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Experimental Use of the Triazavirin Antiviral Medication in Conditions of Group Administration at The Pig-Breeding Unit

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Abstract

Background: The spread of viral and microbial agents is active in Pig-breeding units. Due to illness, animals lose their productivity, which can affect the economy of the enterprise. The purpose of our experiment was to conduct an experimental study of the use of the Triazavirin antiviral medication on piglets in conditions of group administration at the pig-breeding unit and to assess the long-term effects of administering the medication.

Methods: The experiment involved 30 heads of piglets. Upon admission, groups were formed taking into account the condition and age of the animals. Piglets with lesions of the respiratory system and with obvious clinical signs were selected for the experiment. In the first experimental group, experimental piglets received the Triazavirin antiviral medication. In the 2nd (control) group, the experimental animals were not subject to any treatment. In the 3rd experimental group, Tylosin-50 antibacterial medication was used for the treatment of animals. During the experiment, clinical studies and blood tests (biochemical, immunological, hormonal tests) were carried out.

Result: When piglets were given the Triazavirin medication, they demonstrated a stable average daily weight gain and the highest percentage of meat yield. When analyzing the biochemical parameters of animals in the first experimental group, stabilization of several indicators was noted (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, iron, total iron-binding capacity, transferrin saturation coefficient). In the case of Triazavirin administration, there was an increase in the level of free thyroxine and triiodothyronine, a decrease in thyroid-stimulating hormone, and cortisol.

Conclusion: Based on the results of clinical studies, the authors recommend using the Triazavirin medication as part of complex and etiological therapy in the treatment of the respiratory system of pigs affected with diseases of a viral nature.



Introduction

Pig-breeding units are characterized by significant overcrowding and large livestock of animals [1-3]. This leads to an active spread of viral and microbial agents. Animals fall ill and decrease productivity, which results in serious economic losses [4,5]. The profitability of production is the most important indicator of the industry; therefore, it is necessary to develop both therapeutic and preventive measures to prevent diseases of various etiologies with the use of modern, more effective, and safe medications [6-8].

Viral diseases, including the diseases of the respiratory system, can cause serious harm to the body and result in complications, and therefore, the growth, development, and formation of the body can be seriously impaired [9-11]. The influence of an infectious agent negatively affects the immune, respiratory, digestive, and other systems, which leads to developmental delay, a decrease in live weight, a violation of the quality of meat products, and other economic damage [12-14].

The authors aimed to conduct an experimental study of the use of the Triazavirin antiviral medication on piglets in a group administration at a pig-breeding unit, and to assess the long-term effects of administering the medication. The experiment included the study of biochemical, hormonal, immunological parameters of the blood of pigs with signs of respiratory system damage after taking the Triazavirin antiviral medication and the Tylosin-50 antibacterial medication.

Methods

The study was carried out in 2017 in the Interfaculty educational and scientific laboratory of biotechnology of the Federal State Budgetary Institution of Higher Education Izhevsk State Agricultural Academy (FSBEI HE Izhevsk State Agricultural Academy). The experiment was carried out at the Vostochny pig-breeding unit LLC in the Republic of Udmurtia.

The work with animals was carried out following the general ethical principles of conducting experiments on animals and the provisions of the Status of the European Convention for the Protection of Vertebrate Animals used for Experiments or Other Scientific Purposes (ets No. 123) (Strasbourg, March 18, 1986) [Rus., Eng.] (as of 15.03.2010) [15].

During the experiment, experimental groups of piglets were formed, according to the principle of analogs. The animals were kept in the same zoo-hygienic conditions, had the same feeding ration, according to age and feeding technology. The feeding was carried out through the WEDA system. The experimental animals were not given antibiotics in their feed.

The average temperature in the room where the experimental animals were kept during the period of the experiment was +20.3⁰ C.

The experiment involved 30 pigs: 10 heads in the 1st experimental group, 10 heads in the control group (2nd experimental group), and 10 heads in the 3rd experimental group. The animals (piglets) were admitted to the unit at the age of 98 days and with an average weight of 32.52 kg. Upon admission, groups were formed taking into account the condition and age of the animals. Piglets with lesions of the respiratory system and with obvious clinical signs were selected for the experiment. The experimental piglets were kept in a separate pen and had no contact with other animals. After the experiment, they were transferred to the general building.

