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The use of ferrous succinate in combination with vitamins A and E for the prevention of toxic liver dystrophy in piglets

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ABSTRACT

Noncontagious diseases are among the most widespread health issues affecting livestock at large pig breeding complexes. Statistics indicate that toxic liver dystrophy, rickets, vitamin deficiencies, and porcine stress syndrome prevail in groups of growing-finishing pigs. To date, a number of methods have been proposed to prevent and treat toxic liver dystrophy in pigs. The use of a 0.1% solution of sodium selenite and vitamins A and E, which have antioxidant properties, has become common practice in industrial pig farming in the Middle Volga Region of Russia. In recent years, both domestic and foreign researchers have proved that succinic acid and its derivatives exert antioxidant effects. Therefore, the development of new methods for the prevention and treatment of toxic liver dystrophy in piglets is very important. For the first time, research has been undertaken to determine the effects of ferrous succinate, vitamins A and E, sodium selenite on the hematological and biochemical parameters of sows and piglets produced by them. The effects of these drugs on sow productivity and piglet survival have been determined; histopathological alterations in the organs and tissues of piglets with toxic liver dystrophy have been identified. To prevent toxic liver dystrophy in piglets, the authors have proposed a regimen of administering ferrous succinate in combination with vitamins.

Keywords: prevention, piglets, liver dystrophy, survivability, vitamins A and E, ferrous succinate

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INTRODUCTION

Toxic liver dystrophy in pigs was first described by E. Zemmer, in Estonia, in 1882. He considered the disease to be an infection caused by micrococci found in pig carcasses [1,2,3]. The idea of infectious nature of toxic liver dystrophy was later supported by F. Gutira and J. Marek, who associated its causes with various pathogens [4,5,6]. However, J. Kaarde and other researchers stated that toxic liver dystrophy in pigs was not accompanied by any clinical or pathoanatomical changes typical of infectious diseases. A. Obel attempted to prove the infectious nature of toxic liver dystrophy in pigs by infecting healthy animals with large doses of a suspension of the liver tissue obtained from the piglets that had died due to the disease; all the experiments, however, yielded negative results. When researching into toxic liver dystrophy, K. Sherstoboyev called the disease 'infectious hepatitis of pigs' [7,8,9]. During his bacteriological studies, he managed to isolate from the carcasses of fallen piglets a polymorphic microorganism characterized by successful growth on liquid nutrient media. Although the isolated microorganism was reported to grow in both aerobic and anaerobic conditions, the researcher failed to obtain more than two passages of the causative agent of liver dystrophy in guinea pigs. K. Sherstoboyev explained it by the disease seasonality and the resistance the experimental animals had developed due to a well-balanced green feed diet. The author did not encounter an infectious hepatitis of pigs; he was dealing with salmonellosis and pasteurellosis as secondary infections, while the primary disease in the pigs was toxic liver dystrophy [10,11,12].

The variety of the disease names including those of 'enzootic hepatitis of pigs', 'toxic liver dystrophy', 'nutritional liver necrosis' indicates insufficient knowledge of the health condition.

Toxic liver dystrophy in pigs is enzootic, covers a large number of animals and causes high mortality in pig herds. The disease mainly affects suckling pigs and weaners. Despite its enzootic nature and large numbers of animals affected, the disease does not tend to spread. It is not contagious; biological testing via putting healthy pigs in direct contact with obviously sick ones led to negative results [13,14,15].

To date, various methods have been proposed for the treatment of toxic liver dystrophy in pigs. The existing literature suggests that if the disease occurs, all poor-quality feeds must be excluded, sick animals must be given gastric lavage with warm water and purgative enemas, followed by laxatives; a starvation treatment should be prescribed for the period of 8-12 hours [16,17,18]. To improve digestion functions and ensure gastrointestinal tract decontamination in sick pigs, antibiotics, sulfanilamide and acidophilic drugs must be administered orally; Analgin and Luminal are used to manage nervous signs [19,20].

P. Smirnov prevented the disease, consequently, piglet losses by administering three injections of tissue preparations, obtained according to V. Filatov's method, with a 5-day interval between injections [21].

V. Velikanov and S. Abramov suggest that pigs with toxic liver dystrophy should receive a once-daily intraperitoneal injection of a 0.037% sodium hypochlorite solution, at a dose of 5 ml / kg of body weight, in parallel with enterosorbent SV-1 administered orally in feed at the dose of 1.5 g / kg of body weight, for 9 days.

To prevent liver dystrophy in pigs, V. Baymanov and A. Bagautdinov recommend administering the 'Polysalts of microelements' preparation for 7 days. A single dose per animal contains 0.5 mg of potassium iodide, 3 mg of cobalt chloride, 6 mg of copper sulfate, and 5 mg of manganese sulfate. Similar data have been provided by N. Sevastyanov, who suggests the use of the KhZh-90 sorbent agent in addition to the salts of microelements. I. Donnik points out that intestinal adsorbents contribute to activating and correcting animals' immune system functioning, increasing their body weight gain, and mitigating the effects of toxic substances on their health [21,22,23].

The aim of this study was to investigate the possibility of using ferrous succinate in combination with vitamins A and E for the prevention of toxic liver dystrophy in piglets.

