

pii: S232245682100083-11 Received: 09 October 2021 ORIGINAL ARTICLE

Accepted: 01 December 202

Dynamics of Morphological Indicators of Blood of Piglets under the Influence of Iron Clathrochelate Complex and Cyanocobalamin

Iryna Derkach^{1*}, Volodymyr Dukhnitsky¹, Serhii Derkach¹, Vitalii Lozoviy¹, Vasyl Kostrub¹, Yuliia Losa¹, Igor Fritsky², and Maksym Plutenko²

¹National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine ²Taras Shevchenko National University of Kyiv, Kyiv, Ukraine

*Corresponding authors email address: Irina1215@ukr.net; OCCID: 0000-0002-0149-7923

ABSTRACT

Iron deficiency anemia is one of the most common non-contagious diseases of piglets. Veterinary antianemic drugs have several drawbacks, so finding new medicines is an important current task for scientists. Therefore, the present study investigated the antianemic effect of iron (IV) clathrochelate in the organism of piglets. The subsequent studies included the exploration of its antianemic actions, particularly in combination with cyanocobalamin when this combination was administered to sows for prophylaxis in piglets. The experiment was carried out on 30 suckling piglets during the period of their detention with sows. According to the method of analogue groups, two groups of control (I) and experimental (II, each containing 15 animals) were formed and they were studied for 30 days. The piglets from five sows (three from each) were selected for the experimental group. During the pregnancy of these sows, 10 ml of 10% solution of iron (IV) IV clathrochelate and solution of cyanocobalamin were injected intramuscularly twice 7 and 14 days before their expected farrowing. For prevention of iron deficiency anemia, the traditional solution of iron dextran was administered once intramuscularly to piglets of the control group. The investigative material included the blood samples of piglets considering the dynamics of probable changes in the number of erythrocytes, hemoglobin content and hematocrit, and other morphological indicators and blood indices of piglets. The dynamics of changes in erythrocyte count, hemoglobin content, hematocrit, leukocytes and platelets, indices of blood almost did not differ from the dynamics of these values when using only 10% solution of iron (IV) clathrochelate for pregnant sows. The proposed scheme for the prophylaxis of iron deficiency anemia in piglets, involving simultaneous intramuscular injections of IV clathrochelate and cyanocobalamin to pregnant sows, is somewhat inferior to the previous preventive measures, which included only the intramuscular injections of iron (IV) IV clathrochelate, but it can be recommended as highly effective.

Keywords: Anemia, Cyanocobalamin, Clathrochelate, Hemoglobin, Iron, Piglets, Sows

INTRODUCTION

Although the consequences of an excess of iron in animals and humans are severe pathological conditions, including cancer, the issue of its deficiency is constantly focused on both scientists and owners of animals or livestock farms. All over the world, one of the most common problems with commercial pig farming or private pig farming is iron deficiency anemia in piglets. During this pathology, the average daily gain in sick animals decreases, they lag in development, susceptibility to infections increases, and in severe cases, the mortality of piglets can be increased up to 60-70%. The disease is observed for 5-7 days of life and reaches its maximum development at three weeks of age (Killip and Bennett, 2008; Sidorkin et al., 2007; Zharov and Zharov, 2012).

Anemia is a condition of the body that is characterized by physiological norms of hemoglobin leading to a decrease in the number of erythrocytes, or their functional insufficiency (Killip and Bennett, 2008; Levchenko et al., 2012; Lipiński et al., 2013).

The issue of iron deficiency is of utmost importance in newborn piglets (Bonkovsky and Herbert, 1991; Walter et al., 1997; Karput and Nikoladze, 2001). This is because piglets are the most immature of all farm animals at birth. Their intensive growth is much ahead of the formation of erythrocytopoiesis and the perfection of their functional activity. Hemocytopoietic processes do not provide sufficient erythrocyte production and the synthesis of hemoglobin. During this period, erythrocytopoiesis is inhibited in the spleen and liver, and the process of restructuring the erythrocytopoietic capacity of the bone marrow is activated. This biological feature of piglets is a significant factor that determines their susceptibility to anemia (Svoboda and Drabek, 2005; Sidorkin et al., 2007; Gasanov et al., 2020).

