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PHYSIOLOGICAL AND BIOCHEMICAL RECOVERY MECHANISMS OF THE CHICKEN ORGANISM DURING TREATMENT AGAINST DERMANYSSOSIS WITH COMBINED IVERBUTAN

Indyuhova E. N.[1], Arisov M. V.[1], Maximov V. I.[2], Azarnova T. O.[2]

[1]All-Russian Scientific Research Institute for Fundamental and Applied Parasitology of Animals and Plant – a branch of the Federal State Budget Scientific Institution "Federal Scientific Centre VIEV", Moscow, Russian Federation
[2]Federal State Budgetary Educational Institution of Higher Education "Moscow State Academy of Veterinary Medicine and Biotechnology – MVA named after K. I. Skryabin", Moscow, Russian Federation
E-mail: indyuhova@vniigis.ru

The study of implemented physiological and biochemical recovery mechanisms of the animal organism associated with treatment against ectoparasite infections is an up-to-date sector of modern physiology together with biochemistry and parasitology. Chickens with dermanyssosis are found to have significant homeostatic disruption which is due to excessively intensified lipid peroxidation processes associated with depleted antioxidant activity of blood serum, changes in the endocrine system, and deep rearrangements in metabolic processes and in the blood system. A high 95.5 % therapeutic efficacy was found for the Ivermectin-Butaphosphan-based drug. When it was fed to chickens, we noted all reported blood parameters normalized in a very short time. The biostimulant not only expands the range, but also increases the efficiency of implemented adaptive and compensatory capabilities of the chicken organism during treatment.
Keywords: recovery mechanisms, homeostasis, stress factor, Ivermectin, Butaphosphan, chickens.

INTRODUCTION

The study of implemented physiological and biochemical recovery mechanisms of the animal body associated with the treatment against ectoparasite infections is an up-to-date sector of modern physiology together with biochemistry and parasitology. At the same time, in view of morphophysiological, physiological and biochemical parameters of the chickens' blood, it is possible to predict changes in the metabolic process intensity, and with it, homeostatic disruption of the animal body. The stated above needs to be prevented and corrected, that is, treated. Generalized features of the physiological, biochemical, and ethological status of birds in the industrial sector during treatment against dermanyssosis will allow us to evaluate the efficacy of the new drug Iverbutan based on antiparasitic component Ivermectin and biostimulant Butaphosphan. It can be assumed that combined use of these components will affect the recovery rate of physiological and biochemical functions in animals during treatment of parasitic diseases.

The mode of action of Ivermectin is in its effect on the flow rate of chloride ions through membranes of nerve and muscle cells of the parasite. The main targets are glutamate-sensitive chloride channels, and gamma-aminobutyric acid receptors. Changed

flow of chlorine ions disrupts the conduction of nerve impulses, which leads to paralysis and death of the parasite. The study by X. Xu et al. (2019) found that with a single oral administration of the Ivermectin-based drug in response to experimental infection of chickens with *Dermanyssus gallinae*, reduced reproductive potential and impaired blood digestion were observed in mites. All this evidences a disorder of reproduction processes in poultry red mite population. [1].

After oral administration to birds, Ivermectin is well absorbed in the gastrointestinal tract, enters the systemic circulation, reaches a maximum concentration in the blood after 1 hour and is evenly distributed in organs and tissues. Ivermectin is excreted from the poultry organism with droppings.

The second component of the drug is biostimulant Butaphosphan, which is a source of phosphate. It is known that these groups are required for the synthesis of nucleotides and macroergs [2–5]. This biostimulant is well tolerated [6], does not accumulate in the body, maintains carbohydrate energy metabolism, protein metabolism, and lipid metabolism in the body, activates the immune system, and boosts recovery after pathologies of various nature [7–9].

Previously, pharmaco toxicological properties of the described combined drug [10, 11], and its tolerability in chickens were studied [12].