MATERIALS AND METHODS

The experimental study was carried out at the a pig-breeding complex *Iskra,* an agricultural production cooperative specialized in swine raising and breeding, which is located in Kuzhenersky District of the Republic of Mari El. For the experiment, 3 groups of pregnant sows were formed according to the principle of analogues. Starting 30 days prior to the farrowing, all sows from Group 1 and Group 2 received injections of oil solution of retinyl acetate, at a dose of 20,000 IU, once every 10 days, and a single injection of a 10% oil solution of tocopherol acetate at a dose of 0.005 mg /kg body weight. Sows from Group 1 were additionally given a 0.1% sodium selenite solution at a dose of 0.1 ml / kg of body weight. Besides, sows from Group 1 and Group 2 received a ferrous succinate preparation added to their regular daily ration, at a dose of 3 mg / kg body weight until giving birth, and at a dose of 9 mg /kg body weight until weaning. Group 3 served as a control.

During the study, identical animal feeding and welfare conditions were maintained in line with the zoo-sanitary requirements. Experimental animals were kept in a typical pig house equipped with an automatic drinking water delivery system and mechanical cleaning of manure. Feed distribution was performed manually.

At the start of the study and then every 15 days of the experimental period, a complete clinical examination of all experimental and control animals was conducted; morphological and biochemical tests were performed. Blood samples from piglets and sows were taken from the auricle veins in the morning before feeding.

Hematological blood tests were performed on a Mindray BC-3600 analyzer, and biochemical studies were conducted using a Dirui CS-T240 analyzer. Carcasses of fallen animals were subjected to postmortem examination; samples of internal organs were collected for histological examination.

Causative agents of bacterial infections were excluded by the bacteriological examination of the lymph nodes, tissue samples of parenchymal organs, and gastrointestinal tract of dead piglets; the examination was held in the Republican Veterinary Laboratory.

To perform the histological studies, liver, kidney, myocardium and pancreas tissue samples were collected from three dead piglets. Pathological preparations were fixed in a 10% formalin aqueous solution. To ensure compaction of the tissue blocks, the preparations were embedded in paraffin; the sections were stained with Hematoxylin and Eosin.

The analysis of tissue and cell structure was performed utilizing an *Opton* electron microscope (West Germany), simultaneously with photography using an M-35-W camera. This part of the study was carried out at the Pathological Anatomy Department of Kazan State Academy of Veterinary Medicine named after N.E. Bauman.

Digital data obtained in the study were statistically processed using the Microsoft Excel software package. The significance level of the reliability criterion regarding the research results was determined using the Student's t test.

RESULTS AND DISCUSSION

In the first set of experiments, the best results were obtained for Group 3 where ferrous succinate, vitamin A, vitamin E and selenium were applied; therefore, the second set of experiments was performed using these indicators. For this purpose, 3 groups of pregnant sows (five animals in each group) were formed following the principle of analogues at the agricultural production cooperative (collective farm) *Rassvet*, a pig-breeding complex in Kuzhenersky District of the Republic of Mari El.

Starting 30 days prior to the farrowing, all sows from Group 1 and Group 2 received injections of oil solution of retinyl acetate, at a dose of 20,000 IU, once every 10 days, and a single injection of a 10% oil solution of tocopherol acetate at a dose of 0.005 mg /kg body weight. Sows from Group 1 were additionally given a 0.1% sodium selenite solution at a dose of 0.1 ml / kg of body weight. Besides, sows from Group 1 and Group 2 received a ferrous succinate preparation added to their regular daily ration, at a dose of 3 mg / kg body weight until giving birth, and at a dose of 9 mg /kg body weight until weaning. Group 3 served as a control.

The feed ration analysis revealed a deficiency of lysine, calcium, phosphorus, iron, copper, zinc, cobalt, manganese, iodine, vitamins A, E and B_{12}.

The results of the hematological studies of sows' blood are presented in Table 1.

Table 1 Hematological parameters of blood in experimental sows

Group	Experimental period, days			
	Baseline	15	45	60
Hemoglobin, g/L				
Group 1	88.6±1.16	101.8±2,31	104.4±0.84	102.8±2.03
Group 2	84.8±2.66	102,6±1.13	106.8±2.02	105.5±1.67
Control	86.2±1.32	83.6±2.01	81.7±1.51	79.2±1.02
Red blood cells, 10^{12} /L				
Group 1	4.46±0.26	4.98±0.50	6.62±0.30	6.12±0.38
Group 2	4.36±0.39	5.72±0.35	6.33±0.45	6.27±0.24
Control	3.96±0.40	3.88±0.32	3.80±0.28	3.82±0.36
White blood cells, 10^{9} /L				
Group 1	8.56±0.50	9.46±0.23	12.80±0.61	14.34±0.53

Group 2	9.16±0.33	11.44±0.59+	12.61±0.34	13.22±0.43
Control	9.14±0.28	9.86±0.47	9.42±0.27	9.62±0.33
Hematocrit, L/L				
Group 1	0.33±0.03	0.39±0.04	0.39±0.02	0.40±0.03
Group 2	0.30±0.02	0.41±0.03++	0.39±0.03	0.39±0.02
Control	0.32±0.02	0.33±0.03	0.34±0.02	0.33±0.03

