Economic efficiency of Sinoestrol-2% used for down-calving cows to stimulate non-specific resistance in newborn calves

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Abstract. This article assesses the economic efficiency of using Synoestrol-2% to down-calving cows to stimulate colostral immunity and non-specific resistance in newborn calves. Use of the drug positively affected the health of calves. At the same time, the immuno-biochemical and morphological composition of the blood in newborn calves improved to the first day after born: increased the level of total protein for 9.75% (p<0.05) compared to the control group of calves, albumins – 13.7% (p<0.05), alpha-globulins – 31% (p<0.05), gamma globulins – 21.8% (p<0.05), number of leukocyte increased for 17.2% (p<0.05). Ten days after birth, the content of alpha- and gamma-globulin decreased in the calves of the control and experimental groups, but it was significantly higher in the calves of the experimental group. The number of leukocytes was higher in the calves of the experimental group, mainly due to neutrophils. The first day after birth bactericidal activity of the blood serum, lysozyme activity of the blood serum, neutrophil phagocytic rate was higher compared with similar indicators calves of control group. The incidence of dyspepsia of calves of the experimental group decreased by 1.3 times, the duration of the disease was shorter by 1.7 days compared to calves of the control group. The economic efficiency of the use of the drug Sinoestrol-2% to cows was 3.12 rubles per 1 ruble of expenses.

1. Introduction
The health of newborn animals depends on the health of their mothers. The immune system is formed during the neonatal period. Immunoglobulins, necessary for protection against microorganisms of the external environment, enter the body with maternal colostrum through the gastrointestinal tract and are absorbed through the intestinal wall unchanged. For the maximum amount of immunoglobulins to enter a body, it is necessary to feed the calf in a certain dose in colostrum from clinically healthy cows in the first few hours of their life. Russian scientists offer various methods for producing high-quality colostrum, including influencing the body of pregnant cows before calving with various veterinary drugs, including immunomodulators. In some cases, the price of veterinary drugs is high, and may not be comparable with the positive effect on a body.

Kvapilík J. et al. studied mastitis of dairy cows and financial losses. The inflammations of the mammary gland are the most widespread and economically demanding diseases among all production
diseases in dairy cows. At relatively large variability it is possible to estimate that one case of mastitis occurrence can cause the economic loss of around 9000 CzC. There are involved above all lower revenues from the sale of milk (53%), higher costs on herd recovery (20%) and costs for drugs and cure (14%). The reduction of mastitis incidence and decrease of somatic cell count in milk could improve the economic results of dairy cow rearing [1].

New alternative to the gradual cessation of lactation is to abruptly stop milking at the same time as using cabergoline (CAB), a prolactin inhibitor [2]. Under default conditions, the average net cost of abrupt cessation of milking with CAB was €49.6/cow. The data showed that 90% of the net costs ranged from – €13.7 to €307.8/cow. The average net costs for gradual feeding and gradual milking were €99.1 and €71.5/cow, respectively. Abrupt cessation of milking with CAB saved €49.5 and €21.9/cow on average compared with gradual feeding and gradual milking, respectively. This difference was mainly due to more milk returns and intramammary infections costs during lactation.

Based on the investigated effect of hydroxyselenomethionine (HMBSe), it was shown that milk yields (raw, protein, and lactose) and feed efficiency were improved in a quadratic manner following increased dietary HMBSe addition, whereas energy-corrected milk, 4% fat-corrected milk, and total solid yields tended to be enhanced quadratically [3]. In terms of whole-blood variables, red blood cell and white blood cell levels were increased quadratically, whereas hemoglobin concentration increased linearly with increased HMBSe addition. Plasma nonesterified fatty acid concentrations tended to increase linearly along with HMBSe addition. Plasma superoxide dismutase activity increased quadratically with increased HMBSe addition. The total antioxidant capacity in plasma tended to improve quadratically when cows were fed more HMBSe. Moreover, plasma malondialdehyde concentrations of dairy cows tended to decrease in a quadratic manner when dietary HMBSe increased. The Se concentrations in milk, plasma, and milk/plasma ratio increased linearly following increased HMBSe addition. HMBSe improved lactation performance, health status, and milk Se concentrations in early-lactating dairy cows.

