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Syndrome "Eclampsia" Mechanism of Pregnant Cows and Effectiveness of Antioxidant Preparations

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Introduction

800 dairy cows and heifers of highly productive Holstein-Friesian breed, black and mottled and Simmental breeds with an average annual milk production of 6700 kg participated in experiment. Each group of animals was divided into two subgroups. Down calver heifers and cows in dry period were injected with organ selenium preparations intramuscularly at a dose of 0.01 ml per 1 kg of body weight on the 15th and 45th days, for 30 days with 72 hours interval. The first experimental group received the preparation «Immunoseyv®», the second – «Selenolin®» and the control group didn't use preparations. Interhormonal relationships system and LPO-AOD system imbalance of pregnant cows leads to the development of «eclampsia» syndrome in the last third of pregnancy. This pathological state of clinical manifestation is registers against the background of functional insufficiency placental system and non-enzymatic antioxidant protection level. Compared with clinically healthy animals in concentration of progesterone below a blood 2.2–2.5 times (10.5 ± 2.09 vs. 24.7 ± 4.62 ng/ml), testosterone – 1.85 times (0.7 ± 0.09 vs. 1.3 ± 0.22 ng/ml), estradiol – by 27.0 % (215.0 ± 17.9 vs. 273.4 ± 38.4 pg/ml), cortisol – at 34.0–52.8 % (24.4 ± 3.01 vs. 32.7 ± 5.79 ng/ml) vitamin E – 45.4 %, vitamin C – 20.8 %. MDA content larger than that in healthy animals by 43.3 % (from 1.04 ± 0.14 to 1.49 ± 0.12 mmol / l), the stable metabolites N0* – 31.9 %, MPO activity – 26.6 %, catalase – by 17.3 %, triglycerides – 2.2 times, the lactic acid – 2.5 times, the sorption ability of erythrocytes – 55.1 %. Eosinophilia and thrombocytopenia accompanied these changes. Organ selenium preparations double assignment to parenteral clinically healthy cows in dry period for prevention «eclampsia» syndrome and correction metabolic disorders prevents development of obstetric pathology in 92.8 % of the animals, exceeding to 23.7 % index of control group. Applying «Immunoseyv®» selenium-containing preparation to animals with preeclampsia clinical symptoms and subclinical eclampsia reduces detention afterbirth in 3.2 times and postnatal pathology on 10.0 %.

The maximum increase productivity of animals without the introduction of the practice of dairy production of innovative technologies of selection and breeding of dairy cattle, when are not taken into account the physiological needs of the animals, leads to functional overload the organs and systems of the body, against the background of which develop the disease during pregnancy, and violated the fetal development [1-4]. A number of researchers believe [2,3] that the observed disorders of the reproductive function in cows to increase the genetic potential of dairy productivity is largely linked to the substantial and inadequate shifts in metabolism. Therefore, one of the solutions to the problem of preeclampsia at the end of the pregnancy in highly productive dairy cattle is the study of the role in the pathogenesis of metabolic disorders, leading to the development of subclinical eclampsia [5]. In addition, recently launched the concept [6], claiming that the obstetric pathology in cattle breeds of dairy is a by-product of the