663

In the body of piglets, these iron reserves begin to decrease from the eighth day of life, resulting in a slowdown in hemoglobin synthesis and disruption of external gas exchange. In addition, there are disorders of internal gas exchange. Oxygen hypoxia reduces the secretory function of the stomach and intestines, the activity of proteolytic enzymes, α -amylase and lipase, which causes indigestion, insufficient absorption of acids, carbohydrates, lipids, proteins, and vitamins, as well as macro and micronutrients (Levchenko et al., 2012; Leyshon et al., 2016).

With the development of iron deficiency anemia, erythropoietin activates the function of the red bone marrow, which stimulates DNA synthesis in erythroid cells, stimulates their mitotic activity, reduces the maturation period, and increases hemoglobin synthesis. At the same time, erythropoietin inhibits the production of leukocytes, which leads to a decrease in the number of leukocytes in the blood and the development of immunodeficiency (Karput' and Nikoladze, 2001; Karput' and Nikoladze, 2003). On day 10, the inclusion of iron in the composition of iron proteins in erythroid cells of the bone marrow is reduced. From days 3 to 30 of age, the content of ferritin increases in the serum of animals, which signifies a decrease in the intensity of the use of iron ions in the processes of erythrocytopoiesis (Troshin and Nechaeva, 2007; Ganz, 2013).

The basis of modern prevention of iron deficiency anemia is the intramuscular administration of iron dextran drugs to piglets during the first week of their lives (Karput' and Nikoladze, 2001; Batrakov et al., 2005; Levchenko et al., 2012). Prevention is important because the mortality rate for this pathology is quite high, and, the animals do not realize their own potential productivity after recovery due to the treatment, and the meat loses its nutritional qualities (Andreeva and Serpkov, 2002).

The results of preclinical studies of acute and chronic toxicity of a new compound-iron clathrochelate in rare valence IV were previously reported (Dukhnitsky et al., 2018; Dukhnitsky et al., 2019). During clinical trials of this complex, its antianemic efficacy in piglets was studied (Dukhnitsky et al., 2020). There is a new recent preventive regimen of iron deficiency anemia in piglets based on the results of a study of the antianemic efficacy of iron (IV) clathrochelate for piglets born from sows who were subjected to the administration of this drug during pregnancy. Double injection of 10% iron (IV) clathrochelate solution to pregnant sows 7 and 14 days before the expected farrowing provided a prophylactic effect on iron deficiency anemia in their piglets (Dukhnitsky et al., 2021).

It is known that cyanocobalamin is an antianemic vitamin, required for normal hematopoiesis, with metabolic and hematopoietic functions. In the organism (mainly in the liver), cyanocobalamin is converted into a coenzyme form, adenosylcobalamin, or cobalamide, which is the active form of vitamin B_{12} . Cobalamide promotes the maturation of erythrocytes and participates in the synthesis and accumulation of compounds containing sulfhydryl groups in erythrocytes, which increases their tolerance to hemolysis. It has a positive effect on the function of the liver and nervous system, as well as increasing the ability of tissues to regenerate. Therefore, the next stadium of the present research is to investigate a new scheme for the prevention of iron deficiency anemia in piglets by considering the use of two injectable drugs, the solutions of iron (IV) clathrochelate and cyanocobalamin, for sows during pregnancy.

Thus, the aim of this study was to study the main markers of iron deficiency based on the results of morphological blood parameters of piglets under the administration conditions of the solutions of iron (IV) clathrochelate and cyanocobalamin to the pregnant sows.

MATERIALS AND METHODS

Ethical statement

This study was approved by the Ethical Committee of the National University of Life and Environmental Sciences of Ukraine (Kyiv, Ukraine) and by a mutual (verbal) understanding of the respective farm owners.

Geo-location of the study area

The present study was conducted in the Kyiv district of Ukraine, which is located in the northern part of

Ukraine. The average maximum and minimum temperatures were 25°C and 10°C, respectively. The present study was conducted over a 4-month period from April to July 2021 and the data regarding climatic conditions were retrieved from Regional Meteorological Centre, Kyiv, Ukraine.

Animals and samples

The experiment was carried out on 30 sickling piglets hybrids of Great White and Landrace crossbred pigs aged up to 30 days during the detention period with sows. According to the method of analogue groups, two groups of control (I) and experimental (II, each containing 15 animals) were formed. The duration of the experiment was 30 days. The piglets from 5 sows (3 from each) were selected for the experimental group. During the pregnancy of these sows, 10 ml of 10% solution of iron (IV) clathrochelate and solution of cyanocobalamin (at the rate of 500 mkg active substance per administration recommended by official instructions) were injected intramuscularly twice 7 and 14 days before their expected farrowing.

