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Physiological Effect Of Immunomodulatory Drugs In Combination With Hormonal Stimulation On Maternal Cows.

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ABSTRACT

One of the main tasks of dairy farming is to obtain healthy young, while maintaining the health of the mother. The easiest way to get a healthy and viable young is to prevent diseases in the first weeks and months of life. It is most advantageous to use the mechanism of colostral immunity inherent in nature. The aim of this experiment was the comparison of two prophylactic schemes, including products based on anoxemia bromide and hormonal stimulation at the cows for 3-5 days before calving. This was formed 4 groups of 20 animals each: control, 1st subject, 2nd subject, 3rd test subjects, the 4th subject. Animals of the 1st experimental group was injected intramuscularly Isoxepac at a dose of 6 mg. Animals of the 2nd experimental group were injected intramuscularly Polyoxidonium in the dose of 6 mg. Cows 3-children of the experimental group was injected intramuscularly Isoxepac at a dose of 6 mg subcutaneously 1 ml Sinestrola 2%. Animals the 4th experimental group was injected intramuscularly Polyoxidonium in the dose of 6 mg subcutaneously 1 ml Sinestrola 2%. During the experiment, the 3rd experimental group gave the first portion of colostrum 21% more compared to the control group of cows. With an IG content of 75.36 mg / ml, which is 48.05% more than the control animals of the first portion of colostrum. Based on hematological parameters, the mother cows to which such immunological stimulation is applied are positively different from the control animals. As well as their hematological parameters look more positive than in animals of other study groups. The described hematological changes in experimental groups of animals in the preventive therapy of which an immunomodulatory drug without Synestrol was used are 2% similar to each other, but more positive than in cows of the control group.

Keywords: colostrum, Sinestrol, anoxemia bromide, cows

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INTRODUCTION

There is a direct connection between the physiological state of the cow-mother and the calf received from her. Healthy offspring with high viability can only be obtained from a healthy cow. To newborns, in the first days of life, it is necessary to show special attention and care. It is known that the animals that have been ill at an early age are of little or no use for further reproduction. It is necessary to constantly take care of preservation of health of animals at all technological stages of reception and cultivation of young growth, and also operation of an adult livestock and production of animal husbandry. To solve the problem of diseases of young animals in livestock complexes requires the introduction of a number of veterinary measures, especially in the biological complex "mother-fetus-newborn", reliably ensuring the protection of animals from disease and their productive longevity.

Timely drinking of high-quality colostrum to a newborn calf is important for passive calf immunization, stimulation of intestinal epithelial cell growth [10] and development of intestinal functions [5,6,7]. Many scientists consider the true colostrum to be the first portion of colostrum obtained from a cow immediately after calving [1,2,8]. in addition, the calf loses its ability to absorb immunoglobulins through the intestine. The first colostrum contains immunoglobulins such as IgA, IgM, IgG, IGF-1, lactoferrin and lysozyme. As well as a significant amount of nutrients [7], such as fat-soluble vitamins, vitamin B12 and iron [6,7], protein.

In the later stages of pregnancy is hormonal restructuring of the body, which causes functional and structural changes in the breast. The development of alveolar-lobular apparatus of cow udder and cell proliferation are interesting for our study [13]. Restructuring alveolar tissue cells associated with the formation on their surface specific receptors for various hormones, providing the possibility of synthesis of molecules of certain information RNA, necessary for the biosynthesis of colostrum proteins, primarily immunoglobulins. Along with the induction of local synthesis of proteins and other biologically active substances, the permeability of the alveoli and all parts of the capacitive system of the udder significantly increases, which contributes to the selective transition from blood plasma to the breast secret of many biologically active substances (immunoglobulins, some whey proteins, phospholipids, trace elements, hormones, vitamins) [5]. As calving approaches, the processes of synthesis and selective transition to colostrum of the most important components increase. Especially intensively in the secret of the breast changes the concentration of immunoglobulins. Their greatest diffusion in colostrum is observed 3-9 days before calving.