In this regard, the purpose of the research is to evaluate therapeutic efficacy of combined Iverbutan against dermanyssosis in chickens and to characterize physiological and biochemical recovery mechanisms of their organism during treatment.

MATERIALS AND METHODS

The research was conducted on a Nizhny Novgorod Region poultry farm (Russia). The farm was free from infectious diseases.

Regional climatic characteristics are as follows: the climate is moderately continental; the average air temperature is 5.9 °C during the year; average annual atmospheric pressure is 748 mm Hg, and relative humidity is 74 %. The average wind speed is 1.7 m/s. The total average annual precipitation is 386.95 mm.

Based on the results of the parasitological survey [13] in the poultry buildings, two shops were selected where Hy-Line chickens were kept. The first shop with replacement young chickens of the said cross, aged 70 days, with dermanyssosis was an experimental group. At the same time, a decreased body weight, pale mucous membranes, comb and earrings, and loss of plumage were observed in the chickens. The infection intensity was 11.7±1.05 specimens/bird. Ectoparasites were found on the poultry, and in other sites, namely, cage equipment gaps, the floor, etc. The second poultry building with healthy birds (replacement young chickens) aged 70 days was a control group.

The feeding level and keeping conditions of the chickens from the experimental and control groups corresponded to the applicable zootechnical standards. The replacement young birds were kept in triple-deck cages.

The experimental birds received Iverbutan orally by a group method with drinking water at a daily dose of 400 μg of Ivermectin per 1 kg of the bird weight, which corresponds to 1 mL/L of drinking water. This drug contains 0.4 % of Ivermectin and 10.0 % of Butaphosphan as active substances, as well as excipients.

To prepare a therapeutic solution, Iverbutan in a single dose as calculated on the number of the treated birds is diluted in ¼ of the daily intake of drinking water. The prepared therapeutic solution is fed against dermanyssosis three times: twice with a 24-hour interval, and repeated single treatment of the chickens was given at 14 days. The drug efficacy was recorded 14 days after re-treatment. The treatment effectiveness was evaluated by the ratio expressed as a percentage between the number of ectoparasites in the experimental group before and after treatment. At the same time, the physiological and ethological status of the birds from two groups was monitored. The control chickens did not receive the drug.

Blood was taken from the chickens before Iverbutan, and at 10 and 20 days after re-treatment with the drug. Blood was taken individually from the axillary vein of 10 randomly selected birds from the experimental and control groups, into sterile test tubes. The down feathers and feathers were preliminarily pulled out, and the blood sampling site was disinfected with 70 % ethyl alcohol.

Morphophysiological, and physiological and biochemical blood parameters were determined according to common methods. [14]. The research used homeostatic boundaries for the above blood parameters in chickens of egg breeds according to the data from I. P. Kondrakhin (2004) [14] and I. V. Nasonov et al. (2014) [15].

Methods for determining ethological characteristics in the chickens were observation with recording their motor activity, and evaluation of the chickens' reactions to various stimuli [16].

All bird manipulations were performed in accordance with international regulatory requirements [17, 18].

Digital material was processed statistically using a Student's t-test with the Microsoft Excel. The results were considered significant at $P \leq 0.05$ (* – $P<0.05$; ** – $P<0.01$; *** – $P<0.001$).

RESULTS AND DISCUSSION

It is known that a complex of deep physiological and biochemical changes develops in the animal organism with parasitosis which is accompanied by oxidative stress, endocrine changes, impaired blood morphophysiology, inactivated physiological compensatory and adaptive reactions, etc. [19–23]. This obviously creates unfavorable conditions for further growth and development of individuals, realization of their productive and reproductive potential, especially in the industrial sector. Therefore, a complex of therapeutic and preventive measures is required aimed at correcting the physiological and biochemical status of the birds, especially in case of parasitic diseases.

