Effectiveness of various treatment regimens for calves with dyspepsia in Novgorod region

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Abstract. The situation with dyspepsia of young animals in the postnatal period in agroindustrial companies of Russia remains tense due to a high mortality rate. Specialists are not always able to cover a wide range of drugs currently available on the market, although the success in combating the disease depends on a timely introduction of highly effective drugs and various combinations of treatment regimens into practice. The paper presents the findings of studies on the use of various treatment regimens for dyspepsia of newborn calves, with the inclusion of an immunomodulator. The studies have shown high therapeutic efficacy of both antibacterial drugs Cobactan and Neopen, and their use in combination with the drug Phosprenyl. Laboratory studies of morphological and biochemical parameters of blood demonstrated significantly improved concentration and percentage of the drugs. In the course of treatment with basic drugs, the immunomodulator Phosprenyl enhanced their action and positively affected the percentage composition of the leukoformula. Daily clinical examination of young experimental animals showed that treatment with Cobactan, especially in combination with Phosprenyl, is most effective in terms of fastening recovery and safety of calves.

1. Introduction
Gastrointestinal tract disorders of newborn calves are very common today and are the primary factor for livestock safety. The immunity of newborn calves to diseases is low due to both the absence of immunoglobulins in the blood and negative effects of various intoxicants during the prenatal period. There is a need for a more purposeful and effective solution to long-standing problems, and a decrease in morbidity and increase in safety of young cattle are among the main ones. In addition, in heifers recovered from dyspepsia, which has not only bacterial but also bacterial-viral etiology, further productivity can decrease by 18% [1, 2].

The most common causes of the gastrointestinal diseases of newborn calves are unbalanced feeding of pregnant cows and heifers, violation of zoohygienic rules of feeding and keeping newborn calves. It is necessary to take a more responsible approach to the prevention of diseases, to observe the rules of sanitization during disinfection of places where calves are kept, and to use new disinfectants with pronounced antibacterial activity against various types of bacteria [3].

To date, there are many different drugs and methods of treating this disease, but it is necessary to constantly improve all therapeutic and prophylactic methods with due regard to the factors that provoke the disease. Essential for solution of this problem are drugs designed to increase immunity, activate protective and adaptive properties of the body of calves, increase their resistance to infection and prevent morbidity. Modern immunomodulatory drugs (IMD) are able not only to treat immunodeficiency caused by infection, stress, etc., but also to have a complex positive effect on the overall condition of the animal.
Unique properties of the drugs that increase antiviral, antioxidant and anti-inflammatory activities can stimulate the growth and development of young animals [4, 5].

One of these drugs considered in the paper is IMD Phosprenyl that belongs to natural drugs made using unique technologies that employ phosphorylation of polyrenols extracted from ecologically safe pine needles. The main active ingredient of Phosprenyl is sodium polyrenyl phosphate. Polyrenols and their derivatives are characterized by synthesis directly in cells, where they play a vital role in the enzymatic process of combination of sugar residues with organic molecules. Polyrenonols are integral components built into biological membranes that affect numerous characteristics. [6, 7].

Due to this structure, the drug helps to stimulate natural resistance, enhance the immune response to vaccines, and have antibacterial, antiviral and anti-inflammatory properties [8].

However, antibacterial drugs are undoubtedly the main drugs in treatment of calves suffering from dyspepsia. Cobactan 2.5% is an antibacterial drug that belongs to cephalosporins. Cefkinoma sulfate, which is part of the drug structure, belongs to the 4th generation cephalosporins with wide range of antibacterial effects on most gram-positive and gram-negative bacteria [9].

Neopene, also used in our studies, contains procaine benzylpenicillin and neomycin sulfate, which are capable of acting synchronously with these two substances to provide the highest overall effect [10]. These antibacterial drugs are not a novelty on the Russian market, however, the study of their effectiveness alone and in conjunction with the immunomodulator (IMD) Phosprenyl in treatment of young cattle of the Ayrshire breed in Novgorod region refers to unexplored and relevant area.

2. Purpose of study
The study aimed at identifying the most effective drugs and treatment regimens in conjunction with an immunomodulator for diseases of the gastrointestinal tract of young cattle, which increase safety of animals.

3. Materials and methods
The studies were conducted on Ayrshire calves on the farm of the production site at Novgorod Research Institute of Agriculture.

Two experiments were performed, for each experiment two groups of calves were selected according to the principle of conditional analogs after clinical examination and the presence of pronounced clinical signs of the disease (n=10 in each). In the first experiment, Cobactan was used in one group of calves, and Cobactan in conjunction with Phosprenyl were used in the second group. In the second experiment, the antibiotic treatment regimen included Neopen (group I) and Neopen in combination with IMD Phosprenyl (group II).