An important role in the body of the animal play female sex hormones - estrogens (estron, estriol, estradiol). Structures-targets for estrogen are the genitals-ovaries, oviducts, uterus, vagina, mammary glands. Estrogens stimulate their growth and development. Under the action of estrogens the growth of ducts, lobes and alveoli of mammary glands was found [9,14]. In addition, estrogens are involved in the regulation of metabolic processes, increase the content of phospholipids in the blood, increase protein synthesis and the accumulation of muscle tissue, increase the body's resistance to harmful effects, enhance regeneration in tissue damage, improve higher nervous activity. The molecular mechanisms of the biological action of estrogens are their penetration into the target tissue cells, where they bind to a specific non-nuclear protein estrophilin, forming a hormone-receptive complex. After activation, it is transported to the nucleus, where, as a result of binding to the nuclear acceptor, RNA biosynthesis changes and changes characteristic of hormone-sensitive tissue develop, protein synthesis is activated.

It is known that in utero the fetus is able to develop normally only in conditions of constantly increasing content of the complex of hormones, and primarily estrogen in its internal and external environment. After birth the body does not need hyperharmonie the background, and the available hormonal reserves are excreted. In the body of a newborn contains a very large amount of estrogen hormones. According to modern concepts, estrogens stimulate the proliferation of glandular epithelium and milk passages in the intrauterine period [9,13,14].

In early work, we studied the action of some immunomodulatory drugs on the organism of calves, as well as on the concentration of immunoglobulins in colostrum of cows mothers as well as the establishment of the optimum dose Sinestrola 2% [3,11,12].

Sinestrol is a synthetic analogue of the female hormone estrone. It has the effect of endogenous estrogen produced by the female body. Sinestrol in estrogenic activity equivalent to the folliculin 10 000

UNITS. Excretion is by the kidneys, depending on the physiological state (phase of the menstrual cycle), age and other conditions, the rate of excretion of various.

The active substance of drugs Isoxepac and Polyoxidonium is anoxemia bromide. It is a true immunomodulator which: increases reduced and reduces increased immunological activity; acts on phagocytes and natural killers; stimulates the production of IL-1β, IL-6, TNF-α and β-interferons; stimulates the process of phagocytosis, with the lack of humoral immunity - the production of antibodies; restores immune responses in secondary immunodeficiency; increases the resistance of the body against local and generalized infections; it has anti-inflammatory effect; it is a detoxicant, antioxidant, stabilizes cell membranes.

MATERIALS AND METHODS

The experiment was conducted in the summer (June-August) 2018 in the conditions of a typical farm of the Nizhny Novgorod region of dairy orientation. Located in the Dalnekonstantinovsky district of the Nizhny Novgorod region, SEC "Nizhegorodets". The object of the study was Holstein cows at late pregnancy and blood samples obtained from them. Of the selected animals was formed five groups of twenty animals each: control, 1st subject, 2nd subject, 3rd test subjects, the 4th subject. Groups were formed from clinically healthy animals on the principle of pairs-analogues. When selecting animals for the experiment, the following parameters of animals were taken into account: the number of pregnancies (2-3), the volume of previous lactation, the number of inseminations, the physiological state (clinically healthy animals were selected). Schemes of administration of drugs to cows of the formed groups:

- the control was injected intramuscularly isotonic solution of sodium volume of 2 ml.
- Guinea pig - Isoxepac intramuscularly introduced at a dose of 6 mg.
- a test subject was injected intramuscularly polyoxidonium in the dose of 6 mg.
- experimental - Isoxepac intramuscularly introduced at a dose of 6 mg subcutaneously 1 ml Sinestrola 2%.
- test subject was injected intramuscularly polyoxidonium in the dose of 6 mg subcutaneously 1 ml Sinestrola 2%.

Administration of drugs of both groups to animals was carried out 3-5 days before calving.

During the experiment, the volume of the first portion of colostrum was noted and the level of immunoglobulins in it was investigated. To do this, immediately after milking the cow in sterile glass containers after preliminary testing for mastitis, 50 ml of colostrum was taken. For laboratory blood analysis of cows, the sample was taken from the tail vein immediately before administration of the drug and immediately after the hotel.

For laboratory blood tests were carried out on the hematological analyzer CT 2000, Sysmex, Europe, GmbH. The content of common colostrum immunoglobulins (Ig) was determined by the method with sodium sulfite described in the Handbook "methods of veterinary clinical laboratory diagnosis" edited by Professor I. p. Kondrakhin [4].

The resulting digital material was subjected to statistical processing using conventional parametric methods, the degree of reliability was determined by the student's t-criterion using the Microsoft Excel application package (2007).