Thus, single specimens of gamasid mites were found on the experimental birds (infection intensity, 0.53±0.15 specimens/bird) at two weeks after re-treatment with Iverbutan. The drug efficacy level reached 95.5 %, which indicates its high therapeutic efficacy. The control birds remained free from ectoparasites.

In response to various environmental factors, certain physiological and biochemical mechanisms are activated that unite functional systems. These systems provide the body adaptation to new conditions by moving to a new level of functioning and maintaining homeostasis [24, 25]. In the industrial sector, poultry is exposed to many extreme stress

factors. Biological stress factors (viruses, parasite agents, etc.) constitute a special group among them. In the presented study, *D. gallinae* (an aggressive haematophagous ectoparasite) is a stress factor of extreme strength [26].

The dynamics in the physiological and biochemical, and morphophysiological blood parameters of the Hy-Line chickens during dermanyssosis treatment with Iverbutan is presented in the Table below.

It is known that the regulation of all physiological and biochemical processes, and the adaptability of the body to changing environmental conditions pertains to the neuroendocrine system. Thus, the endocrine glands produce a wide range of hormones that are responsible for such processes [27]. The chickens were found to have functional stress of the adrenal cortex during a developed stress reaction, which was expressed in increased corticosterone and cortisol secretion that caused metabolic process alteration, particularly, they stimulated the protein decay in muscles, the conversion of amino acids and glycerol into glucose, as well as the synthesis of gluconeogenetic enzymes [28]. The presented study considered cortisol content in the blood of the chickens. On day 10 after the drug administered to the test chickens, a decreased cortisol concentration was registered in the blood as compared to the baseline of the hormone in question. Thus, its concentration on days 10 and 20 was 0.43±0.02 mcg/dL versus 0.31±0.02 mcg/dL in the control ($P<0.01$) and 0.28±0.02 mcg/dL versus 0.27±0.02 mcg/dL in the control, respectively. The detected changes in the concentration of the stress-associated hormone in the replacement young experimental birds within the above periods may be associated with the stress response decrement in their body [29]. The described changes in its concentration may also be associated with Butaphosphan, which is consistent with the evidence base by F. J. van der Staay et al. (2007) [30].

Another group of hormones that provides the adaptation of the body to extreme environmental stimuli is iodine-containing thyroid hormones. They are necessary for the functioning of almost all organs and tissues; thyroid hormones are involved in various physiological and biochemical processes; they regulate metabolic process intensity, oxygen consumption by tissues, thermogenesis, energy balance, bone tissue metabolism, and nervous system development, affect the exchange of glycosaminoglycans and proteoglycans in the connective tissue, contribute to the effects of somatotropic hormone, and stimulate erythropoiesis, testis and ovarian cell differentiation, oocyte steroidogenesis and maturation, the growth of cartilage tissue, plumage, etc. We determined the concentration of triiodothyronine in the chickens' blood as the most active form of thyroid hormones [31]. During dermanyssosis treatment, a 12.2 % ($P<0.05$) and 11.8 % increase in free triiodothyronine was found at 10 and 20 days respectively versus the control.

It is known that possible behavioral reactions in animals can be assessed by the functional activity of the endocrine glands. The thyroid gland activity has a direct impact on behavior [32]. Thus, aggressiveness, excessive sensitivity to various environmental stimuli, anxiety, and excessive vocalization were recorded in the chickens with dermanyssosis as compared with the behavior of the control birds. At 20 days after re-treatment with the drug, the ethological status in the experimental birds did not differ from the control.

Changes in morphophysiological, physiological and biochemical blood parameters and ethological status in the experimental chickens (see Table) indicate that the described free triiodothyronine concentrations are physiologically optimal for the studied birds.