In [4] the authors considered the effects of biotin dietary supplementation, intramuscular vitamin B12 (VB12) injections, and beginning at the prepartum period on feed intake and lactation performance in postpartum dairy cows. When VB12 was given, the cows had greater feed intake, better lactation performance and lower body weight loss in the postpartum period compared with animals without injection of VB12. The VB12-injected cows had lower plasma nonesterified fatty acids and β-hydroxybutyrate concentrations but higher plasma superoxide dismutase activity compared with cows without VB12. Cows fed a biotin supplement had higher milk protein yield (6 and 8 wk) and lactose yield (6–8 wk), compared with animals without biotin. However, under the present experimental conditions, authors found no additive effect of a combined supplement of biotin and vitamin B12 on lactation performance of dairy cows.

Prophylactic and economic efficiency of Hexamine for dry cows and calves was examined in [5]. The authors found that the drug Hexamine has a stimulating effect on erythropoiesis, increased activity of the antioxidant system and indicators of nonspecific resistance. The authors noted an increase content of microelements (Se, Co, Cu, Mn, Fe) and a decrease content of heavy metals in the blood of animals. The economic efficiency of the use of the drug Hexamine was 4.54 rubles per 1 ruble of costs.

Use in the diets of young cattle optimal dosage of enzyme-bacterial additive Amprobac in the amount of 0.70 wt.% of mixed feed makes it possible to increase an average daily weight gain by 10.7%, to reduce the feed efficiency ratio by 1.0–8.0% and to increase a feed conversion efficiency by at least 8% [6]. The effect of the new Russian drug Prevention NA on the body of cows and calves obtained from them, as well as economic efficiency was particularly considered in [7].

The glandular substance and follicles of the ovaries, placental tissues, and adrenal cortex synthesize a complex of sex hormones - estrogens (estrone, estriol, and estradiol). The biological effect of estrogens is associated with the formation of the genital area (uterus, fallopian tubes, and vagina) and the development of secondary sexual characteristics [8]. After using of estrogens to animals, observed grow the ducts, lobes and alveoli of the mammary glands. The effect of estrogen on the cells of the immune
system has been proven [9]. Estrogens have anabolic effects associated with increased protein synthesis in the body, delayed nitrogen excretion.

There are studies on the effect of estrogen on the content of blood lipoproteins [10]. In vitro experiments have been shown that estradiol, estriol, and estrone inhibit UV-induced oxidation of methylene oleate, as well as free radical oxidation of biological lipoprotein membranes. Some estrogen metabolites and synthetic estrogens had a similar antioxidant effect, while catechol-estrogens reduced tocopherol radicals and inactivated lipid radicals more efficiently than alpha-tocopherol and ascorbic acid [11].

In our previous experiments, we used a synthetic analogue of female sex hormone estrone-based Sinoestrol-2%. We have evaluated the economic efficiency of thymogen, roncoleukin, polyoxidonium in livestock enterprises on the clinical and physiological state of the body, physiological and biochemical parameters and non-specific resistance of pregnant cows and calves obtained from them [12, 13].

The aim of this study is to determine the economic efficiency of Synoestrol-2% after its use for pregnant cows to stimulate colostral immunity and increase non-specific resistance in newborn calves.

2. Materials and methods
The experimental part were performed on down-calving cows and their new-born calves at farming enterprise Mir (Dalnekonstantinovsky district of Nizhny Novgorod region, Russia). The experimental work was conducted in the spring and summer of 2014-2018 years. The studying objects were 10 down-calving cows of black-motley breed selected based on the principle of analogs. Selected cows were divided into control and experimental groups. Cows of the experimental group were exposed to subcutaneous injection of Synoestrol-2% given as a single dose of 1 ml 3-9 days before calving. The animals from the control group were exposed to subcutaneous injection of sodium chloride physiological solution given as a single dose of 1 ml 3-9 days before calving. We tested clinical and physiological state of down calving cows and calves. Also we determined titratable acidity and the content immunoglobulin’s in colostrum of the first milk yield. Blood for research was taken from newborn calves one day, ten and thirty days after birth.