RESULTS AND DISCUSSION

Data on the number of immunoglobulins in the colostrum of cows of the control and experimental groups are presented in figure 1. It shows that the highest concentration of immunoglobulins is observed in cows of the 3rd experimental group, the rate is higher than in control animals by 48% and 15.9% than in animals of the 4th experimental group. We also see that the difference between the 1st and 2nd experimental groups is insignificant, but in the group of animals in preventive therapy of which polyoxidonium was used, the deviation of the mean value is less than in the animals of the 1st experimental group. It is worth noting the

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difference of 18.41% between the 1st and 3rd experimental group, which shows the efficiency of Sinestrola 2% in the preventive scheme.

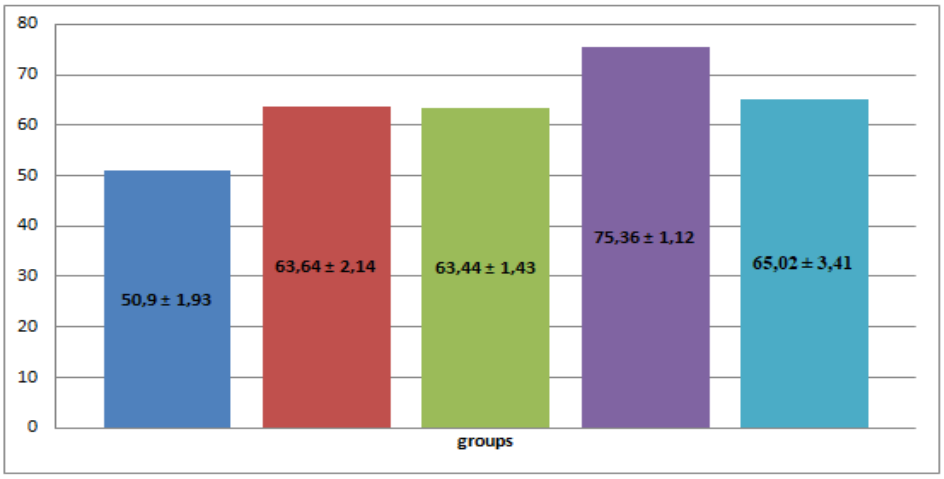

Figure 1-Concentration of Ig in the first portion of colostrum

Figure 2 shows the volume of the first portions of colostrum from cows of the observed groups. From it we see that cows in preventive therapy which has been used Sinestrola 2%, give a greater amount of colostrum in the first milking in comparison with animals to which the drug was not used. And the difference is on average 25%.

It should be noted that in the Russian Federation in recent years there is no similar information. And to estimate these figures by comparison with other dairy farms is not yet possible.

The results obtained in the laboratory study of the blood of cows of the 1st and 2nd experimental groups are presented in table 1. It can be seen that the red blood cell content in cows of the 2nd experimental group after calving increased by 23.1% compared to the first study, which is higher by 13.31% than in the control group and 19% higher compared to the 1st experimental group. On average, the number of leukocytes in animals of the 1st experimental group increased by 24.18%, which is 15.66% higher than in animals of the 2nd experimental group. But at the same time, the number of leukocytes does not go beyond the permissible limits, as it happened in the control group. The increase in the total number of leukocytes was due to the growth of segmental cells in both the 1st and 2nd experimental groups by 57.56% and 67.88%, respectively. Also, the number of rod cells increased by 28.57% and 30.77%. We can see an increase in the number of erythrocytes in the 2nd experimental group by 23.1% and hemoglobin by 13.08%, while in the animals of the control and the 1st experimental group these indicators increased less intensively.

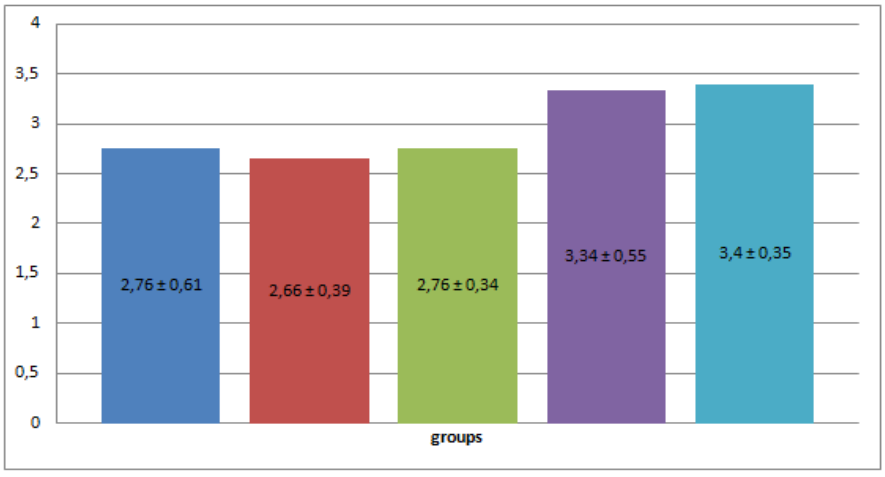

Figure 2 - volume of the first portion of colostrums

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In General, it can be concluded that the groups in the preventive therapy of which immunostimulatory drugs have been used have milder changes in the leukocyte formula, compared with control animals that do not go beyond the physiological norm.