Obviously, increased endocrine activity of the thyroid gland in the experimental chickens affected the RBC parameters. The analysis of these data makes it possible to objectively assess possible changes in the metabolic process intensity, and the extent of the body defenses, and to characterize the physiological state of the birds as a whole. Before treatment, the test birds showed a decrease in erythrocytes by 15.1 % ($P<0.001$), and hemoglobin concentration by 14.2 % ($P<0.001$) versus the healthy birds. Significant changes in the RBC parameters in the chickens are due to daily blood loss during the poultry red mite parasitism and the high sensitivity of erythrocytes to oxidative stress [33]. At the same time, the acid-base balance is disregulated in the birds, and the metabolic processes slow down leading to decreased synthesis of macroergs. During treatment, we can observe activated erythropoiesis, a positive upward trend in erythrocytes and hemoglobin concentration. Thus, 20 days after the repeated feeding of Iverbutan to the chickens, an increase in erythrocytes and hemoglobin was found versus their baseline parameters. The described changes are obviously due to adequate activation of the thyroid gland function that produces thyroid hormones. Thus, after treatment on day 20, an 11.8 % increase in free triiodothyronine was detected in the experimental chickens' blood versus the control group. This causes the stimulated erythropoietin synthesis and, accordingly, the maturation of erythrocytes in the red bone marrow [34]. Previously, we found that the erythropoietin concentration was 3.9 times lower ($P < 0.001$) in hens of egg breeds during the *D. gallinae* parasitism versus the healthy birds [20].

In addition, thyroid hormones stimulate the immune function. Before treatment, the chickens showed a decrease in leucocytes by 21.1 % ($P<0.01$) versus the control. Along with this, the following was found in the leucogram of the experimental birds: a decrease in eosinophiles by 3.6 ($P<0.001$), monocytes, by 1.4 ($P<0.01$), basophiles, by 1.8 ($P<0.05$) and pseudoeosinophiles, by 7.7 % ($P<0.01$), and an increased percentage of lymphocytes by 16.3 % ($P<0.001$) versus the control. However, pseudoeosinophiles, monocytes and basophiles were within the lower values of the physiological range [14]. The described changes in the leucogram may be due to stress response chronization, in particular, the long-term effect of glucocorticoids on white blood cells in the chickens [35]. Corticosteroid hormones are known to accelerate eosinophile apoptosis [36]. On day 10 and 20 of the study, normalized number of leucocytes and the white blood cell ratio were detected in the blood of the experimental chickens. Thus, on day 20 after treatment, the number of leucocytes in the experimental chickens' blood was $20.30 \pm 0.63 \times 10^9$/L versus $19.20 \pm 0.79 \times 10^9$/L in the control. Many studies have noted that Butaphosphan optimizes the immune function in animals [7, 8], and stimulates nonspecific resistance [37].

Thus, during treatment with Iverbutan, a positive upward trend in total protein can be observed in the chickens' blood. The baseline of this parameter was significantly lower than the control figures by 12.9 % ($P<0.001$). On day 20 post-treatment, its level in the experimental chickens was 48.97 ± 0.54 g/L versus 49.93 ± 0.55 g/L in the control. The described changes in the total protein are possibly due to an increase in free triiodothyronine in the experimental chickens. It is known that the birds' metabolic

processes and growth intensity positively correlate with the concentration of thyroid hormones in the blood which stimulate anabolic processes in the animal body [34]. The stated above causes a positive growth in total protein in the experimental chickens during treatment, which is required to maintain the body weight for the implementation of the productive potential of the individual.

It can be noted that there is a stable increase in albumins in the experimental chickens during the entire research. This group of proteins maintains oncotic pressure of the blood plasma in the animal organism, forms a reserve of free amino acids and performs a transport function (transfer of some hormones, including thyroid hormones, vitamins, free fatty acids, etc.). The full implementation of the above functions of albumins is especially important in the recovery period.

