mu\text{g/ml}$	33.9±0.21	39.5±0.34	40.2±0.25	42.8±0.16	42.9±0.16	55.8±0.25 p<0.01	44.8±0.29 p<0.01	43.1±0.18	44.0±0.12	44.3±0.15	45.2±0.22	46.0±0.18	45.7±0.17

Legend: p - reliability of the dynamics of indicators from research to research.

## DISCUSSION

The study found that during early ontogeny in healthy calves, stability was noted with subsequent enhancement of the activity of the antioxidant potential of the plasma [15,16] and an increase in the levels of the primary products of lipid peroxidation - acyl hydroperoxides and secondary - tiobarbituric acid-active compounds were stable [17,18], which, apparently, is necessary for this type of productive animals for the development of antistress mechanisms of its homeostasis in the early stages of development [19,20]. The achieved low level of plasma lipid peroxidation causes an unchanged alteration of endotheliocytes [21] and components of the liquid part of the blood, contributing to weak stimulation of plasma hemostasis [22,23].

Very important for optimal fluid properties of blood in healthy calves is the activity of plasminogen, which ensures the equilibrium of fibrin formation and fibrinolysis [24]. This can be confirmed by the absence of signs of thromboses and hemorrhages in healthy calves, which allows the calf organism to respond adequately to unfavorable environmental factors, which usually have a procoagulant effect on hemostasis [25,26].

During early ontogeny, fibrinolytic activity of plasminogen significantly increases with a decrease in the activity of the fibrinolysis inhibitor -  $\alpha_2$  antiplasmin [27]. Obviously, this is a physiological response to the adaptation of the organism [28], which, upon completion of the neonatal phase, requires an increase in fibrinolysis activity [29]. In view of the fact that the general inhibitor of the contact activation of plasma proteases, plasminogen gradually increases with the level of fibrin degradation products remaining in the blood [30], one can think about the optimal functioning of the mechanisms of hemostatic adaptation [31] in these conditions without signs of hypocoagulant hemostasis direction at these times, providing optimal conditions of microcirculation [32,33].

Thus, in calves with a change in diet there is a significant increase in fibrinolysis activity, which is probably an element of the general adaptation process of the organism during early ontogeny.

## CONCLUSION

The physiological dynamics of fibrinolysis in many ways ensures, during the course of early ontogeny, the necessary level of liquid blood properties and the optimal degree of perfusion of the internal organs, which greatly facilitates the metabolism in the calf tissues, contributing to its further growth and development, being an essential element of the final functional maturation of the body in a changing diet.

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