The increase in the number of platelets in animals of the 1st, 2nd and control groups is approximately equal and indirectly indicates the same birth injuries.

Table 1-Hematological parameters of blood of cows of the 1st and 2nd experimental groups, before and after calving

Indicators	Before drug administration			After calving		
	control	1rd experimental	2rd experimental	control	1rd experimental	2rd experimental
White blood cells	12,42±3,74	9,14 ± 1,74	11,15 ± 2,46	15,56±3,71	11,35 ± 1,99	12,1 ± 3,36
Eosinophils	3,2 ± 2,17	1,6 ± 0,55	1,6 ± 0,89	3,2 ± 1,3	1 ± 0	0,8 ± 0,45
Basophils	0 ± 0	0 ± 0	0 ± 0	0,4 ± 0,55	0 ± 0	0 ± 0
Myelocytes	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Young neutrophils	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Band neutrophils	3,2 ± 0,84	2,8 ± 0,45	2,6 ± 1,52	3,2 ± 0,84	3,6 ± 0,89	3,4 ± 1,95
Segmented neutrophils	31,6 ± 17,1	34,4 ± 4,28	33 ± 16,91	44,8±7,79	54,2 ± 4,82	55,4 ± 11,01
Lymphocytes	56,8 ± 14,91	56,6 ± 2,97	57,8 ± 17,44	43,8±7,33	35,6 ± 7,13	35,4 ± 9,34
Monocytes	5,2 ± 1,64	4,6 ± 2,3	5 ± 1,41	4,6 ± 2,7	5,6 ± 3,29	6,25 ± 3,5
Red blood cells	5,72 ±0,81	6,02 ± 0,99	5,67 ± 0,64	6,28±0,43	6,25 ± 0,74	6,98 ± 0,15
Hemoglobin	106 ± 13,95	111,8±14,79	104 ± 3,24	115 ± 8,69	117,4 ± 11,5	117,6 ± 5,46
Platelets	227 ± 58,56	248,2±38,19	230 ± 78,31	444,8 ± 70,4	491,8±82,44	486,4 ± 108,01
Hematocrit	29,44±3,69	30,6 ± 3,83	30,4 ± 1,71	34,7 ± 2,2	35,98 ± 2,3	35,78 ± 0,8
Lymphocytes /Segmental Neutrophils	1,8 ± 1,01	1,67 ± 0,29	2,55 ± 2,08	0,98±0,33	0,67 ± 0,18	0,7 ± 0,44
Band neutrophils / lymphocytes	0,06 ± 0,01	0,05 ± 0,01	0,05 ± 0,03	0,07±0,02	0,11 ± 0,04	0,09 ± 0,06
Total lymphocyte	7,3±3,48	5,14 ± 0,74	6,47 ± 3,59	6,89±2,38	4,11 ± 1,42	4,27 ± 2,29
count Average platelet	6,26 ± 1,04	5,5 ± 0,93	6,42 ± 0,24	6,4 ± 0,31	7,04 ± 0,49	6,6 ± 0,37
volume Average anisocytosis	17,46 ± 1,62	16,22 ±0,99	16,9 ± 1,12	16,84 ± 1,68	15,62 ± 0,44	17,58 ± 1,29
ESR	2,6 ± 1,34	2,2 ± 1,64	1,8 ± 1,3	1,4 ±0,55	1,4 ± 0,55	1 ± 0

The results of hematological studies of the 3rd and 4th experimental groups of cows are presented in table 2. It shows that the number of red blood cells in the blood of animals of the 3rd and 4th experimental groups increased by 8.07% and 9.11%, respectively, which is similar to the indicators of control animals. But less by 15% than in animals of the 2nd experimental group.