Table 1 shows that in all sows hemoglobin level was below the lower limit of normal, namely 84.8-88.6 g / L, while the normal range is 99-119 g / L. In addition, the sows had low hematocrit levels. By the 15th day of experiment, the hematological parameters had changed as follows. In Group 1, the red blood cell count increased by 1.12 times and was (4.98 ± 0.50) 10^{12} /L ($p < 0.05$); the white blood cell count increased by 1.11 times and reached (9.46 ± 0, 23) 10^9 /L ($p > 0.05$); hemoglobin level rose to 101.8 ± 2.31 g / L ($p < 0.01$), and hematocrit increased to 0.39 ± 0.04 L / L ($p < 0.05$). In sows from Group 2, on the 15th day the red blood cell count increased to 5.72 ± 0.35 × 10^{12} / L ($p < 0.05$), and white blood cell count increased to 11.44 ± 0.59 × 10^9 / L ($p < 0.05$), hemoglobin concentration increased by 1.21 times ($p < 0.05$), and hematocrit rose by 1.33 times ($p < 0.01$). The results of analyzing the respective parameters in control sows indicate that the number of red blood cells on the 15th day of experiment decreased to (3.88 ± 0.32) 10^{12} / L, while the white blood cell count increased by 1.08 times; the concentration of hemoglobin fell to 83.6 ± 2 , 01 g / L compared with the baseline values, and the hematocrit level increased slightly.

On the 45th day of the study, changes in the hematological parameters were similar to those of the 15th day. In Group 1, the red blood cell count significantly increased to 6.62 ± 0.30 10^{12} / L ($p < 0.001$), while the white blood cell count was 12.80 ± 0.61 10^9 / L; hemoglobin concentration increased by 1.18 times ($p < 0.001$) compared to baseline. The hematocrit level slightly went down and was 0.39 ± 0.02 L / L ($p > 0.05$).

In Group 2, on the 45th day of the experiment, the following significant alterations ($p < 0.001$) in hematological parameters were recorded. The number of red cells increased by 1.45 times (6.33 ± 0.45 10^{12} / L), hemoglobin concentration increased by 1.26 times (106.8 ± 2.02 g / L), the white blood cell count went up by 1.38 times (12.61 ± 0.34 10^9 / L), and hematocrit increased by 1.29 times (0.39 ± 0.03 L / L) in comparison with the initial values.

In the control, sows' blood parameters changed as follows: the red blood cell count decreased to 3.80 ± 0.28 10^{12} / L, the hemoglobin level was 81.7 ± 1.51 g / L, the white cell count slightly decreased to 9.4 ± 0.27 · 10^9 / L, while hematocrit slightly increased by 1.06 times compared with the baseline values.

On the 60th day of the experiment, compared to the 45th day, the red cell count in the blood of sows from Group 1 slightly decreased and was (6.12 ± 0.38) 10^{12} / L ($p < 0.001$), the white cell count went up to (14.34 ± 0.53) 10^9 / L ($p < 0.001$) which was 1.68 times higher than the baseline level. Changes in hemoglobin and hematocrit concentrations were significant; the hemoglobin level increased to 102.8 ± 2.03 g / L ($p < 0.001$), and hematocrit rose by 1.23 times and amounted to 0.40 ± 0.03 L / L ($p < 0.05$) compared to baseline.

On the 60th day of the study, hematological parameters of sows from Group 2 tended to change compared with the baseline values: the red blood cell count significantly increased ($p < 0.001$) by 1.44 times and amounted to 6.27 ± 0.24 10^{12} / L, the level of hemoglobin increased by 1.24 times and was 105.5 ± 1.67 g / L ($p < 0.001$), the white blood cell count increased by 1.44 times and was 13.22 ± 0.43 10^9 / L ($p < 0.001$), and hematocrit increased by 1.3 times and was 0.39 ± 0.02 L / L ($p < 0.05$). In the control, the red blood cell count slightly decreased to 3.82 ± 0.36 10^{12} / L, and hemoglobin concentration went down to 79.2 ± 1.02 g / L. The white blood cell count increased by 1.05 times and amounted to 9.62 ± 0.33 · 10^9 / L, hematocrit increased by 1.03 times and reached 0.39 ± 0.02 L / L compared to the baseline values.

The baseline parameters generally did not go beyond the physiological norm, with the exception of segmented neutrophils: their level slightly exceeded the upper limit of normal.