The following indicators were determined in calves during carrying out of scientific and economic experiment. Hematologic indicators was estimated on in vitro blood analyzer XT 2000, (Sysmex, GmbH). The excretion of leukogram was determined by counting in blood smears of different types of white blood cells stained by Romanovsky-Gimza. Biochemical indicators were detected as the level of total protein in the serum of animals by means of a biochemical analyzer AU480 (Olympus, Japan).

Immunologic indicators included determining immunoglobulins on an analyzer Minicap (Sebia, France). Bactericidal activity of blood serum was examined using Escherichia coli test culture (microbial strain O111). Lysozyme activity was measured using a Micrococcus lysodeikticus test culture in the modification of USRIEVM (Ukrainian Scientific-Research Institute of Experimental Veterinary Medicine), and neutrophil phagocytic rate was analyzed by a Staph. albus., T lymphocytes – by E-rosette assay and B lymphocytes – via EAC-rosette assay.

The resulting digital material was subjected to statistical processing using conventional parametric methods. The degree of confidence was determined by Student’s t-test employing the Microsoft Excel (2007) software package and STAT 3 software program [14].

Hygienic conditions of keeping animals corresponded to natural temperature and humidity conditions of atmospheric air in all seasons of the year. The dairy farm is safe by infectious and invasive cattle diseases.

Diets for cows and calves provided the needs of the body in energy and nutrients, mineral elements and vitamins according to the norms of feeding. The structure of the diet for dry cows (live weight 500 kg and planned yield of 5000 kg) included 5.5 kg of hay, 7 kg of clover-timothy hay, 12 kg of corn silage, 5.0 kg of fodder beet, 3.0 kg of a mixture of concentrates, 0.3 kg of fodder molasses, 100 g monocalcium phosphate.
Newborn calves were fed mother's colostrum after occurrence sucking reflex for 10-12 minutes, at a dose of 1.5 kg per 1 calf’s. Calves were fed mothers colostrum before 7 day age (6 kg/day), mother’s milk (6 kg/day) before 2 weeks age, oatmeal. Three week old calves were habituating to hay.

We used the formulas to calculate economic efficiency [15]. Economic damage (U) resulting from reduced animal productivity:

\[ U_1 = M_z \times (V_z - V_b) \times T \times C, \]  

where, \( M_z \) – total count of calves; \( V_z \) – average daily weight gain of healthy calves, kg; \( V_b \) – average daily weight gain of morbus calves, kg; \( T \) – average duration of observation of changes in animal productivity, days; \( C \) – unit purchase price, Rub. Economic damage (U) resulting from death or slaughter:

\[ U_2 = N \times G \times C, \]  

where, \( N \) – count of morbus and necessity slaughter calves; \( G \) – average body weight of calves; \( C \) – unit purchase price, Rub. Total economic damage (U):

\[ U = U_1 + U_2, \]  

where, \( U_1 \) – economic damage resulting from reduced animal productivity; \( U_2 \) – economic damage resulting from death or slaughter. Costs of veterinary measures (Z\(_v\)), Rub:

\[ Z_v = N \times C, \]  

where, \( N \) – count of animals; \( C \) – amount of expenses for drug. Prevented economic damage (P\(_a\)):

\[ P_a = U_k - U_o, \]  

where, \( U_k \) – total economic damage by control group; \( U_o \) – total economic damage by experimental group. Economic efficiency (E):

\[ E = P_a - Z_v, \]  

where, \( P_a \) – prevented economic damage; \( Z_v \) – costs of veterinary measures. Economic efficiency of veterinary measures per one ruble of expense (E\(_e\)):

\[ E_e = E / Z_v. \]  

3. Results and discussion

The use of a synthetic analogue of estrone-Synoestrol-2% parenterally injected to cows in the period 3-9 days before calving has a positive effect on the clinical and physiological state of newborn calves received from them.