Before treatment and on the day of clinical recovery, blood was taken from each calf from the jugular vein to study morphological and biochemical parameters. Calculations of the average blood counts before treatment were carried out in the two experiments to obtain more reliable results, which were control in the studies. The drugs were injected intramuscularly, in doses in accordance with the instructions – Phosprenyl (0.1 ml per 1.0 kg of live weight), Cobactan (1.5 ml per 1 head), and Neopen (1 ml per 20 kg of live weight).

4. Results
Blood is a universal biological medium of the body, which provides information about the health of animals, and the composition of certain substances and elements reflects all the processes in the body (table 1).
Table 1. Morphological and biochemical blood parameters in calves with dyspepsia during various treatment regimens, experiment I.

| Blood parameter         | Before treatment (average values) | Day of clinical recovery | Day of clinical recovery |
|-------------------------|-----------------------------------|--------------------------|--------------------------|
|                         |                                   | treatment: Cobactan       | treatment: Cobactan + Phosprenil |
|                         |                                   |                           |                           |
| RBC, mln/mm³            | 7.59±0.69                         | 6.83±0.26***              | 7.02±0.02                |
| WBC, thou./mm³          | 16.31±3.1                         | 10.33±1.04***             | 13.06±2.4                |
| Hemoglobin, g%          | 9.9±0.76                          | 11.21±0.32                | 11.40±0.09               |
| DC, %                   |                                   | 51.44±5.96***             | 49.82±4.97               |
| Lymphocytes             | 69.84±6.0                         |                           |                          |
| Eosinophils             | 0.85±0.06                         | 2.05±0.6                  | 0.40±0.08***             |
| Band neutrophils        | 2.22±0.3                          | 1.81±0.12***              | 1.40±0.05***             |
| Segmented neutrophils   | 47.25±1.4                         | 34.85±5.18***             | 30.4±5.33                |
| Alkali reserve, vol. %  | 45.69±3.4                         | 47.92±4.88***             | 49.31±2.95               |
| CO₂                     | 69.60±4.0                         | 71.81±4.6                 | 73.30±3.2***             |
| Total protein, g/l      |                                   |                          |                          |

* Р <0.05; **Р <0.01; ***Р <0.001

Table 1 shows high RBC count at the beginning of the experiment compared to reference values, which is characteristic of dyspepsia with significant fluid loss. During treatment with the drug Cobactan, experimental animals exhibited a decrease in the total number of RBC (by 10.4%) with a simultaneous decrease in the number of WBC (by 36.8%), which indicates reduction of the inflammatory process in the body.

Prior to treatment, hemoglobin in sick calves showed the lower limit of reference values for calves. When using Cobactan or Cobactan + Phosprenil, Hb concentration increased by 12.3–12.5% and thus provided higher oxygen saturation levels.

WBC, as an element responsible for the immune response to viruses, first exceeded reference values for young animals of the postnatal period. The treatment regimens used, especially those with an immunomodulator, reduced WBC number by 35.8% and 40.2%, respectively. This suggests a decrease in viral infection in the body.

Eosinophils are cells capable of digesting antigens and antibodies, and treatment with antibacterial drugs, as potential allergens, often leads to an increase in their number, which is proved by the analysis of the results obtained. IMD Phosprenyl used in the treatment regimen hypothetically reduces the allergic reaction to Cobactan.

An increased concentration of neutrophils, both band and segmented, is characteristic of various bacterial infections. In our studies, treatment with Cobactan reduced the concentration of band and segmented neutrophils by 22.6% and 35.6%, respectively, and treatment with Cobactan + IMD reduced their concentration by 58.6% and 55.4%, respectively.

The blood of animals is characterized by relative constancy of the pH value which depends on concentration of hydrogen ions. Such constancy is obvious, since any processes in the body are impossible without enzyme systems, the activity of which is closely related to the pH value. This pattern was considered in the analysis of blood alkali reserve in non-treated calves, and its concentration in this period was found to be lower compared to reference values (46–66 vol.% CO₂). On the day of clinical recovery, alkali reserve in both groups increased by 4.9% and 7.9%, respectively, and reached reference values.

The total protein in blood serum shows not only deficiencies in feeding but also reflects the overall condition of the calves’ bodies, including the condition of calves with diseases. At the beginning of the experiment, total protein was 69.60 g/l compared to reference values of 72–86 g/l. On the day of clinical recovery, the concentration of total protein in calves from group I increased by 3.2%, and this indicator in Phosprenyl treated calves increased by 5.3% and reached reference values.
In the second experiment, the drug Neopen, which contains active substances such as penicillin and neomycin, exhibited synergistic antibacterial effect (table 2).