In Group 1, a statistically insignificant ($p > 0.05$) increase of 1.04 times in the number of stab neutrophils was observed on the 15th day of experiment, as well as a 1.09-fold decrease in segmented neutrophils ($p < 0.05$), while lymphocytes ($p > 0.05$) went down by 1.03 times, and eosinophils ($p > 0.05$) decreased by 1.1 times. On the 45th day of the study, there was a statistically insignificant decrease in the number of stab neutrophils in this group ($p > 0.05$) to 4.8 ± 0.27%. The number of segmented neutrophils significantly decreased by 1.25 times ($p < 0.001$), the number of lymphocytes reduced by 1.01 times ($p < 0.05$), the number of eosinophils decreased by 1.05 times ($p > 0.05$), while the number of monocytes increased by 1.45 times ($p > 0.05$) compared with the baseline. On the 60th day of the experiment, an insignificant increase in the number of stab neutrophils to 6.2 ± 0.28% ($p > 0.05$) and a rise in the number of eosinophils to 3.6 ± 6.30% ($p < 0.05$) were recorded. The number of segmented neutrophils decreased to 36.2 ± 1.02% ($p < 0.001$), the concentration of lymphocytes increased by 1.29 times ($p > 0.05$), and that of monocytes increased by 1.72 times ($p > 0.05$) compared with the initial values. In Group 2, the number of stab neutrophils decreased by 1.1 times ($p > 0.05$) by the 15th day of the study and then gradually increased reaching the value of 9.2 ± 0.36% ($p > 0, 05$) on the 60th day, which was 1.53 times higher than the baseline. The number of segmented neutrophils significantly decreased on the 15th day of the study - by 1.05 times ($p < 0.05$) - and kept falling to 32.8 ± 1.55% ($p < 0.001$) by the 60th day. On the 15th day, the number of eosinophils increased by 1.13 times compared with the baseline parameter ($p > 0.05$). The pattern continued until the 60th day of the experiment, when the number of eosinophils was 1.35 times higher compared to the initial value ($p > 0.05$). Similar changes occurred in the concentrations of lymphocytes and monocytes, the number of which in the course of the study did not significantly increase ($p > 0.05$) and reached the levels of 67.4 ± 1.51% and 3.6 ± 0.29%, respectively, on the 60th day. In the control group, the following picture was observed. The number of stab neutrophils did not change significantly throughout the experiment. There was a gradual increase in the number of segmented neutrophils, so on the 15th day of the study, their number increased by 1.01 times, and on the 60th day – by 1.20 times compared

with the baseline parameters. On the 15th day, the number of lymphocytes decreased by 1.13 times compared with the baseline values, but then their number gradually increased and, on the 60th day of the study, reached 56.7 ± 1.07%, which was 1.04 times higher than baseline. The number of eosinophils increased slightly and was 2.7 ± 0.33% on the 60th day of the study, and the number of monocytes increased by 1.27 times.

Along with hematological parameters, dynamics of blood biochemical parameters is of considerable interest. Table 2 presents the data resulting from the analysis of levels of total protein and protein fractions in the blood serum of sows from the farm under research. The data indicate that total protein concentrations in the blood of sows were at the lower limit of normal in all groups of animals, which was primarily due to an unbalanced diet.

In Group 1 of sows, an increase in the total protein content was recorded as early as on the 15th day of the study. This pattern continued throughout the entire experimental period, and, at the end of the study, the total protein level was 81.1 ± 0.88 g / L ($p < 0.05$). Similar changes were observed in Group 2, where, on the 15th day of study, the total protein level increased by 2.02% ($p > 0.05$) compared to the baseline value of (74.1 ± 0.70 g /L); by the 60th day the total protein level amounted to 82 ± 0.44 g / L ($p < 0.001$), which was 1.1% higher than in Group 1 (81.1 ± 0.88 g / L) and 11.2% higher than in the control. In the control group, total protein content increased by 1.5% by the 15th day of study, and the value of 74 ± 0.81 g / L was recorded on the 45th day. On the 60th day, a slight increase to 74.4 ± 0.49 g / L in the total protein concentration was found in the sows' blood.

The analysis of concentrations of individual protein fractions in sows' blood serum revealed lower concentrations of albumins, alpha globulins and beta globulins, and a higher content of gamma globulins compared with the reference values used in veterinary medicine. On the 15th day of the study, the sows from Group 1 demonstrated a significant increase in the levels of albumins (by 30.5%) ($p < 0.001$), alpha globulins (by 66.1%) ($p < 0.01$), beta globulins (by 6.4%) ($p > 0.05$), as well as a statistically insignificant decrease in the concentration of gamma globulins (by 25.2%) ($p > 0.05$). This pattern continued up to the 45th day of experiment. On the 60th day, the albumin levels increased to 35.91 ± 0.56 g / L ($p < 0.001$); the content of alpha globulins was 50.7% higher (13.23 ± 0.64 g / L) ($p > 0.05$), and that of beta-globulins was 23.9% (13.34 ± 0.84 g / L) ($p > 0.05$) higher compared with the initial parameters.

Table 2 Values of the content of total protein and protein fractions in sows' blood serum

Group	Experimental period, days			
	Baseline	15	45	60
Total protein, g/L				
Group 1	73.3±1.06	77.18±0.86	81.2±1.03	81.1±0.88
Group 2	74.1±0.70	75.6±0.64	80.5±0.71	82.0±0.44
Control	73.7±0.51	74.8±1.05	74.0±0.81	74.4±0.49
Albumins, g/L				
Group 1	25.51±0.69	33.30±1.01	34.34±0.92	35.91±0.56
Group 2	23.29±1.21	33.64±0.77	33.53±0.37	36.22±0.45
Control	22.32±0.67	23.33±0.35	22.87±0.91	21.49±0.66
Alpha globulins, g/L				
Group 1	8.82±0.55	14.65±0.9	12.66±0.50	13.29±0.64
Group 2	9.37±0.77	15.45±0.40	15.79±0.34	14.09±0.48
Control	8.72±0.24	9.89±0.49	11.23±0.38	12.02±0.29
Beta globulins, g/L				
Group 1	10.77±0.44	11.46±0.51	18.88±0.6	13.34±0.84
Group 2	10.26±0.28	13.16±0.47	20.91±0.74	14.04±0.62
Control	9.49±0.33	10.36±0.59	12.41±0.36	12.012±0.28
Gamma globulins, g/L				
Group 1	25.74±0.34	19.25±1.11	18.11±0.6	16.74±0.42
Group 2	23.22±1.01	19.47±0.91	17.22±0.48	17.04±0.33
Control	24.28±0.66	24.02±0.73	21.86±0.79	20.16±0.58