According to the traditional scheme of prevention of iron deficiency anemia, on the second day of life, the piglets of the control group were administered iron dextran drug uniferon in a dose of 1 ml per animal (200 mg per injection).

Maintenance, feeding, care, and all manipulations o the animals were carried out according to generally accepted norms, taking into account the age and physiological development of animals. The experiment was conducted in accordance with the principles of humanity set out in the directive of the European Community.

The active substance of the drug used in sows to form the experimental group is iron in the rare valence IV and in the form of clathrochelate. It is a macrobicyclic complex in which a metal ion is "packaged" in a nanocapsule, which prevents interaction with the vast majority of reagents, including bioligands, and also shields the metal from other environmental factors. The synthesis of unique iron (IV) clathrochelate compounds was first reported by Tomyn et al. (2017). We have conducted preclinical studies of its acute and chronic toxicity, cumulative properties, and some clinical studies (Dukhnitsky et al., 2019; Dukhnitsky et al., 2020; Dukhnitsky et al., 2021).

The solvent rheopolyglucine we used is a plasma-substituting colloidal solution of dextran (a polymer of glucose) that contains, in addition to dextran, sodium chloride, and water for injections.

The piglets were observed for one month. On the 1, 5, 9, 12, and 30 days of piglets' life of, monitored hemoglobin content and morphological indices of blood were monitored, which was in accordance with the recognized methods.

Statistical analysis

Microsoft excel was used for the descriptive statistics. The results were analyzed statistically using ANOVA followed by Duncan's test to determine the significant differences. For all statistical calculations, the significance was considered as the value of p < 0.05. The correlation was calculated with Pearson's coefficient test.

RESULTS AND DISCUSSION

As a result of the studies, no stillbirths and clinical signs of anemia were observed. During the experiment, there were no pallor of mucous membranes (with a yellowish tinge), tousled hair, dry or wrinkled skin in piglets, as well as accelerated heart and respiratory rates. In all piglets during the experiment, there was no lag in growth, digestive disorders, inactivity, which are the characteristics of anemia. The animals actively sucked sows, naturally occupied the teats with a higher level of lactation, which contributed to their rapid growth and development.

It should be specified that the animals of the experimental group were more active than the piglets of the control group, which was previously confirmed by other researchers who noted a decrease in the motility and duration of suckling sow's milk due to a deficiency of iron in the body of suckling piglets (Pristupa et al., 2013). In addition, on day 30 of the experiment, the body weight of piglets in the experimental group was higher than that of piglets in the control group.

Indicators, such as erythrocyte count, hemoglobin content, and hematocrit (Table 1) were particularly informative for the diagnosis of iron deficiency anemia. The number of erythrocytes in the blood is one of the most important indicators that characterize the blood system. Erythrocytes are formed from reticulocytes after they leave the bone marrow. An increase in the number of erythrocytes in the blood, called erythrocytosis, is one of the characteristic laboratory signs of erythremia and indicates heart and lung disease, and a decrease in the number of erythrocytes is the main criterion for anemia.

Moreover, all researchers conclude that one of the most important complex compounds created by nature is hemoglobin. This is a complex protein that contains a non-protein (prosthetic) group named heme, which, in turn, contains about 4% hemoglobin. Heme is a bioinorganic chelate complex of iron (II) with a tetradentate ligand porphyrin, has a spatial structure. Iron binds to the protein part (globin) in the fifth orbital in heme, and its sixth orbital is free and may contain various low molecular weight ligands. Therefore, its main function includes the transport of oxygen from the lungs to the tissues and the removal of carbon dioxide from the organs. Decreased hemoglobin levels lead to the disruption of all these processes. Proverbially, a sign of anemia is low hemoglobin, and its increase indicates a deficiency of oxygen saturation of tissues, significant loads.

The hematocrit shows the relationship between plasma volume and blood cells, and blood indices characterize the relationship between their hemoglobin and red blood cells saturation according to normal and pathological conditions. The decrease and increase of hematocrit are observed during the anemia and erythremia, respectively.