actions of those mechanisms that are necessary to carry out the genetic program of pregnancy and fetal development [7]. The source of damage to the tissue structures of the organs of reproduction in this case may be, it would seem, normal pregnancy processes of metabolism, in particular, the intensification of processes of free radical oxidation, aimed to increase the synthesis of prostaglandins and steroid hormones, involving the formation and accumulation of Reactive forms of oxygen (superoxide, hydroxide, radicals, hydrogen peroxide), serving Universal nonspecific metabolic link in the development of many pathological conditions [8]. Moreover, in recent years, it is becoming increasingly apparent involvement in the pathogenesis of functional disorders of the Reproductive System in mammals not only active metabolites of oxygen, but such free radicals, such as nitric oxide [9], which is a universal regulator of physiological functions of the body and the metabolism of cells, including protective-adaptive reactions to stress and adaptive responses of the Organism [10,11]. Therefore, the study "oxidative stress", affecting the system of half-AO3, and nitrogen oxides in the genesis of obstetric-gynecological pathologies in the relationship with the status of the endocrine system and scant body of animals unique nutrient element - selenium, controlling in the composition of proteins and peptides level of peroxide oxidation, the synthesis of nucleic acids and proteins, lipid metabolism, the processes of homeostasis and hormonogenesis, participating in the formation of the immune defense [12], is one of the first places in addressing issues related to preserving their fertility. The purpose and methodology of research. The purpose of the work is the development of the syndrome "eclampsia", determine the impact of drugs on the Selenium hormonal, oxygen-antioxidant and biochemical status of cows and give clinical assessment of their role in the prevention of preeclampsia pregnant women. The experiments were performed in Saratov State Agrarian University named after N. I. Vavilov, as well as in the farms of different organizational and legal forms of ownership of the Saratov region in the period 2009-2016, the experiment involved 800 cows and heifers dairy high-yielding cows Holstein-Friesian, black and diverse and Simmental breeds. In the experiments were the cows with the annual dairy productivity of 6,700 kg. A group of clinically healthy animals accounted for cows with normal arterial pressure (ADF - 98.1 ± 1.63 mmhg), the lack of signs of edema and the presence in the urine protein in the range of 0.6 ± 0.07 g/l. In the group with heavy course of preeclampsia in combination with symptoms of subclinical eclampsia were classified animals with complete its complex of symptoms: arterial hypertension (ADF - 136,1 ± 2.85 mmhg), proteinuria (protein in the urine - 3.0 ± 0.49 g/l), swelling in the area of the pelvic limbs, abdominal wall, dewlap. In the group with subclinical eclampsia were classified cows with individual clinical symptoms of preeclampsia (ADF - 118,7 ±3.01 mmhg, protein in the urine - 1.1 ± 0.44 g/l). Deep cows and cows in the dry period were injected selenorganic drags intramuscularly in a dose of 0.01 ml per 1 kg of mass of the body of 15-th and 45-th days, within 30 days with an interval of 72 hours. The first treatment group entered the drug "Immunoseyve®", the second - "Selenolin ®, the control group cows' drugs are not used. For hematological studies of blood taken before the morning feeding. Biochemical blood tests conducted on the analyzer, CIBA-CORING 288 BLOOD GAS SYSCEM (USA). Statistical analysis of data was conducted using standard Microsoft Excel 2000 SPSS 10.0.5 for Windows. The results of the research. Determined that the development of preeclampsia in cows took place against the background of the placental insufficiency, shown by indicators of endocrine status, indicating a low content in peripheral blood of steroid hormones (Table 1).

Table 1: Hormonal blood parameters in pregnant cows during eclampsia and subclinical eclampsia.

Indicator	Clinically healthy	Eclampsia of pregnant	The syndrome of "eclampsia"
Progesterone, ng/ml	24,7 ± 1,62	10,5 ± 2,00**	11,2 ±4,30**
Testosterone, ng/ml	1,3 ±0,02	0,7 ±0,09*	1,2 ±0,33
Estradiol, PG/ml	273,4 ± 18,40	215,2 ± 17,90*	270,1 ± 15,40
Cortisol, ng/ml	32,7 ± 1,79	24,4 ± 1,01*	21,4 ± 1,47**
The index P/e	90	50	40

As can be seen from the above data, in cows with mild pathological process (or at an early stage of development) the concentration of the progesterone was lower than that of clinically healthy animals, in 2,4 times (10.5 ± 2.09 ng/ml against 24.7 ± 4.62 ng/ml, $p < 0.05$), testosterone - 1.7 times (0.7 ± 0.09 ng/ml against 1.3 ± 0.22 ng/ml, $p < 0.05$), estradiol - 1,3 times (KZT1 215.0 ± 17.9 pg/ml against 273,4 ± 38.4 pg/ml), cortisol - 1,3 times (24.4 ± 3.01 ng/ml against 32.7 ± (5.79 ng/ml). Back in the subsequent compensatory mechanisms of functional activities placental complex lead to enhance the synthesis of testosterone and estradiol and improve their content in the blood of cows of the third group (with a full triad complex of symptoms of preeclampsia) up to the level of clinically healthy animals. However, the concentration of the progesterone (11.2 ± 4.31 ng/ml) and cortisol (21.4 ± 3.47 ng/ml) remains low. The index of the ratio of progesterone with estradiol in cows with pathology of pregnancy was lower than that of animals with physiological its passage, in 1.8-2.2 times.