The Triazavirin antiviral medication was administered to the animals of the 1st experimental group orally, with feed at the rate of 1.0 g per head for 7 days. With the technological and intensive rearing of piglets, it is difficult to determine the dosage of medications individually, so the question arose about the group administration of the medication. For this, a fodder mass of a mushy consistency was made (the compound feed was mixed with water to obtain a homogeneous mass). The medication was added to this mixture and mixed until it was evenly distributed over the volume of the compound feed.

In the 2nd (control) group, the experimental animals were not subject to any treatment.

In the 3rd experimental group, Tylosin-50 antibacterial medication was used for the treatment of animals. It was used according to the instructions. The calculation of the dosage was made by body weight, on average 6.5 ml per head, which was injected intramuscularly, once a day, for 7 days (Table 1). During the experiment, clinical studies and blood tests (biochemical, immunological, hormonal) were carried out. The experimental piglets were handed over to Uvinsky meat-packing plant LLC, according to the technological plan, on the 178th day of life and fattening of animals. Blood was drawn from piglets after the experiment on the 178th day at slaughter. Biochemical studies were carried out on an automatic biochemical analyzer LABIO-300 (China). The level of hormones was determined on an automatic enzyme immunoassay analyzer Alisei (SEACsrl, Italy). Reagent kits made by Alkor Bio Company LLC (Russia, St. Petersburg) were used for the quantitative enzyme immunoassay in the blood serum for the thyroid-stimulating hormone (TSH), triiodothyronine (T₃), free thyroxine (T₄, picomole/l), and cortisol. Immunological studies were carried out on a Clima MC-15 RAL biochemical analyzer (Spain), using reagent kits made by Vital Development

Corporation OJSC (Russia, St. Petersburg) for determining the concentration of immunoglobulins A, M, G in blood serum by the immunoturbidimetric method.

Experiment No.	Dosage	Number of animals	Administration method	Administration mode
1st experimental group	1.0 g of the Triazavirin medication, per day	10	Orally	0.5 g twice a day, for 7 days
2nd experimental group (control group)	No medicinal preparations were administered	10	-	-
3rd experimental group	Tylosin-50, 6.5 ml per head	10	Intra-muscular	Once a day, for 7 days

Table 1: Experiment diagram

Mathematical and statistical processing of the results was carried out using the method of variation statistics using the Student's t-test. Data are presented as mean \pm standard error of the mean. The calculations were performed on a personal computer using the Microsoft Excel 7.0 program for statistical analysis.

Results

For the experiment, animals with classical, obvious signs of respiratory tract diseases were selected. The noted symptoms included the presence of cough, sneezing and snorting, labored breathing, wheezing and shortness of breath, discharge from the nostrils of various nature, apathy, weakness, decreased appetite, ears drooping, blurred eyes, body temperature above normal (Table 2).

Group No.	Body temperature, °C Day 1	Body temperature, °C Day 2	Body temperature, °C Day 5	Body temperature, °C Day 8
1st	38.6	38.8	38.2	36.8
2nd	39.5	39.2	39.1	38.8
3rd	38.9	39.1	38.5	36.5

Table 2: Average body temperature of piglets during the experimental period.

In the 1st experimental group, experimental piglets received the Triazavirin antiviral medication by 0.5 g in the morning and the evening per head at the age of 98 days, the daily dose was 1.0 g. As early as on the second day, signs of improvement were noted. The animals were more active, ate food, moved around the corral. On the fifth day, there was a decrease in body temperature and normalization of breathing; the shortness of breath and wheezing were already absent, but there was a slight cough, discharge from the nostrils, sneezing, and slight fatigue. By the eighth day, the main pathological clinical signs were gone. The condition of the animals had stabilized, the body temperature was within the normal range (Table 2).

In the 2nd (control) group, treatment of experimental animals was not performed. On the second day, there was an increased body temperature, wheezing, shortness of breath, and nasal discharge. The signs characteristic of respiratory diseases increased. By the fifth day, there were no signs of improvement. On the eighth day, the main group of animals practically did not move, the feed was consumed by animals only for 10% of the specified volume. The body temperature dropped from 39.1 to 38.8^o C. After the clinical examination on day 8 and the end of the experiment, to prevent death, the animals were treated according to the therapeutic protocols approved by the farm.