It is known that blood cells also include platelets and leukocytes. The main function of the platelets is to participate in blood clotting, and an increase in the content of the leukocytes may be a sign of infections (bacterial, viral, and fungal), acute inflammatory processes in organs, traumatic tissue damage, thyroid disease, and acute bleeding, malignant tumors.

Indicator	Day of research	Control	Iron (IV) clathrochelate + cyanocobalamin
Hemoglobin (g / l)	1	81.3 ± 0.62	87.9 ± 3.01
	5	71.8 ± 0.74	$89.8 \pm 4.70^{**}$
	9	79.2 ± 1.60	$55.7 \pm 0.24 **$
	12	70.5 ± 1.99	$51.7 \pm 0.92^{**}$
	30	117.1 ± 1.75	$76.0 \pm 1.58^{**}$
Hematocrit (vol%)	1	31.8 ± 0.64	$27.8 \pm 0.97 *$
	5	30.0 ± 0.13	23.7 ± 0.64 **
	9	31.8 ± 0.64	17.2 ± 0.20 **
	12	32.9 ± 0.51	15.0 ± 0.14 **
	30	40.7 ± 0.62	25.5 ± 0.17 **
Erythrocytes (10 ¹² /L)	1	3.9 ± 0.08	3.8 ± 0.16
	5	3.6 ± 0.13	3.5 ± 0.09
	9	3.8 ± 0.11	3.0 ± 0.01
	12	3.7 ± 0.10	$2.8 \pm 0.02 **$
	30	6.3 ± 0.12	$5.0 \pm 0.07 **$
Leukocytes (10 ⁹ /L)	1	5.3 ± 0.14	5.4 ± 0.41
	5	7.1 ± 0.11	$9.8 \pm 0.12 **$
	9	7.5 ± 0.26	9.9 ± 0.50
	12	7.7 ± 0.24	6.7 ± 0.23
	30	9.8 ± 0.13	9.4 ± 0.31
Plateles (10 ³ /mm ³)	1	391.3 ± 9.94	407.2 ± 29.62
	5	474.2 ± 8.18	521.8 ± 24.56
	9	498.9 ± 5.88	$624.8 \pm 13,70$ **
	12	485.0 ± 9.77	907.5 ± 15.53**
	30	457.5 ± 7.58	450.5 ± 10.17

Table 1. Hemoglobin content, hematocrit, and morphological parameters of piglets' blood under the action of iron and cyanocobalamin

Control group: Uniferon to the piglets, iron (IV) clathrochelate + cyanocobalamin, Experimental group: Iron (IV) clathrochelate, rheopolyglukine + cyanocobalamin to the sows, *p < 0.05, **p < 0.01, differences are likely to be in relation to the control group, $x \pm SE$, n = 15.

According to Table 1, the significantly higher hemoglobin content in the blood of piglets in the experimental group at the first and fifth days of life was respectively by 1.08 and 1.25 (p < 0.05) times, compared to hemoglobin content in the blood of piglets in the control group. In contrast, the hemoglobin content in the blood of piglets in the experimental group was significantly 1.42, 1.36, and 1.54 (p < 0.05) times lower at days 9, 12, and 30, respectively, compared to the control group. This tendency of changes in the hemoglobin content of piglets' blood in the experimental group under the influence of iron (IV) clathrochelate and cyanocobalamin differs slightly from the dynamics under the influence of piglets in the studies (Derkach, 2021), it was noted that the hemoglobin content in the blood of piglets in other periods it did not differ from the control. However, under different prevention schemes in all periods of the study, the content of hemoglobin in the blood of piglets in the control and experimental groups was within physiological values.

During the entire study period, the hematocrit was probably higher in the piglets of the control group, and the highest difference was on days 9 and 12 by 1.85 and 2.19 times, respectively. Such data coincide with previous studies (Derkach, 2021), according to which the hematocrit was probably higher in the control group during the whole period of the study, and the difference was also the highest on days 9 and 12 by 1.7 and 1.9 times, respectively. The findings of the current study indicated that the value of hematocrit in the blood of piglets of the experimental group was within physiological values.