Proceeding from the fact that in the mechanisms of development of preeclampsia on the background of subclinical eclampsia (syndrome of "eclampsia-preeclampsia") in dairy cows the central place occupies the revitalization of the oxidative stress and free radical oxidation, we have carried out studies on the use of a new antioxidant drug "Immunoseyve®" as an element with antioxidant

action for the prevention of this pathological condition of pregnant cows. Indicators of the status of the system half-AO3 are presented in table 2.2. It follows from the table that in cows with pathology of pregnancy already at the initial stage of its development was an increase in the content in the blood of intermediate peroxidation lipids - dam at 43.0% (1.04 ± 0.14 to 1.49 ± 0.12 μmol/l, p < 0.05), and the activation of the antioxidant protection as a compensatory response to the damaging effect of lipid peroxidation products. The activity has increased by 14.3%, the contents of the stable metabolites of nitrogen oxide trap - At 38.0%, vitamin C - by 24.1%. At the same time, the content of vitamin E, not synthesized in the body, decreased by 13.1% (11.2 ± 0.89 to 9.9 ± 1.20 mmol/l), which is associated with a significant flow of his to neutralize the toxic products of lipid peroxidation. When the syndrome of "eclampsia-preeclampsia" there is a high level of activity of enzymatic link antioxidant protection in complex with the nitrogen oxide trap. Nonenzymatic power management of continuing decline: blood levels of vitamin E is reduced to 7.7 ± 0.93 μmol/l, or 44.5 % (p < 0.01), vitamin C - to 12.0 ± 1.69 mmol/l, which is lower than that of healthy animals, 20.8%. As a result, the received data show that the pathology of pregnancy in cows, clinically manifested complex of symptoms of preeclampsia, develops on the background of subclinical eclampsia and revitalization processes peroxidation lipids (increase in the blood, DAM, the activity of enzymes AO3 and stable metabolites of N0, the accumulation of toxic metabolic products, violations of the functions of the liver and kidneys (proteinuria, reducing the ratio of content in the blood urea and creatinine clearance). Analysis of the data showed that the pregnancy in cows with the syndrome of "eclampsia-preeclampsia" ended with the pathological childbirth in 8.3% of cases and the development of the inflammatory process in the genital organs at 25.0% of the animals. When twice the intramuscular injections of cows during the period of dead trees new antioxidant organoselenium drug "Immunoseyve®" pathological births have not been registered, and inflammatory processes in the uterus diagnosis in 7.2% of cases (Table 2). Consequently, the appointment of the antioxidant of "Immunoseyve®" cows, passing in the dead wood with clinically normal course of pregnancy, would prevent the development of obstetric pathology in 92.8% of the animals.

Table 2: Some indicators of the state of the LPO-AOD system in cows with physiological and pathologic course of pregnancy.

Indicator	Clinically healthy	Gestosos of pregant	The syndrome of "eclampsia"
Malonic dialdehyde, mkmol/l	1.04 ±0,14	*1,49 ±0,12	1,48 ±0,14
Gap, mm 0-8N/Limin	14,6 ± 1,54	17,2 ± 2,11	18,4 ±2,58
Catalase, mm H_20_2/Limin	30,1 ± 1,26	34,4 ± 0,93	35,3 ±2,44
Vitamin E, μmol/l	11,2 ± 0,89	9,9 ± 1,20	7,7 ±0,93
Vitamin C, mmol/l	14,5 ± 5,73	18,1 ± 4,02	12,0 ± 1,69
N0*, μmol/l	60,1 ±8,02	83,0 ±7,87	79,3 ±8,19