In the third experimental group, antiviral therapy was not used for the treatment of animals. For treatment, we used the Tylosin-50 antibacterial medication, from the macrolide group. On the second day, during the clinical examination, there were signs of damage to the respiratory system: shortness of breath, wheezing, sneezing, discharge from the nostrils, apathy, fatigue, body temperature of 39.1^o C. By the fifth day, the first signs of improvement in the condition of the animals had appeared. The appetite had improved, the animals were active, there was no wheezing, the temperature had gradually decreased to 38.5^o C. On the eighth day, there were no signs of damage to the respiratory system, the body temperature was within normal limits, there were no wheezing, coughing, and shortness of breath, no discharge from the nose was observed, the animals were active, with a good appetite, the feed consumption was almost 100% (Table 2).

The experiment involved animals aged 98 days and with an average live weight of 32.31 kg. Later, growth and average daily weight gain (ADWG) were monitored until the full completion of the growing and fattening cycle. The control weighing was performed at 98 days (at the time of receipt of the animals), at 123 days, and 178 days (on the day of slaughter). At the meat processing plant, the output of meat without the head, legs (autopodia), skin, and internal organs were calculated (Table 3).

At the farm, a ready-made compound feed was used for feeding animals according to age and weight: piglets of the preweaning period, up to 35-40 days of age received SK-3, piglets from 41 days to 90 days were fed with SK-4, piglets from 71 to 120 days were fed with SK-5, and piglets from 116 to 200 days were fed with SK-6.

During the experiment, from day 98 to day 123, we measured the maximum weight gain in the first group that received the Triazavirin antiviral medication, by 1.177 kg. In the third group that received the Tylosin-50 antibacterial medication, the weight gain was lower (1.156 kg), but in the percentage ratio in the 1st and 3rd

groups, the increase amounted to 3.62%. In the period from 123 to 178 days, the greatest weight gain was observed in the 3rd group, by 0.531 kg and 0.87%. The weight gain in the 2nd group amounted to 0.445 kg and 0.72%.

Indicators		Group No.		
		1st	2nd	3rd
Indicators at the beginning of the experiment, 98 days	Average live weight, kg	32.52	32.5	31.9
	Average daily gain, kg	1.177	1.108	1.156
	Average daily gain, %	3.62	3.4	3.62
Indicators at the end of the experiment, 123 days	Average live weight, kg	61.94	60.2	60.8
	Average daily gain, kg	0.445	0.036	0.531
	Average daily gain, %	0.72	0.06	0.87
Indicators for the slaughter period, 178 days	Average live weight, kg	86.4	80	90
	Average daily gain, kg 80 days	0.67	0.594	0.726
	Average daily gain, %	0.78	0.74	0.81
Meat yield, kg	Meat yield, kg	56.08	51.8	56.2
	Meat yield, %	64.91	64.75	62.44

Table 3: Control weighing and live weight gain of piglets of experimental groups

For 80 days of keeping (98 to 178 days), the largest average live weight was achieved by piglets of the 3rd group, the second place was occupied by the animals of the 1st group, and the indicators of the 2nd control group were the smallest. The maximum ADWG was also noted in the 3rd group that received the Tylosin-50 antibacterial medication, amounting to 0.726 kg and 0.81%. The ADWG in the 1st group equaled 0.67 kg and 0.78%. At slaughter, the highest percentage of meat yield was observed in the 1st experimental group that received the Triazavirin antiviral medication, equaling 64.91%. The meat yield in the control group was 64.75%, and the lowest indicators were observed in the 3rd group that had received the Tylosin-50 antibacterial medication (62.44%).

From the above data, it can be concluded that the use of the Triazavirin antiviral medication leads to a stable ADWG and a higher percentage of meat yield at slaughter. These indicators reflect the effectiveness of the use of the Triazavirin antiviral medication.

The experiment was carried out on piglets at the age of 98 days when the animals were admitted to the pig-breeding unit. Some indicators of blood serum at the time of slaughter are quite interesting. The use of antiviral and antibacterial medications at 98 days and further fattening up to 178 days of age, until the complete completion of the growing and fattening cycle, give a picture of the long-term effectiveness of treatment and the state of health of the body after the experiment.