The number of erythrocytes in the blood of piglets of the experimental and control groups on the first and fifth days of life did not differ and was within physiological values. However, in the critical period of manifestation of iron deficiency (on days 9 and 12 of life) the number of erythrocytes was lower in the blood of piglets in the experimental group probably by 1.27 and 1.32 times, compared to the control group. However, on day 30 of the experiment, this difference decreased and amounted to 1.26 times. A similar trend of changes in this indicator was when iron (IV) clathrochelate alone was used for pregnant sows. At the time piglets aged 1, 12, 30, and 60 days, there was no difference between the piglets of the experimental and control groups regarding the number of erythrocytes and it was within physiological values. However, in the critical period of iron deficiency (on days 5-9 of life) this indicator was probably lower in the blood of piglets of the experimental group by 1.2 times, compared to the control group (Derkach, 2021).

It is necessary to emphasize that the results of the current experiments concur with the conclusions of other studies (Levchenko et al., 2012). According to their data, the content of hemoglobin in the blood of piglets 50-70 g/l and the number of erythrocytes up to 2.5-3.0 T/l indicate the presence of iron deficiency anemia in piglets.

The dynamics of changes in the number of leukocytes were similar to the previous studies. More specifically, leukocytes in the blood of piglets of the control and experimental groups were almost the same during days 1-30. On days 5 and 9, the number of leukocytes was higher in the blood of piglets of the experimental group by 1.38 (p < 0.05) and 1.32 times, respectively. On day 12, this indicator was lower by 1.15 times. In the current study addressing the effect of only iron (IV) clathrochelate (Derkach, 2021), the changes in the number of leukocytes were characterized by the fact that on days 5 and 12 of life in the blood of piglets in the experimental group, their rate was higher by 1.2 times than the control.

The number of platelets in the blood of piglets of the experimental group on days 1 and 5 almost did not differ from the number of platelets in the blood of piglets of the control group. However, it respectively increased by 1.25 and 1.87 times on days 9 and 12 (p < 0.05), compared with the control group. According to a previous study, the number of platelets in the blood of piglets of the experimental group differed from that in the blood of animals of the control group only on day 12 and was higher by 1.7 times (Derkach, 2021).

Furthermore, a number of characteristics of erythrocytes and other blood cells (Table 2) were used for the diagnosis of anemia. Thus, average erythrocyte volume (MCV) is an indicator of the presence of microcytosis or macrocytosis of erythrocytes. The average hemoglobin content in the erythrocyte (MCH) is an indicator that is a sign of the presence of normochromic, hypochromic, or hyperchromic anemia. The average concentration of hemoglobin in the erythrocyte (MCHC) is an indicator to diagnose anemia. Erythrocyte distribution width (RDW-CV) is an indicator that evaluates erythrocyte anisocytosis (quantification of erythrocytes by size).

Indicator	Day of research	Control	Iron (IV) clathrochelate + cyanocobalamin
	1	72.4 ± 0.29	73.0 ± 0.83
	5	67.6 ± 0.86	$69.2 \pm 0.55*$
MCV (µm ³)	9	64.0 ± 0.61	56.2 ± 0.59
	12	59.1 ± 0.34	$51.5 \pm 0.40 **$
	30	57.5 ± 0.50	$48.6 \pm 1.01^{**}$
RDW (%)	1	15.2 ± 0.21	$14.4 \pm 0.12*$
	5	16.2 ± 0.22	16.8 ± 0.10
	9	19.0 ± 0.21	31.7 ± 1.38
	12	16.6 ± 0.45	$38.0 \pm 0.31^{**}$
	30	15.3 ± 0.46	$30.8 \pm 0.24 **$
MCH (pg)	1	20.2 ± 0.20	$22.9 \pm 0.43^{**}$
	5	18.4 ± 0.18	$26.7 \pm 0.93^{**}$
	9	18.1 ± 0.20	18.4 ± 0.18
	12	17.2 ± 0.21	16.5 ± 0.26
	30	16.7 ± 0.15	$15.6 \pm 0.23^{**}$
MCHC (%)	1	27.09 ± 0.26	29.5 ± 0.79
	5	28.2 ± 0.28	$38.4 \pm 1.09 **$
	9	28.0 ± 0.26	30.9 ± 1.98
	12	29.1 ± 0.25	$32.7 \pm 0.19 **$
	30	29.0 ± 0.19	$31.4 \pm 0.07 **$
MPV (µm ³)	1	8.4 ± 0.08	9.1 ± 0.14 **
	5	8.0 ± 0.08	8.3 ± 0.19
	9	8.2 ± 0.15	$7.6 \pm 0.04 **$
	12	8.5 ± 0.18	8.9 ± 0.37
	30	8.9 ± 0.06	$7.5 \pm 0.15^{**}$
PDW (%)	1	18.0 ± 0.11	17.8 ± 0.18
	5	18.4 ± 0.20	$18.6 \pm 0.13 **$
	9	17.4 ± 0.19	17.1 ± 0.15**
	12	17.2 ± 0.20	16.9 ± 0.12
	30	17.0 ± 0.18	$16.0 \pm 0.04 **$
PCT (%)	1	0.4 ± 0.02	$0,4 \pm 0.01$
	5	0.4 ± 0.01	$0,4 \pm 0.02$
	9	0.3 ± 0.01	$0,4 \pm 0.02^{**}$
	12	0.3 ± 0.02	$0,3 \pm 0.02$
	30	0.4 ± 0.03	$0.3 \pm 0.01^{**}$