**Table 2.** Morphological and biochemical blood parameters in calves with dyspepsia during various treatment regimens, experiment II.

| Blood parameters          | Before treatment (average values) | Day of clinical recovery | Neopen | Neopen + Phosprenyl |
|---------------------------|-----------------------------------|--------------------------|--------|---------------------|
| RBC, mln/mm$^3$           | 7.59±0.69                         | 9.31±0.02**              | 11.40±0.91† |
| WBC, thous./mm$^3$        | 16.31±3.1                         | 12.44±0.91*              | 11.31±0.6*** |
| Hemoglobin, g%            | 9.9±0.76                          | 11.33±0.27               | 11.50±0.06 |
| DC, %                     | 69.8±6.0                          | 50.71±1.51               | 55.02±4.43 |
| Lymphocytes               | 69.84±6.0                         | 50.71±1.51               | 55.02±4.43 |
| Eosinophils               | 0.85±0.06                         | 0.30±0.07***             | 0.30±0.07*** |
| Band neutrophils          | 2.22±0.3                          | 1.30±0.13**              | 0.70±0.06*** |
| Segmented neutrophils     | 47.25±1.4                         | 37.72±1.6***             | 35.32±2.39* |
| Alkali reserve, vol. % CO$_2$ | 45.69±3.4                         | 53.76±6.10               | 55.55±4.25 |
| Total protein, g/l        | 69.60±4.0                         | 62.90±2.80               | 43.11±5.10 |

* P <0.05; **P <0.01; ***P <0.001

When treated with Neopen, blood test showed RBC number increased by 1.72 mln/mm$^3$. IMD Phosprenyl used in the treatment regimen increased this indicator by 3.81 mln/mm$^3$, while Hb concentration increased in both groups, which shows the stimulating effect of drugs on the hematopoietic function of the body.

At the beginning of the experiment, WBC count in sick calves exceeded the upper limit of reference values by 4.31 thous./mm$^3$. On the day of clinical recovery, the excess was only 0.44 thous./mm$^3$ in animals from group I, and WBC number in calves from group II reached reference values.

Severe development of the disease primarily causes an increase in the total number of segmented neutrophils, which is proved by the result obtained – their concentration at the beginning of treatment was 47.25%, exceeding the upper limit by 35%. The appearance of band neutrophils reduces successful prognosis of the disease. During treatment, the concentration of band neutrophils decreased in both groups, but this was most effective when IMD Phosprenyl was included in the treatment regimen – by 85.7% relative to the indicators in calves from group I. The number of segmented neutrophils also decreased in both Neopen treated and Neopen + Phosprenyl treated calves.

In the second experiment, reserve alkali in the blood of treated calves increased insignificantly and was within reference range. The concentration of total protein in animals which treatment regimen included Phosprenyl decreased sharply by 61.4% compared to the control, but this indicator is not reliable. The results of the therapeutic efficacy of the drugs used in the study are presented in table 3.

**Table 3.** The results of the therapeutic efficacy of various treatment regimens.

| Parameters                      | Treatment regimen | group I | group II |
|---------------------------------|-------------------|---------|---------|
|                                 | Cobactan          | Cobactan + Phosprenyl | Neopen | Neopen + Phosprenyl |
| Number of animals in a group, heads | 10                | 10      | 10      | 10                  |
| Fallen animals, heads           | 1                 | 0       | 1       | 1                   |
| Clinical recovery, days         | 5                 | 4       | 6       | 5                   |
| Recovered animals, heads        | 9                 | 10      | 9       | 9                   |
| Therapeutic efficiency, %       | 90                | 100     | 90      | 90                  |
The results of the study showed that all drugs used for treatment exhibited high therapeutic efficacy, compared to the average mortality rate from dyspepsia on the farm, which amounted to 19.8%. In the first experiment, the condition of Cobactan treated calves improved on the fourth day of treatment, and the main symptoms of the disease disappeared on the fifth day. IMD Phosprenyl used in the treatment regimen fastened recovery by one more day.

In comparison with the average statistical data obtained on the farm, where animals were treated with generally accepted therapeutic regimens, the clinical recovery of calves used in the second experiment occurred 3–4 days earlier, although it was inferior to the indicators of animals used in the first experiment.

5. Conclusion
The study carried out on newborn calves with dyspepsia in Novgorod region has shown high therapeutic efficacy of the drugs Cobactan and Neopen. These antibacterial drugs neutralized the main pathogenic properties of dyspepsia, and combined therapy with IMD Phosprenyl significantly improved homeostasis, immune resistance, and the clinical state of calves.

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