The content of gamma globulins significantly decreased by 34.9% compared to the baseline parameter and reached 16.74 ± 0.42 g / L ($p < 0.05$). In Group 2, a consistent increase in albumin concentration from 23.29 ± 1.21 g / L (baseline) to 36.22 ± 0.45 g / L (60th day) was observed, which was statistically reliable ($p < 0.001$). On the 15th and 45th days, the alpha globulin level significantly increased ($p < 0.01$) by 64.8% and 68.5%, respectively, compared with baseline, and was 14.09 ± 0.48 g / L ($p > 0.05$) on the 60th day of the experiment. There was also a significant increase ($p < 0.01$) in the concentrations of beta globulins during the experiment. The level of gamma globulins significantly decreased, from 23.22 ± 1.01 g/L (baseline) to 17.04 ± 0.33 g/L, by the 60th day ($p < 0.05$).

The following changes in the content of protein fractions were found in the blood serum of the control animals. The level of albumins slightly increased by 4.5% on the 15th day, and then decreased by 3.7% on the 60th day compared to baseline. The level of alpha globulins kept slightly increasing during the entire experiment. Thus, on the 45th and 60th days, the parameter was 28.7% and 37.8% higher, respectively, than the baseline value. By the 15th and 45th days, the content of beta globulins rose by 9.2% and 30.8%, respectively compared to baseline. On the 60th day, it went down by 3.2% in comparison with the 45th day of experiment. The concentrations of gamma globulins gradually decreased during the experiment and reached 20.16 ± 0.58 g / L by the 60th day. Table 3 shows the data on the levels of total calcium, inorganic phosphorus and glucose in the sows' blood.

The total calcium concentrations kept increasing significantly (p <0.001) in both experimental groups. Thus, on the 15th day of the study, the total calcium level increased by 1.10 times and was 2.33 ± 0.04 mmol / L in Group 1, while in Group 2 it increased by 1.08 times and amounted to 2.43 ± 0.04 mmol /L. On the 45th day, the total calcium content was 2.76 ± 0.11 mmol / L in sows from Group 1, and 2.81 ± 0.08 mmol / L in sows from Group 2. By the end of the experiment, the total calcium level was 45.5% higher than baseline in sows of Group 1, and 25.3% higher that baseline for Group 2. In sows from the control, the total calcium content did not change significantly during the experiment.

Regarding the changes in the inorganic phosphorus level, it increased by 1.23 times in Group 1, while in Group 2, on the contrary, it decreased by 1.07 times (p <0.01) on the 15th day of experiment. On the 45th day, the inorganic phosphorus concentration was close to baseline (p <0.01) in Group 1, whereas in Group 2 it did not change significantly compared to the data of the 15th day (p> 0.05).

Table 3 Values of total calcium, phosphorus and glucose concentrations in sows' blood

Group	Experimental period, days			
	фон	15	45	60
Total calcium, mmol / L				
Group 1	2.11±0.05	2.33±0.09	2.76±0.11	3.07±0.04
Group 2	2.25±0.08	2.43±0.04	2.81±0.08	2.82±0.07
Control	2.29±0.07	2.26±0.08	2.38±0.04	2.25±0.06
Inorganic phosphorus, mmol / L				
Group 1	1.57±0.04	1.93±0.06	1.56±0.07	1.61±0.11
Group 2	1.77±0.09	1.65±0.0	1.66±0.05	1.58±0.03
Control	1.75±0.05	1.85±0.07	1.74±0.06	1.96±0.11
Glucose, mmol / L				
Group 1	2.28±0.24	3.35±0.2	3.36±0.20	3.91±0.41
Group 2	2.18±0.19	3.36±0.30	3.42±0.18	4.07±0.44
Control	2.98±0.15	2.67±0.28	2.78±0.26	2.88±0.13

On the 60th day of the experiment, the concentration of inorganic phosphorus was 1.61 ± 0.11 mmol / L (p <0.01) in the blood of sows from Group 1, and 1.58 ± 0.03 mmol / L (p < 0.001) in sows from Group 2, which was 2.5% higher and 10.7% lower, respectively, compared to baseline. In the control, the inorganic phosphorus level slightly increased and, by the end of the experiment, reached 1.96 ± 0.11 mmol / L, which exceeded the upper limit of the physiological norm.

Blood glucose levels in sows from both groups increased in the course of the experiment. For sows in Group 1, the content of blood glucose was 3.35 ± 0.29 mmol / L (p <0.01) on the 15th day, and 3.91 ± 0.41 mmol / L (p <0.001) on the 60th day of the experiment, which exceeded the initial value by 71.5%. In sows from Group 2, the blood sugar level was 3.36 ± 0.30 mmol / L on the 15th day, 3.42 ± 0.18 mmol / L (p <0.001) on the 45th day, and 4.07 ± 0.44 mmol / L (p <0.001) on the 60th day, which was 4, 1% higher than that in Group 1. The blood glucose level in sows of the control group remained below the lower limit of normal.