Table 2. Blood indices of piglets under the action of iron and cyanocobalamin

MCV: Mean erythrocytes volume, RDW: Red blood cell distribution width, MCH: Mean corpuscular hemoglobin concentration, MCHC: Mean corpuscular hemoglobin concentration, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Platelet crit, Control group: Uniferon to the piglets, iron (IV) clathrochelate + cyanocobalamin, Experimental group: iron (IV) clathrochelate, rheopolyglukine + cyanocobalamin to the sows; *p < 0.05, **p < 0.01, differences are likely to be in relation to the control group; $x \pm$ Standard error, n = 15.

667

To cite this paper: Derkach I, Dukhnitsky V, Derkach S, Lozoviy V, Kostrub V, Losa Y, Fritsky I, and Plutenko M (2021). Dynamics of Morphological Indicators of Blood of Piglets under the Influence of Iron Clathrochelate Complex and Cyanocobalamin. World Vet. J., 11 (4): 663-669. DOI: https://dx.doi.org/10.54203/scil.2021.wvj83

The average erythrocyte volume in piglets of the experimental group differed most from that of piglets in the control group on day 12, which was lower by 1.15 (p < 0.05) times, while during other experimental periods this indicator did not differ significantly. Similar to the dynamics of changes in the number of erythrocytes, the trend of changes in this indicator was observed in previous studies (Derkach, 2021). In particular, on days 9 and 12, the mean of erythrocyte volume in the piglets of the experimental group was probably lower by 1.3 and 1.2 times, respectively, compared to the control group.

The width of erythrocyte distribution in the blood of piglets of the experimental group initially did not differ from the control during the first five days. However, this parameter was respectively higher by 1.67, 2.29, 2.01 times on days 9, 12, and 30 of the study, compared to that of the control group. In previous studies (Derkach, 2021), the dynamics of the width of the distribution of erythrocytes almost did not differ between the control and experimental groups because this parameter was higher in piglets of the experimental group, slightly on day 5, and already by 1.3 times on day 9, by 2.6 times on day 12, and by 2.0 times on day 30, compared to the control, while almost no different from the control on the 60th day.

The average hemoglobin content in one erythrocyte was higher probably by 1.45 times in the piglets of the experimental group on the fifth day of age. The concentration of hemoglobin in the erythrocytes of piglets in the experimental group differed the most on day 5 and was higher probably by 1.36 times. In previous studies (Derkach, 2021), the dynamics of indicators that characterize the hemoglobin content- the concentration of hemoglobin in erythrocytes and the average hemoglobin content in one erythrocyte did not differ during the study period, this parameter was higher by 1.2 times in piglets of the control group to the same extent in both periods on days 12 and 30.

The mean platelet volume varied during the study period within physiological values, which correlates with previous studies (Derkach, 2021). In particular, when piglets aged 9 and 12 days, this parameter was probably lower by 1.2 times in animals of the experimental group, 1.5 times on day 30, 1.2 times on day 60, compared to the control group. The dynamics of platelet width and platelet crit were similar to previous results of clinical trials of iron (IV) clathrochelate when administered to pregnant sows, in particular in piglets of the experimental group these indicators almost did not differ from those in control animals during the study period and were within physiological values. Finally, literature analysis shows that the number of studies addressing iron in the form of high valences has increased in recent years (Lubianova, 2010; England et al., 2014; Kaplia, 2015). However, the mechanism of its pharmacological effects on the body has not yet been sufficiently studied. Only a small number of scientific works on this topic are available. It should be noted that for the current study was the first research including preclinical and clinical studies of iron in valence IV and in the form of clathrochelate with studying its antianemic effect.