In the animal organism, all types of metabolism are directly interacted with each other. The transformations of metabolic waste-products of carbohydrates, proteins and lipids are interconnected and interdependent. At 20 days after the triple treatment with the drug, an increased alanine aminotransferase and aspartate aminotransferase activity by 11.8 % ($P<0.01$) and by 1.9 % (within the reference range) was observed in the chickens' blood, respectively, versus the control. The observed changes in the enzyme activity obviously contribute to increasing the potential and efficiency of communication between carbohydrate and protein metabolisms, which is especially important for timely implementation of compensatory reactions as the central components of adaptation mechanisms in the experimental chickens. In particular, alanine aminotransferase supports functioning of the glucose-alanine shunt, and aspartate aminotransferase supports the ingress of substrates into the tricarboxylic acid cycle [38].

It should be noted that enzymes are actively involved in the adaptation processes to various stress factors. Thus, an increased alkaline phosphatase activity within the reference range evidences the boost of carbohydrate energy metabolism, including through a glucose-alanine shunt [39]. At 10 and 20 days after the triple treatment, the chickens showed an upward trend in the alkaline phosphatase activity by 3.6 % and 6.8 %, respectively, versus the control. The stated changes in enzyme activity may also be partly associated with more intensive growth of bone tissue [40]. The latter is associated with increased secretion of triiodothyronine in the experimental chickens.

It is known that muscle tissue is the main depot of amino acids that are actively involved in maintaining gluconeogenesis in various critical body conditions. Previously, in our studies, we considered the creatinine concentration in the blood of chickens with dermanyssosis as a nonspecific marker of muscle dystrophy that develops under the influence of long-term high concentrations of glucocorticoids [41]. In the presented study, the creatinine concentration and the creatine phosphokinase activity in the experimental chickens tend to decrease versus these pre-treatment parameters. At 20 days after the triple treatment, the creatinine concentration was 35.66 ± 0.84 μmol/L versus 37.02±1.02 μmol/L in the control, and the activity of creatine phosphokinase was 1,758.1 ± 51.19 U/L versus 1,801.79 ± 45.18 U/L in the control.

In the experimental chickens, intensified lipid metabolism can be observed during treatment. In case of dermanyssosis, profound changes are observed in lipid metabolism of the chickens, in particular, lipase activity increases by 1.3 ($P<0.01$), and cholesterol

decreases by 1.4 (P<0.001) and triglycerides by 22.0 % (P<0.001) versus the healthy birds. Cholesterol and triglycerides in the experimental chickens were within the lower values of the physiological range. The described lipid metabolism profile indicates a trend towards the depletion of energy reserves, triglycerides. Their post-treatment cholesterol concentration tended to increase; it was 3.18 ± 0.05 mmol/L versus 3.37 ± 0.07 mmol/L in the control on day 20 of the study. This obviously causes an increase in the cholesterol synthesis rate and optimization of its consumption for producing steroid hormones. Perhaps, this is to a greater extent for the synthesis of reproductive hormones required to implement the productive and reproductive potential of individuals [9], especially after an extreme stress factor. Also, a positive trend in triglycerides was detected in the experimental chickens' blood: pre-treatment triglycerides were 4.89 ± 0.06 mmol/L versus 6.27 ± 0.12 mmol/L in the control (P<0.001), and post-treatment triglycerides were 6.40 ± 0.09 mmol/L versus 6.36 ± 0.10 mmol/L in the control. These changes evidence optimized energy processes in terms of adequate consumption of triglycerides [42]. After treatment, the representatives from the experimental group showed a decrease in lipase activity versus the control values.

Glucose is the most important carbohydrate required for the normal physiological processes in the body. The chickens with dermanyssosis were found to have a significant increase in glucose by 8.6 % (P<0.05), and a decrease in total protein by 12.9 % (P<0.001) and triglycerides by 22.0 % (P<0.001) versus the control. The stated above is obviously due to activated gluconeogenesis in response to high cortisol concentrations in the blood of the experimental chickens (pre-treatment). This can also be considered as a pronounced compensatory function [22]. The glucose concentration in the experimental chickens' blood during treatment tended to increase (within the reference range). Additionally, this monosaccharide is a key source of energy which is especially needed by the organism in the recovery phase. As a result of the complete oxidation of glucose, the body receives necessary energy in the form of high-energy phosphorus compounds (ATP and GTP) for various functions. The comparison of pre- and post-treatment carbohydrate energy metabolism indicators evidences its intensification versus the control.