Biochemical parameters of blood serum at the time of slaughter in the three experimental groups are stable (Table 4). Several indicators correspond to the physiological norm and practically do not differ in all experimental groups; these indicators are cholesterol, creatinine, urea, gamma-glutamyl transpeptidase

(GGTP), lactic dehydrogenase (LDH). Aspartate aminotransferase (AsAT) in the control group corresponds to the normal indicators. In the first group its level is increased by 18.46%, and in the third group by 41.03%, but it remains within the average values. Alanine aminotransferase (AlAT) in the first group corresponds to the average values of the norm, and in the second and third groups, it exceeds the upper threshold by 19.15% and by 13.19%, respectively. The level of alkaline phosphatase (AP) in all three experimental groups exceeds the average: in the first group the excess amounts to 55.11%, in the second group to 96.14%, and in the third group to 77.27%. In the first group, the value is as low as possible and is close to the physiological norm. The iron level in all experimental groups is much lower than the average, but in the first experimental group that received an antiviral medication, the indicator is the highest. In the first group, the iron level is higher than in the control group by 11.63%, and in the third group, it is lower than the control group by 10.47%. The level of total iron-binding capacity (TIBC) in all three experimental groups is high. It exceeds the average values for pigs by 91.64% in the first group, by 99.36% in the second group, and by 78.46% in the third group. During the experiment, the level of transferrin saturation coefficient (TSC) in all groups was low, below the lower limits of the average indicators (Table 4).

The parameter under study	Normal value (taken from literature)	1st group Triazavirin	2nd group control	3rd group Tylosin
Cholesterol, mmol/l	2.1-3.5	2.44±0.12	2.44±0.075	2.6±0.0035*
Creatinine, µmol/l	70-208	142.6±11*	166±0.95	152.8±4.8**
AsAT, units/l	15-55	46.2±2.97*	39±1.92	55±5.7**
AlAT, units/l	22-47	43.6±4.398**	56±1.61	53.2±0.66
Urea, mmol/l	2.9-8.8	5.4±0.51*	4.3±0.08	5.6±0.478**
AP, units/l	41-176	273±25.892**	345.2±2.22	512±8.949***
GGTP, units/l	31-52	37.2±5.67	37.67±1.54	44±1.031***
LDH, units/l	160-425	368.6±10.1*	340.2±1.34	270±18.8***
Iron, µmol/l	28-36	19.2±2.22	17.2±1.02	15.4±0.51
TIBC, µmol/l	44.1-62.2	119.2±2.07*	124±1.1	111±3.459***
TSC, %	23.9-80.8	15.8±0.3055**	14±0.55	13.858±0.26

Note: * - $P \geq 0.950$, ** - $P \geq 0.990$, *** - $P \geq 0.999$

Table 4: Biochemical parameters of piglets' blood serum in the experimental groups at the slaughter period (178 days)

When assessing the protein fractions of blood and groups of immunoglobulins, one can evaluate the immunological status of animals (Table 5). We see that the total protein, albumins, globulins slightly change their values, but those values do not go beyond the limits of physiological norms. The A/G coefficient exceeds the average values but is stable in all experimental groups.

When determining the concentration of immunoglobulins A, M, and G in the blood serum, very

low values are detected that do not reach the lower level of the physiological norm. During the experiment, IgA was not detected in the blood serum of animals. In the groups that had received antiviral and antibacterial medications (the first and the third groups), the level of Ig M was lower than in the control group by 23.65% and 1.2%, respectively. The level of immunoglobulin G had increased in the first group by 62.02%, and in the third group, it had decreased by 17.71%, comparing with the control group. All of the above values are below the average range of the physiological norm (Table 5).

The analysis of some hormonal parameters of the blood serum of experimental animals demonstrated some changes. The TSH level in the first experimental group had decreased by 23.85%, and in the third by 29.23%, comparing with the control group. T4 in the first experimental group had increased by 4.87%, and in the third, it had decreased by 5.68%. Similar tendencies can be noted for T₃ which had increased by 74.27% in the first group and decreased by 65.53% in the third group comparing with the control group. Cortisol had decreased in the 1st and 3rd groups by 10.84% and 21.36%, respectively (Table 6).

The parameter under study	Normal value (taken from literature)	1st group Triazavirin	2nd group control	3rd group Tylosin
Total protein, g/l	58-89	72.2±0.113*	74.2±0.86	72.8±1.2
Albumin, g/l	23-40	38.4±1.17	39.4±0.51	37.8±0.3155**
Globulin, g/l	39-60	33.8±2.13	34.8±0.86	35±2.47
A/G coefficient	0.7-1	1.16±0.08	1.136±0.04	1.11±0.11
Ig A, g/l, (mg/ml)	2.34	-	-	-
Ig M, g/l, (mg/ml)	1.47	0.51±0.05	0.668±0.01	0.66±0.02
Ig G, g/l, (mg/ml)	12	5.95±0.84*	3.66±0.09	3.012±0.3*

Note: * - P ≥ 0.950, ** - P ≥ 0.990, *** - P ≥ 0.999

Table 5: Biochemical parameters of piglets' blood serum in the experimental groups at the slaughter period (178 days)