The data on the levels of vitamins A and E, conjugated and unconjugated bilirubin, ketone bodies and selenium are given in Table 4.

Table 4 shows that all sows had low levels of vitamins A and E, selenium, and high levels of unconjugated bilirubin and ketone bodies. Conjugated bilirubin was found in the blood serum of all sows.

Throughout the experimental period, the levels of vitamins A and E increased in the sows of experimental groups. Thus, on the 15th day of study, in Group 1, the vitamin A concentration was 2.87 times (p <0.001) higher and that of vitamin E was 1.74 times (p <0.001) higher than the baseline; in Group 2, levels of vitamins A and E exceeded the initial values by 2.69 times and 2.07 times (p <0.001), respectively. On the 45th day, the level of vitamin A in Group 1 slightly decreased to 1.24 ± 0.04 μmol / L (p <0.001), and on the 60th day it increased again to 1.50 ± 0.06 μmol / L (p <0.001). By the end of the study, the level of vitamin E in Group 1 was 2.16 times higher than baseline and amounted to 7.06 ± 0.29 μmol / L (p <0.001). A similar pattern was observed in Group 2, where, on the 60th day, the vitamin A content reached 1.42 ± 0.09 μmol / L (p <0.001), which was 2.33 times higher than baseline, while the vitamin E level exceeded the baseline by 2, 37 times and amounted to 7.18 ± 0.44 μmol / L (p <0.001). In the control group, the vitamin A content did not change significantly, while vitamin E concentration decreased by 11.8% compared with baseline by the 60th day.

A statistically significant decrease in the conjugated bilirubin level was observed: in Group 1, it fell by 2.43 times on the 15th day and by 6.55 times on the 45th day, while in Group 2 it decreased by 2.69 times and 4.9 times, respectively, compared with baseline (p < 0.001). On the 60th day, no conjugated bilirubin was detected in the blood serum of sows from either Group 1 or Group 2. In the control group, in contrast, the conjugated bilirubin level on the 15th day of study (2.13 ± 0.08 μmol / L) was 7% higher than baseline, and on the 60th day, it was 1.70 ± 0. 05 μmol / L.

Table 4 Values of the content of vitamins A and E, conjugated and unconjugated bilirubin, ketone bodies, and selenium in sows' blood

Group	Experimental period, days			
	Baseline	15	45	60
Vitamin A, μmol / L				
Group 1	0.55±0.07	1.58±0.09	1.24±0.04	1.50±0.06

Group 2	0.61±0.04	1.64±0.08	1.39±0.06	1.42±0.09
Control	0.51±0.05	0.49±0.06	0.44±0.02	0.46±0.04
Vitamin E, μmol / L				
Group 1	3.26±0.06	5.66±0.19	6.51±0.33*	7.06±0.29
Group 2	3.03±0.26	6.28±0.34	6.97±0.20*	7.18±0.44
Control	3.14±0.48	3.06±0.18	2.91±0.14	2.77±0.17
Conjugated bilirubin, μmol / L				
Group 1	2.16±0.15	0.89±0.09	0.33±0.02	-
Group 2	1.91±0.07	0.71±0.06	0.39±0.04	-
Control	1.99±0.07	2.13±0.08	1.76±0.08	1.70±0.05
Unconjugated bilirubin, μmol / L				
Group 1	15.05±0.01	12.26±0.34	9.32±0.18	9.02±0.33
Group 2	14.36±0.30	10.88±0.42	7.92±0.29	8.14±0.17
Control	14.77±0.32	16.09±0.54	13.64±0.21	14.46±0.25
Ketone bodies, g/L				
Group 1	0.048±0.004	0.037±0.002	0.025±0.0004	0.004±0.0002
Group 2	0.050±0.003	0.044±0.003	0.0242±0.0002	0.009±0.0001
Control	0.045±0.011	0.047±0.004	0.038±0.005	0.051±0.004
Selenium, μmol / L				
Group 1	0.31±0.03	0.96±0.07	1.01±0.08	0.88±0.07
Group 2	0.28±0.04	0.34±0.08	0.49±0.05	0.51±0.03
Control	0.37±0.05	0.25±0.03	0.29±0.03	0.28±0.04

Significant changes also occured in the unconjugated bilirubin concentrations in the sows' blood. In Group 1, its amount was 12.26 ± 0.34 μmol / L ($p < 0.001$) on the15th day of experiment and 9.32 ± 0.18 μmol / L ($p < 0.001$) on the 45th day, which was 38.2% lower compared with baseline. On the 60th day, the level of unconjugated bilirubin in the blood was 1.67 times lower than baseline, and had the value of 9.02 ± 0.33 μmol / L ($p < 0.001$). In Group 2, the level of unconjugated bilirubin was 10.88 ± 0.42 μmol / l ($p < 0.001$) on the 15th day of experiment, which was 1.32 times lower than baseline; on the 45th day, it was 7.92 ± 0.29 μmol / L ($p < 0.001$), which was by 1.81 times lower than baseline, and on the 60th day the level of unconjugated bilirubin was 8.14 ± 0.17 μmol / L ($p < 0.001$), which was 1.76 times lower than baseline. In the control, its amount increased by 1.09 times to 16.09 ± 0.54 μmol / L on the 15th day, and was 14.46 ± 0.25 μmol / L on the 60th day.