The body temperature of calves obtained from cows, which were injected with a synthetic analogue of estrone before calving, was higher than the body temperature of calves obtained from cows, which were injected isotonic sodium chloride solution by 0.6°C, the heart rate was lower by 7.7 beats/min. The frequency of respiratory movements in calves included in the experimental groups one day after birth was similar. The appearance of a confident standing posture in animals included in the control group was realized after 89 min, in animals included in the experimental group after 81 min, which is 7.1 min faster than control. The appearance of a suckling reflex in calves included in the control group occurred after 111 min, in calves included in the experimental group 9.8 min faster (Table 1).

Studies have shown that in calves of the experimental group, 1 day after birth, there is a significant increase in blood levels of total protein by 9.75%, as well as its fractions: albumin by 13.7%, alpha globulin by 31%; gamma globulins by 21.8% compared to calves obtained from cows that were injected isotonic sodium chloride solution before calving (Table 2). The level of serum beta-globulins in the calves of the experimental group was reduced by 11.7%, the hemoglobin level was increased by 4.1% compared with the calves of the control group. However, these data were not reliable.
Table 1. Clinical and physiological indicators of calves after using Synoestrol-2%.

| Indicator                        | Age, days | Group of calves |            |            |
|----------------------------------|-----------|-----------------|------------|------------|
|                                  |           | Control         | Experimental |            |
| Body temperature, °C             | 1         | 38.4 ± 2.32     | 39.0 ± 0.16 |            |
|                                  | 10        | 38.7 ± 0.18     | 38.8 ± 0.20 |            |
|                                  | 30        | 38.8 ± 0.10     | 38.8 ± 0.18 |            |
|                                  | 1         | 120 ± 3.80      | 112 ± 3.92  |            |
| Puls, beats per minute           | 10        | 134 ± 2.92      | 128 ± 4.10  |            |
|                                  | 30        | 128 ± 3.90      | 124 ± 4.12  |            |
|                                  | 1         | 46 ± 1.54       | 48 ± 1.21   |            |
| Breath per minute                | 10        | 42 ± 2.12       | 40 ± 1.56   |            |
|                                  | 30        | 38 ± 1.96       | 36 ± 1.69   |            |

The appearance of a confident standing posture, min: 87.9 ± 8.8 vs. 80.8 ± 8.2
The appearance of suckling reflex, min: 110.8 ± 10.8 vs. 101.0 ± 11.5

*≤0.05 as compared to control.

Table 2. Biochemical and immunological parameters of calves blood after using Synoestrol-2%.

| Indicator                          | Group     | 1            | 10           | 30           |
|------------------------------------|-----------|--------------|--------------|--------------|
| Total protein, g/l                 | control   | 54.71 ± 1.24 | 56.81 ± 0.87 | 57.24 ± 1.32 |
|                                   | experimental | 60.60 ± 1.32* | 67.95 ± 1.23* | 62.10 ± 1.28* |
| Albumins, g/l                      | control   | 17.44 ± 0.51 | 20.86 ± 0.58 | 23.94 ± 0.65 |
|                                   | experimental | 19.82 ± 0.74* | 22.12 ± 0.27* | 24.82 ± 0.56 |
| Alpha-globulins, g/l               | control   | 13.62 ± 0.43 | 12.73 ± 0.13 | 11.53 ± 0.53 |
|                                   | experimental | 17.85 ± 0.63* | 14.32 ± 0.64 | 13.71 ± 0.84 |
| Beta-globulins, g/l                | control   | 7.52 ± 0.36  | 7.48 ± 0.52  | 6.92 ± 0.49  |
|                                   | experimental | 6.64 ± 0.35  | 7.06 ± 0.18  | 6.74 ± 0.39  |
| Gamma-globulins, g/l               | control   | 16.13 ± 0.39 | 15.72 ± 0.38 | 14.85 ± 0.44 |
|                                   | experimental | 19.75 ± 0.55* | 18.45 ± 0.21* | 16.83 ± 0.64 |
| Bactericidal activity, %           | control   | 35.8 ± 2.4   | 37.4 ± 3.2   | 40.5 ± 2.9   |
|                                   | experimental | 38.9 ± 3.9*  | 39.7 ± 2.4   | 41.9 ± 2.8   |
| Lysozyme activity, %               | control   | 15.9 ± 1.7   | 16.7 ± 1.9   | 19.9 ± 2.1   |
|                                   | experimental | 17.1 ± 1.3*  | 17.8 ± 1.5   | 20.4 ± 1.4   |
| Neutrophil phagocytic rate, %      | control   | 36.8 ± 0.99  | 42.3 ± 1.39  | 44.5 ± 1.54  |
|                                   | experimental | 40.6 ± 1.24* | 42.8 ± 1.29  | 44.9 ± 1.69  |
| Phagocytic index, %                | control   | 1.12 ± 0.09  | 1.44 ± 0.06  | 1.58 ± 0.07  |
|                                   | experimental | 1.46 ± 0.10* | 1.50 ± 0.08  | 1.56 ± 0.21  |