The parameter under study	1st group Triazavirin	2nd group control	3rd group Tylosin
TSH, μIU/ml	0.099±0.006	0.13±0.002	0.092±0.014**
T4, pmol/l	14.21±0.31*	15.55±0.081	12.78±0.209***
T3, nmol/l	3.59±0.76*	2.06±0.012	0.71±0.55197**
Cortisol, nmol/l	576±20.95***	646±1.76	508±1.14

Note: * - P ≥ 0.950, ** - P ≥ 0.990, *** - P ≥ 0.999

Table 6: Indicators of the level of hormones in the piglets' blood serum in experimental groups at the slaughter period (178 days)

Discussion

In the pig industry, antibacterial medications are widely used, and antiviral medications are not used directly. In our experiment, we compare the Triazavirin antiviral medication with the Tylosin-50 antibacterial medication.

The analysis of the condition and clinical picture of the experimental animals shows that the first signs of

improvement and stabilization of physiological parameters were noted in the first group on the second day. In the third group, positive dynamics were observed by the fifth day of the experiment.

When analyzing the ADWG in the three experimental groups, we note a stable increase and the highest percentage of meat yield at slaughter in the first group. These indicators reflect the effectiveness of the Triazavirin antiviral medication. Significant crowding and physiological immaturity of piglets allow pathogenic agents to actively spread and cause diseases [1, 4, 9]. Viral infections affecting the digestive, respiratory, immune, and other systems are particularly dangerous. When affected by viruses, many systems and organs don't function properly, the food metabolism and mineral metabolism are disturbed, and the work of the liver, bone marrow, spleen, thymus, thyroid gland, pituitary gland, and adrenal glands is disrupted [2, 5, 12]. The analysis of biochemical parameters of blood serum allows us to assess the functional activity of several organs and metabolic processes in the first place [6, 8, 14]. When analyzing the biochemical parameters at the slaughter of animals in the first experimental group, we noted the stabilization of AsAT, AlAT, and AP, and an increase in the level of iron, TIBC, and TSC. In the third experimental group, there was a deterioration in the indicators of AsAT, iron, TIBC, TSC, and improvement of AlAT and AP parameters. For growing animals, the indicators of iron, TIBC, and TSC are important. These indicators are associated with the work of the thyroid and parathyroid glands, with the liver and spleen, and the hypothalamus. Young and growing piglets experience iron deficiency accompanied by the development of iron deficiency anemia. From our experiment, we can see that infectious agents can also negatively affect the metabolism and assimilation of iron, and the development of anemia. Indicators of protein fractions of blood serum such as proteins, albumins, globulins, remain on average at the same level in all three experimental groups. Immunoglobulins A, M, and G are of interest to us. Immunoglobulin A plays a great role in protecting the mucous membranes of the respiratory system from pathogenic agents. On day 178, Ig A was not detected in the samples. Immunoglobulin M was kept at the same level in animals before and after the experiment in all groups, but the average physiological parameters had not been reached. Immunoglobulin G is involved in protecting the body from viral and bacterial infections. Ig G reached its maximum value in the first group but did not rise to the average physiological indicators. These data indicate the immunosuppressive state of animals when diseases of the respiratory system occur at an early age. In the

first group, we noted an increase in the level of T₄ and T₃, and a decrease in TSH and cortisol, which is a positive result during the experiment. It is this picture that is the most physiologically reliable and reflects the stable function of the hypothalamic-pituitary system and the thyroid gland. At the slaughter of animals on day 178, we observed the suppression of all indicators in the third group in the analysis of blood serum for hormones. Over the past period after the experiment, the indicators did not stabilize when using tylosin. Based on the results of clinical studies, we recommend using the Triazavirin medication as part of complex and etiological therapy in the treatment of the respiratory system of pigs affected with diseases of a viral nature. When piglets are given the Triazavirin medication, they demonstrate a stable ADWG and the highest percentage of meat yield. When analyzing the biochemical parameters of animals in the first experimental group, stabilization of several indicators (AsAT, AlAT, AP, iron, TIBC, TSC) was noted. Indicators of protein fractions of blood serum (proteins, albumins, globulins, immunoglobulins A, M, G) indicate the immunosuppressive state of animals. In the case of Triazavirin administration, there was an increase in the level of T₄ and T₃ and a decrease in TSH and cortisol.

Competing Interests

None.

Author Contributions

All authors contributed equally.

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