Therefore, the current study aimed to analyze the higher antianemic efficiency of iron (IV) drugs, compared to the traditional Iron dextran drugs. The findings revealed the dynamics of morphological changes in the blood of piglets during 30 days under the influence of iron (IV) clathrochelate in combination with cyanocobalamin and the influence of iron (IV) clathrochelate alone. The peculiarity of the studies was that these drugs were not injected into the suckling piglets, and injected into the pregnant sows in order to prevent iron deficiency anemia in their piglets.

Two injections of 10% solution of iron (IV) clathrochelate and cyanocobalamin to pregnant sows on days 7 and 14 before the expected farrowing provide a prophylactic effect against iron deficiency anemia in the born piglets. The dynamics of changes in erythrocyte count, hemoglobin content, hematocrit, leukocytes and platelets, indices of blood did not differ significantly from the dynamics of these values when using only 10% solution of iron (IV) clathrochelate for pregnant sows.

CONCLUSION

The proposed scheme for the prophylaxis of iron deficiency anemia in piglets, which involves simultaneous intramuscular injections of iron clathrochelate (IV) and cyanocobalamin to pregnant sows is somewhat inferior to the prevention scheme, which provides for intramuscular injections of only iron (IV) clathrochelate, but can be recommended as highly effective. This is confirmed by the results of dynamics of morphological indicators of blood of piglets under the influence iron clathrochelate complex and cyanocobalamin. We have established the indicators such as erythrocyte count, hemoglobin content, hematocrit, leukocytes and platelets, indices of blood are within physiological limits. Therefore, these preventive measures can be applied at pig farms.

DECLARATION

Competing interests

The authors declare that they have no competing interests.

Authors' contribution

All authors contributed equally in present study.

Ethical consideration

Ethical issues (including plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy) have been checked by the authors.

REFERENCES

Andreeva A, and Serpkov A (2002). Kak predotvratiť alimentarnuju anemiju porosjat. Zhivotnovodstva, 2: 87.

Batrakov A, Travkin O, and Jakovleva E (2005). Profilaktika alimentarnoj anemii u. Veterinarija, 12: 44-45.