*≤0.05 as compared to control.

The first day after birth bactericidal activity of the blood serum, showing the general effect of antimicrobial protection factors in calves of experimental group, was higher by 8.6%, lysozyme activity of the blood serum was higher by 7.5% compared with similar indicators calves of control group. 10 days after birth, the calves of the all groups experienced an increase in the level of albumin and total protein. The level of beta-globulins did not undergo age-related changes in the control group, but in the
experimental group it increased, the level of alpha-globulins and gamma-globulins decreased. It should be noted that in calves obtained from cows that were injected with a synthetic estrone analog before calving, the level of total protein significantly increased by 9%, albumin by 6%, alpha globulin by 12.5%; beta-globulin decreased by 5.6%; gamma globulin increased by 17.4% compared with calves obtained from cows that were injected with isotonic sodium chloride solution. The hemoglobin content was 5.8% higher (Table 2).

Bactericidal activity of blood serum and lysozyme activity of blood serum in calves of all groups tended to increase, but in calves of the experimental group, these indicators were higher by 6.1 and 6.6%, respectively, compared with the control (Table 2).

The level of total colostrum immunoglobulins in cows of the control group was 40.6 g/l, and in cows of the experimental group 46.5 g/l, that is, in cows of the experimental group, this indicator was higher by 14.5 compared to the control group. The formation of high-quality colostrum can be explained by the fact that under the influence of estrogen, the number of membrane receptors for oxytocin in mammary gland tissues increases. Oxytocin stimulates contraction of cells surrounding the alveoli of the mammary gland. This causes the movement of milk into the alveolar duct system and leads to its release, stimulating lactation.

The level of total protein in calves of the experimental group compared with the control was higher due to the gamma-globulin fraction. In this experiment, in calves obtained from cows that were injected with a synthetic analogue of estrone 1st day after birth, the leukocyte count was significantly higher by 17.2% compared with the calves of the control group. The absolute and relative number of T cells in calves of the experimental group exceeded the values of similar indicators of calves in the control group by 20 and 10.6%, respectively. Differences in blood hemoglobin level were not significant, as well as in the number of red blood cells. On the tenth day of life, the leukocyte count in the calves of the experimental group was higher mainly due to neutrophils. On the thirtieth day of life, the morphological blood parameters of the calves of the control and experimental groups were similar to each other.

At the beginning of the first month of life, in the group of calves obtained from cows injected with Sinoestrol-2%, there was a disease of simple dyspepsia in three out of five calves, in the group of calves obtained from cows injected with an isotonic solution of sodium chloride - four out of five, then there is an incidence in the experimental group was 1.3 times lower. The calves of the experimental group fell ill after one day, the duration of the disease was shorter by 1.7 days compared with the control. The survival of calves in the experimental groups is 100%.