The level of ketone bodies gradually decreased in both experimental groups during the experiment. In Group 1, it was 0.037 ± 0.002 g / L ($p < 0.05$) on the 15th day, and 0.025 ± 0.0004 g / L ($p < 0.001$) on the 45th day, which was 48% less than baseline; on the 60th day, the level of ketone bodies 91.6% ($p < 0.01$) lower than baseline. In Group 2, it decreased by 1.14 times (0.047 ± 0.004 g / l) ($p > 0.05$) on the 15th day, by 2.08 times (0.024 ± 0.0002 g / L) ($p < 0.05$) on the 45th day, and by 5.55 times (0.009 ± 0.0001 g / L) ($p < 0.001$) on the 60th day compared with baseline. In the control group, the level of ketone bodies did not change significantly and remained above the upper limit of normal.

During the analysis of dynamics in selenium levels in the blood of sows, the most noticeable changes were observed in Group 1 because sows from that group received injections of a 0.1% sodium selenite solution. Thus, in Group 1, the selenium level was 0.96 ± 0.07 μmol / L ($p < 0.001$) on the 15th day of the experiment, 1.01 ± 0.08 μmol / L ($p < 0.001$) on the 45th day, and 0.88 μmol / L ($p < 0.001$) on 60th day, which exceeded the baseline values by 2.84 times. In Group 2, the selenium level only increased by 21.4% ($p > 0.05$) on the 15th day compared to baseline. On the 60th day, the selenium concentration was 0.51 ± 0.03 μmol / L ($p < 0.01$), which was 42.0% less than the respective parameter in Group 1 and 82% more than in the control ($p < 0.001$).

The analysis of changes in the activity of some enzymes in the blood serum of sows, the following findings were obtained. On the 15th day of experiment, the activity of aspartate aminotransferase in Group 1 decreased by 1.73 times and was 52.8 ± 6.25 U / L ($p < 0.001$), while in Group 2, it went down by 1.19 times and was 75.2 ± 4.55 U / L ($p < 0.001$). On the 45th day, its activity in Group 1 was 58.7% lower than baseline, and in Group 2 it was 41.8% ($p < 0.001$) lower than baseline. On the 60th day, the activity of aspartate aminotransferase reached the level of 35.2 ± 4.12 U / L ($p < 0.001$) in Group 1 and that of 41.8 ± 3.22 U / L ($p < 0.001$) in Group 2, which was lower than baseline by 2.59 and 2.14 times, respectively. In the control, the aspartate aminotransferase level gradually increased and reached 106.1 ± 6.35 U / L on the 60th day of the experiment.

Similar dynamics were observed in the activity of alanine aminotransferase in the sows' blood serum. Thus, in Group 1 its activity was 95.3 ± 8.18 U / L ($p < 0.005$) on the 15th day and 84.8 ± 7.15 U / L ($p < 0.001$) on the 45th day, which was 34.8% lower than baseline. In Group 2, the alanine aminotransferase activity was 110.5 ± 10.11 U / L ($p > 0.05$) on the 15th day and 92.8 ± 6.52 U / L ($p < 0.001$) on the 45th day. On the 60th day, its activity level significantly decreased compared to the initial values ($p < 0.001$) - by 36% in Group 1 and by 30.3% in Group 2. In the control, the level of alanine aminotransferase activity was 128.6 ± 10.24 U / L on the 15th day, 134.2 ± 9.43 U / L on the 45th day, and 130.6 ± 8.36 U / L on the 60th day, which was 6.5% higher than the initial values.

In Group 1, the activity of glutamate dehydrogenase decreased by 1.12 times (32.7 ± 4.18 U / L) ($p < 0.01$) on the 15th day, by 1.24 times (29, 4 ± 4.44 U / L) ($p < 0.001$) on the 45th day, and by 1.15 times (31.8 ± 3.25 U / L) ($p < 0.001$) on the 60th day of the experiment compared to baseline. In Group 2, the activity of this enzyme significantly decreased during the experiment and reached 33.3 ± 2.47 U / L by the 60th day, which was 27.3% lower than baseline ($p < 0.001$).

In Group 1, the level of alkaline phosphatase also fell significantly, namely by 1.25 times (40.1 ± 3.55 U / L) ($p < 0.01$) on the 15th day, by 1.42 times (35 , 6 ± 4.09 U / L)

(p <0.001) on the 45th day, and by 1.38 times (36.4 ± 2.46 U / L) (p <0.001) on the 60th day of the study in comparison with the baseline. In Group 2, its activity decreased by 9.7% (p <0.001) on the 15th day, 27.5% (p <0.001) on the 45th day, and by 30.9% (p <0.001) on the 60th day compared to baseline.

Significant changes were found in amylase activity dynamics. In Group 1, the parameter increased by 1.31 times (131.2 ± 10.14 g· h / L) (p <0.001) on the 15th day of experiment, by 1.40 times (139.9 ± 12.62 g · h / L) (p <0.001) on the 45th day, and by1.36 times (135.8 ± 9.84 g · h / L) (p <0.001) on the 60th day as compared with the baseline. In Group 2, the amylase activity kept significantly increasing during the entire experiment (p <0.001) and exceeded the initial level by 63.4% on the 60th day. In the control, the levels of glutamate dehydrogenase, alkaline phosphatase and amylase activity did not change significantly.