In the control group of animals turned out to be 75.0%. The manifestation of obstetric pathologies was reduced to 3.47 times. The morphological and biochemical blood analysis before putting experience and at the final stage of the pregnancy has shown that the appointment of the antioxidant drug "Immunoseyve®" is accompanied by significant changes in the mi- in cows hemomorphological and biochemical status. Thus, the number of leukocytes in the blood of cows decreased by 18.9%, the eosinophils - in 2.1 times (p < 0.05), the monocytes - at 2.31%, while increasing the relative number of neutrophils by 12.8%, the lymphocytes - 7.7% and platelets - 12.5%. Also trend toward lower sorption ability of erythrocytes, hemoglobin and hematocrit. Changing the quantitative characteristics of the formed elements of blood with the positive shifts in the platelet link of homeostasis under the influence of the antioxidant drug "Immunoseyve®", there is a decrease in the body of animals of endogenous toxicity included focal, improving uteroplacental blood flow, which contributes to the activation of the exchange of substances between the blood of mother and fetus. Change the biochemical parameters of blood of the moat was characterized by primarily increasing content in the blood of selenium at 78.4% (p < 0.001), vitamin E - 58.1%, vitamin C - on 231,6% (P < 0.05) and glucose - at 28.0% (P < 0.05). The manganese concentration in the blood of cows has increased by 21.2% (P < 0.01), copper - by 11.4%, zinc - to 32.8% (P < 0.02) and is associated with the protein of iodine - by 7.4%. The Dam depositum decreased by 17.8%. Analysis of the data showed that the appointment of sick cow's eclampsia antioxidant drug "Immunoseyve ®" reduced the expression of the pathology of descent act in these animals from 25.0% to 1.1%, or 3.24 times, and the development of postpartum endometritis - 1.22 times (Table 3). The use of antioxidant drug "Immunoseyve ®" animals with clinical symptoms of preeclampsia in combination with subclinical eclampsia in terms of its treatment-and-prophylactic actions proved to be more effective in comparison with the appointment of his animals, only patients with subclinical eclampsia. The data show that in the appointment of the antioxidant drug "Immunoseyve®" dry cows against the backdrop of subclinical eclampsia and of preeclampsia in pregnant are activating the exchange of trace elements, energy processes, improve the antioxidant status, decreased activity of lipid peroxidation. Studied the application of new injectable HFA formulation compositional liposomal forms of selenorganic drug "Immunoseyve®" (composition: nanoselen, lactoferrin and filler, Pharmacological group - medications selenium) is deeply cows and heifers. Noted its positive impact on the operational activities of

the placental complex, as evidenced by the increase in the content in the blood of estradiol-17r by 49.7% (270,1 ± 25.4 pg/ml up to 404,5 ± 108.2 pg/ml) and cortisol - at 39.0% (21.4 ± 3.47 ng/ml to 29.7 ± 2.52 ng/ml), as well as improving the work of the thyroid gland (increase in the content of the associated with Bel- k iodine with 4,03 ± 0.15 μg% to 4.33 ± 0.12 μg% or 7.4%). At the same time, it should be noted that the expressed changes in the functional activity of the liver and kidneys on the basis of the indicators of the content of urea, creatinine and aminotransferase activity is not registered. Conclusions. The research proved that the appointment of antioxidant means cows, passing in the dead wood with clinically normal course of pregnancy, would prevent the development of obstetric pathology in 92.8% of the animals. In the control group of animals turned out to be 75.0%. The manifestation of obstetric pathologies was reduced to 3.47 times. Therefore, recovery scheme of the functional activity of all organs and systems of the body when clinically distinct complex of symptoms of preeclampsia and manifestation of subclinical eclampsia the polyorgan pathology, must include not only the antioxidant therapy, but other means of influencing the normalization of the major parts of the pathological process.

Table 3: The antioxidant effect of selenium on the course of childbirth and the postpartum period in cows.

Indicator	Groups of animals, the drug		Drugs are not used
	«Selenolin®»	«Immunoseyve®»	
The number of animals	380	320	100
Pathology of childbirth and the postpartum period, %	32,0	19,0	56,0
The detention of the afterbirth, %	6,8	4,8	13
Endometritis, %	14,3	10,7	22,0
Subinvolution of uterus, %	13,7	8,5	33,0

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