Table 3. Average daily gain weight (g) in calf body after using Sinoestrol-2% (n = 5).

| Group of calves | 0-1   | 1-2   | 2-3   | 3-4   | 4 average |
|-----------------|-------|-------|-------|-------|-----------|
| Control         | 540.0 ± 14.12 | 524.0 ± 12.56 | 505.0 ± 11.33 | 650.0 ± 17.58 | 554.8 ± 12.92 |
| Experimental    | 616.0 ± 15.28* | 630.0 ± 10.31* | 553.0 ± 12.41* | 700.0 ± 13.62 | 624.8 ± 10.74 |

*≤0.05 as compared to control.

The calves of the experimental group had a higher average daily gain in body weight. At the end of the first month of life, he was higher by 14.0; at the end of the second 20.3; at the end of the third 9.5% relative to the calves of the control group. At the end of the fourth month of life, the gain in these groups of calves was similar (Table 3). In this experiment, Synoestrol-2% at a dose of 1 ml per animal was injected parenterally to cows 3-9 days before calving. The drug is released in 10 ml vials. The retail cost of 1 dose was 15 rubles. During the experiment, the diagnosis of simple dyspepsia was made in the control group by 4 calves, in the experimental group by 3 calves. For the treatment of animals, the following scheme was used: glucose solution 40% in a dose of 250 ml intravenously 2 times a day, 2 days; a solution of gentamicin sulfate 4% at a dose of 6 ml orally, 2 times a day with an interval of 12 hours, 5 days; 9-valent serum against pasteurellosis, salmonellosis, escherichiosis, parainfluenza-3 and infectious rhinotracheitis of cattle - 40 ml intramuscularly, once; algalin solution 50% in a dose of 500 mg intramuscularly 2 times a day, 3 days. The average cost of treating 1 calf was 453.5 rubles (Table 4).
Table 4. Costs of veterinary measures.

| Drug                          | Volume of drug per course, ml | Cost, Rub. |
|-------------------------------|-----------------------------|-----------|
| Synoestrol-2%                 | 1.0                         | 15.0      |
| Glucose solution, 40%         | 1000.0                      | 100.0     |
| Gentamicin sulfate solution, 4% | 60.0                        | 96.0      |
| 9-valent serum                | 40.0                        | 150.0     |
| Analgin solution, 50%         | 12.0                        | 17.5      |

Table 5. The results of the production test of the drug Sinoestrol-2%.

| Group of calves               | Control       | Experimental |
|-------------------------------|---------------|--------------|
| Count of animals              | 5             | 5            |
| Count of morbus calves        | 4             | 3            |
| Necessity slaughter           | -             | -            |
| Dead calves                   | -             | -            |
| Body weight of newborn calves, kg | 30.4±1.4   | 29.2±1.2     |
| Body weight of calves in the end of experiment, kg | 99.19±2.9 | 106.67±2.7 |
| Body weight gain, kg          | 68.79         | 77.47        |
| Average daily gain of calves, g | 554.8±12.92 | 624.8±0.74  |

The economic efficiency of using the studied drug in the technology for obtaining and growing calves is presented in Table 5. The use of Synoestrol-2% allowed reducing the number of cases of disease and reduce the duration of the course of simple dyspepsia of calves. There was a decrease in the cost of buying drugs. The economic efficiency of the use of the drug Sinoestrol-2% to cows was 3.12 rubles per 1 ruble of expense.

4. Conclusion
From the presented data, it can be concluded that the use of Synoestrol-2% to cows 3-9 days before calving stimulates colostral immunity and non-specific resistance and is cost-effective in production conditions. Maternal colostrum is a source for calves of nutrients and immune factors including immunoglobulins, lysozyme, and immune cells. The level of immunoglobulins of the first milk yield in cows of the experimental group was higher by 14.5%. Studies have shown that in calves of the experimental group, 1 and 10 day after birth, there is a significant increase in the immunoglobulins of blood serum by 21.8 and 17.4%. The first and tenth day after birth bactericidal activity of the blood serum, showing the general effect of antimicrobial protection factors in calves of experimental group, was higher by 8.6 and 6.1%, lysozyme activity of the blood serum was higher by 7.5 and 6.6% compared with similar indicators calves of control group. Increased immunity in calves led to a decrease in the incidence of dyspepsia and an increase in the average daily gain weight.

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