The results of this study indicate that under identical feeding and maintenance conditions, the administration of ferrous succinate, tocopherol, retinyl acetate and sodium selenite to pregnant and lactating sows does not adversely affect either clinical and physiological body condition of the animals or the ways they express their maternal instincts.

Table 5 Sow productivity traits

Group	Number of sows used in the experiment	Total number of piglets born	Number of piglets per sow	Piglet body weight
Group 1	5	63	12.6±0.89	1.24±0.06
Group 2	5	66	12.8±0.76	1.23±0.08
Control	5	65	12.4±0.34	0.98±0.06

The data presented in Table 5 show that treatment of sows with the abovementioned drugs during the late gestation period has a positive effect on the piglet birth weight.

Piglets produced by the experimental sows had higher birth weights than newborn piglets of sows from the control group. The pattern continued until weaning time.

Table 6 presents the data on piglet survival during the experiment.

Table 6 Piglet survival in the experiment

Group	Piglet mortality before 45th day of age		Survival, %
	Total	Including toxic liver dystrophy as a cause of death	
Group 1	2	-	96.8
Group 2	2	-	97.0
Control	18	11	72.3

Table 6 shows that piglet mortality and survival rates were similar in Group 1 and Group 2 involved in the experiment. Thus, the piglet survival rates were 96.8% and 97% in Group 1 and Group 2, respectively, whereas in the control it was 72.3%.

During the research and production experiments, we performed postmortem examination of 44 carcasses of suckling and weaned piglets with signs of toxic liver dystrophy. Most of the lost piglets had good and medium body weights. In sick piglets, red spots appeared on the skin of the back, abdomen and nose, which eventually became blue and violet in color. Skin yellowing was recorded in some animals, and the necropsies revealed yellow discoloration of the subcutaneous tissue and serous membrane covering internal organs.

The postmortem examination of the fallen piglets exhibited venous stasis in the mesenteric veins and serous covering of the stomach and intestines, as well as indications of acute catarrhal gastroenterocolitis. Mesenteric and portal lymph nodes were found to be enlarged, swollen, and grayish-red in color, with a smoothed follicular structure pattern; many of the nodes had punctate hemorrhages on their cut surfaces. In some animals, the development of diffuse diphtheria colitis with signs of ulceration was discovered. Additionally, 2 out of 25 dissected animals had catarrhal bronchopneumonia of a confluent nature.

Significant changes were observed in the liver of the fallen animals. Acute venous congestion within the liver was found, along with the variegated coloration of the organ due to dark red areas alternating with grayish-white ones. The cut surface of the liver tissue was reddish-brown and wet. The gallbladder was filled with thick bile of dark green color.

A histological examination of the liver revealed the preservation of the lobular and beam structure pattern. Some areas of the interlobular tissue contained small clusters of lymphoid histiocytes. Intralobular capillaries and central veins were full of blood.

The examination demonstrated the presence of parenchymal cells with signs of protein and fatty degeneration, as well as necrobiosis and necrosis, in most lobules. Experimental piglets exhibited poorly expressed protein dystrophy and fatty change in the liver, as well as noticeable proliferation of the interlobular connective tissue.

In the kidneys of the control animals, vessels of the glomeruli were filled with blood to varying degrees, while in the lumen of their capsules an increased amount of the granular eosinophilic mass was found along with the epithelium of convoluted tubules with signs of protein dystrophy. Moderate edema of the interstitial tissue was also observed.

Furthermore, protein dystrophy and fatty degeneration of cardiomyocytes, and moderate edema of the interstitial tissue were noted in the myocardium of the control animals. In experimental piglets, most of the muscle fibers in the myocardium did not have any noticeable changes. Fatty degeneration of individual muscle fibers was recorded. Necrobiosis of exocrynocytes and endocrynocytes, edema of interstitial tissue, and fibrinoid

necrosis of the blood vessel were found in the pancreas of the control animals.

The results of our study indicate that in the case of administering ferrous succinate, retinyl acetate and tocopherol acetate, sodium selenite to sows during the late gestation and lactation periods, the piglets produced by the sows do not suffer from degenerative changes of parenchymal organs or pancreas.

CONCLUSION

The use of ferrous succinate, retinyl acetate, tocopherol acetate, and sodium selenite contributes to the normalization of the morphological and biochemical blood parameters in sows.

In the case of administering ferrous succinate, retinyl acetate and tocopherol acetate, sodium selenite to sows during the late gestation and lactation periods, the piglets produced by the sows do not have degenerative changes of the parenchymal organs or pancreas.

An effective way to prevent toxic liver dystrophy in piglets and improve sow productivity is the treatment of sows with oil solution of retinyl acetate at a dose of 20,000 IU, administered intramuscularly once every 10 days, starting 30 days prior to farrowing; tocopherol acetate solution at a dose of 0.005 mg / kg of body weight, administered intramuscularly, once; ferrous succinate administered daily through the feed at the dose of 0.3 mg / kg of body weight.

Conflict of interest

The authors declare that there is no known conflict of interest associated with this publication.

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