- Bonkovsky S, and Herbert L (1991). Iron and the Liver. The American Journal of the Medical Sciences, 301(1): 32-43. DOI: https://www.doi.org/10.1097/00000441-199101000-00006
- Derkach I (2021). Comparative efficacy of iron-containing drugs in the prevention of iron deficiency anemia in piglets. NV LNU of Veterinary Medicine and Biotechnology. Series: Veterinary Sciences, 23(102): 66-71. DOI: https://www.doi.org/10.32718/nvlvet10210
- Dukhnitsky V, Derkach I, Derkach S, Plutenko M, Fritsky I, and Derkach S (2018). Determination of the accumulative toxicity parameters of iron (IV) on white mice. Ukrainian Journal of Ecology, 8(2): 308-312. DOI: <u>https://www.doi.org/10.15421/2018_343</u>
- Dukhnitsky V, Derkach I, Plutenko M, Fritsky I, and Derkach S (2019). Acute toxicity of the iron clathrochelate complexes. Regulatory Mechanisms in Biosystems, 10(3): 276-279. DOI: <u>https://www.doi.org/10.15421/021942</u>
- Dukhnitsky VB, Kalachniuk LH, Derkach IM, Derkach SS, Plutenko MO, and Fritsky IO (2020). Iron(IV) hexahydrazide clathrochelate complexes: The chronic toxicity study. Ukrainian Journal of Ecology, 9(3): 18-23. DOI: <u>https://www.doi.org/10.15421/2020 3</u>
- Dukhnitsky V, Derkach I, Derkach S, Lozovyi V, Kostrub V, Losa Yu, Fritsky I, and Plutenko M (2021). Bilkovyi spektr syrovatky krovi porosiat za vplyvu preparativ ferumu. Visnyk Poltavskoi Derzhavnoi Ahrarnoi Akademii, 1: 101. DOI: <u>https://www.doi.org/10.31210/visnyk2021.01.31</u>
- England J, Bigelow O, Katherine M, Heuvelen V, Farquhar E, Martinho M, Meier K, Frisch J, Münck E, and Que L (2014). An ultrastable oxoiron (IV) complex and its blue conjugate base. Chemical Science, 5: 1204-1215. DOI: <u>https://www.doi.org/10.1039/C3SC52755G</u>
- Ganz T (2013). Systemic iron homeostasis. Physiological Reviews, 93(4): 1721-1741. DOI: https://www.doi.org/10.1152/physrev.00008
- Gasanov AS, Amiov DR, Muhutdinova DM, Ovsjannikov AP, Churna ZG, and Shamsutdinova NV (2020). Anemia and drugs used in its treatment and prevention. Available at: <u>https://kazanveterinary.ru/en/</u>
- Karput' IM, and Nikoladze MG (2001). Iron metabolism in healthy and sick piglets with alimentary anemia. Bulletin of the Academy of Agrarian Sciences of the Republic of Belarus, 4: 73-77.
- Karput' IM and Nikoladze MG (2003). Diagnosis and prevention of alimentary anemia of piglets. Veterinary Medicine, 4: 34-37.
- Kaplia AA (2015). The influence of iron ions on ATP-hydrolases activity of cell membranes of rat colon smooth muscle and kidney. Ukrainian Biochemical Journal, 87(1): 83-90. DOI: <u>https://www.doi.org/10.15407/ubj87.01.083</u>
- Killip S, and Bennett M (2008). Iron Deficiency Anemia American Family Physician, 78(8): 671-678.
- Lipiński P, Styś A, and Starzyński R (2013). Molecular insights into the regulation of iron metabolism during the prenatal and early postnatal periods. Cellular and Molecular Life Sciences, 70(1): 23-38. DOI: <u>https://www.doi.org/10.1007/s00018-012-1018-1</u>
- Levchenko VI, Kondrakhin IP, and Vlizlo VV (2012). Vnutrishni khvoroby tvaryn. Chastyna 1. Bila Tserkva, BDAU, pp. 25-30.
- Leyshon BJ, Radlowski EC, Mudd AT, Steelman AJ, and Johnson RW (2016). Postnatal Iron Deficiency Alters Brain Development in Piglets. The Journal of Nutrition, 146(7): 1420-1427. DOI: <u>https://www.doi.org/10.3945/jn.115.223636</u>
- Lubianova IP (2010). Modern concepts about the metabolism of iron from the position of the occupational pathologist. Actual Problems of Transport Medicine, 20(2): 47-57. Available at: http://dspace.nbuv.gov.ua/handle/123456789/23140
- Pristupa TI, Danchuk VV, Danchuk OV, and Kaplunenko VH (2013). Motor activity of suckling piglets with the introduction of iron compounds. Scientific Bulletin of Veterinary Medicine, 12(107): 60-63. Available at: <u>http://nbuv.gov.ua/UJRN/nvvm 2013_12_18</u>
- Sidorkin V, Gavrish V, Egunova A, and Ubiraev V (2007). Diseases of swine. Akvarium print, Moskwa, pp. 50-53.
- Svoboda M, and Drabek J (2005). Iron deficiency in suckling piglets: Etiology, clinical aspects and diagnosis. Folia Veterinaria, 49: 104-111. Available at: <u>https://www.uvlf.sk/document/folia-veterinaria-volume-49-issue-2.pdf#page=47</u>
- Tomyn S, Shylin SI, Bykov D, Ksenofontov V, Gumienna-Kontecka E, Bon V, and Fritsky IO (2017). Indefinitely stable iron (IV) cage complexes formed in water by air oxidation. Nature Communications, 81: 1-8. Available at: https://www.nature.com/articles/ncomms14099
- Troshin AN, and Nechaeva AV (2007). Obtaining a ferromagnetic drug and its prophylactic efficacy in iron deficiency anemia in animals. Scientific Journal of KubSAU, 28(4): 33-42. Available at: <u>http://ej.kubagro.ru/2007/04/pdf/06.pdf</u>

Zharov AV and Zharov JuP (2012). Patologija obmena veshhestv u vysokoproduktivnyh zhivotnyh. Veterinarija, 9: 46-50.

Walter T, Olivares M, Pizarro F, and Muñoz C (1997). Iron, Anemia, and Infection. Nutrition Reviews, 55(4): 111-124. DOI: https://www.doi.org/10.1111/j.1753-4887.1997.tb06462.x