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Table 2 - Hematological parameters of blood of cows after administration of drugs Isoxepac and polyoxidonium, with the use of Sinestrol

Indicators	Before drug administration			After calving		
	control	3rd experimental	4rd experimental	control	3rd experimental	4rd experimental
White blood cells	12,42 ± 3,74	9,78 ± 2,83	11,29 ± 3,45	15,56±3,71	17,12 ± 6,25	16,81 ±7,92
Eosinophils	3,2 ± 2,17	2,6 ± 1	1,8 ± 0,58	3,2 ± 1,3	1 ± 0,82	0,8 ± 1
Basophils	0 ± 0	0 ± 0	0 ± 0	0,4 ± 0,55	0 ± 0	0 ± 0
Myelocytes	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Young neutrophils	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Band neutrophils	3,2 ± 0,84	3,2 ± 0,5	2,8 ± 1	3,2 ± 0,84	3,2 ± 0,58	2,4 ± 0,58
Segmented neutrophils	31,6 ± 17,1	31,2 ± 6,13	33,6 ± 6,43	44,8±7,79	53,2 ± 17,86	54,4 ± 0,58
Lymphocytes	56,8 ± 14,91	56,8 ± 7,75	59,4 ± 6,93	43,8±7,33	37,8 ± 17,23	41,2 ± 4,93
Monocytes	5,2 ± 1,64	6,2 ± 2,65	2,4 ± 0,58	4,6 ± 2,7	4,8 ± 0,82	3,2 ± 1
Red blood cells	5,72 ±0,81	5,95 ± 1,01	5,82 ± 0,99	6,28 ±0,43	6,43 ± 0,83	6,35 ± 0,6
Hemoglobin	106 ± 13,95	108,4 ± 9,22	99,2 ± 0,58	115 ± 8,69	120,4 ± 9,18	105,6 ± 4,36
Platelets	227 ± 58,56	243,8 ±46,22	237,6 ± 5,57	444,8 ± 70,4	391,8±140, 1	364,8±109,22
Hematocrit	29,44 ± 3,69	30,96 ± 4,45	28,26 ± 0,87	34,7 ± 2,2	35,84 ± 3,69	32,04 ± 1,95
Lymphocytes /Segmental Neutrophils	1,8 ± 1,01	1,67 ± 0,26	1,81 ± 0,37	0,98 ±0,33	0,57 ± 0,16	0,77 ± 0,17
Band neutrophils / lymphocytes	0,06 ± 0,01	0,05 ± 0,02	0,05 ± 0,02	0,07 ±0,02	0,13 ± 0,03	0,06 ± 0,04
Total lymphocyte	7,3±3,48	4,8 ± 0,11	6,6 ± 1,08	6,89 ±2,38	3,44 ± 0,96	6,77 ± 2,09
count Average platelet	6,26 ± 1,04	5,9 ± 1,13	5,96 ± 0,56	6,4 ± 0,31	6,56 ± 0,39	6,6 ± 0,76
volume Average anisocytosis	17,46 ±1,62	16,36 ± 0,6	16,36 ± 0,35	16,84 ± 1,68	16,26 ± 0,75	16,66 ± 0,85
ESR	2,6 ± 1,34	1,4 ± 0,58	1 ± 0	1,4 ± 0,55	1,4 ± 0,58	1,2 ± 0,58

The number of leukocytes in animals of the 3rd experimental group increased after calving by 75.05%, which is higher by 26.16% compared to the 4th experimental group. And higher on 50,87% than cows of the 1st experimental group. In the leukogram of the 3rd experimental group, we observe a sharp change in the number of segmented cells, by 70.51%, and a decrease in the number of monocytes by 33.45%. The total number of lymphocytes decreased by 28.33%. A similar picture we see in animals of the 4th experimental group, but the number of lymphocytes slightly increased. However, the change in these indicators in this case is not a pathology and is characteristic of normal calving.

CONCLUSION

Thus, it can be concluded that using prophylactic immunostimulatory therapy combinations of drugs Isoxepac and Sinestrola 2%, 3-5 days before calving, it is possible to obtain a larger volume of the first portion of colostrum, in our case 25%. Which in this case will contain more immunoglobulins. Based on the hematological parameters, the mother cows to which such stimulation is applied, positively differ from the control animals. As well as their hematological parameters look more positive than in animals of other study groups. The described hematological changes in experimental groups of animals in the preventive therapy of

which an immunomodulatory drug without Synestrol was used are 2% similar to each other, but more positive than in cows of the control group.

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