During the entire research, increased α-amylase activity was detected in the blood of the experimental chickens versus the control. Thus, the activity of such enzyme on day 10 and 20 post-treatment was higher by 1.4 (P<0.001) and 1.3 (P<0.01) versus the control. This confirms the intensification of carbohydrate energy metabolism in the experimental chickens.

It is known that thyroid hormones have a pronounced calorigenic effect increasing the oxygen uptake by tissues. The stated above obviously affects lactate dehydrogenase [43]. On day 10 after treatment, the lactate dehydrogenase activity which characterizes anaerobic glycolysis intensity [44] decreases sharply in the chickens compared to the baseline (pre-treatment, 1,524.99 ± 62.68 U/L versus 1,053.47 ± 50.45 U/L in the control, P<0.001). On day 20, this enzyme activity did not differ significantly from the control group (1,043.04 ± 43.30 U/L versus 1,078.04 ± 50.21 U/L in the control). The described changes in lactate dehydrogenase also indicate a tendency to restoration of oxygen supply to tissues due to normalized red blood parameters in the studied birds during the specified period.

It is known that oxidative stress affects the metabolic processes as a result of inactivated enzymes and hormones, and modification of proteins and lipids, etc. [45].

According to the molecular theory of the stress response development due to hypoxia of various nature, the mitochondrial respiratory chain functionality is disrupted and, accordingly, free radical processes and hypoenergetic states are initiated. It is known that stimulation of free radical oxidation leads to a change in the structure and functions of various proteins, lipids and other biological molecules, which subsequently results in initiation and development of inflammatory, allergic and autoimmune processes in the body. The main target for free radicals is polyunsaturated fatty acids that are part of the bilipid membrane scaffold. The stated above leads to activated lipid peroxidation whose mechanism is of a chain nature.

A detailed analysis of lipid peroxidation products determined intensified lipid peroxidation processes in the experimental chickens during the *D. gallinae* parasitism. Thus, the experimental chickens were found to have an increase in lipids with isolated double bonds by 2.3 ($P<0.001$), with diene conjugates by 2.1 ($P<0.001$), triene conjugates by 2.4 ($P<0.001$), oxodiene conjugates by 1.7 ($P<0.01$) and with Schiff's bases by 2.5 ($P<0.001$) versus the control. Additionally, a significant decrease in the antioxidant activity of blood serum by 18.1 % ($P<0.01$) was found in the chickens before treatment as compared with the healthy chickens. This evidences the development of oxidative stress in the chickens in response to stress exposure, the *D. gallinae* parasitism. It is known that even a partial modification of the structural elements of membranes associated with abnormal lipid peroxidation causes a whole range of changes that negatively affect their functionality: increased microviscosity, permeability, changed surface charge, inactivated membrane enzymes, disrupted functional state of membrane receptor complexes, etc. [46]. At the same time, excessively accumulated lipid peroxidation products lead to systemic damage to cellular structures, and the intensive formation of the end products of lipid peroxidation (Schiff's bases) is a sign of irreversible structural changes in cell membranes [47].

At 10 days after treatment, the representatives of the experimental group showed increased antioxidant activity of blood serum versus the baseline (60.10 ± 0.90 % versus 57.90 ± 0.98 % in the control). Further a slight decrease in this consolidated figure was observed (56.0 ± 1.12 % versus 59.0 ± 1.20 % in the control) on day 20 of the study. The studies by F. S. Guimarães et al. (2013) found that the Butaphosphan- and Cyanocobalamin-based drug showed an optimization of the antioxidant system in cattle [48]. The uneven increase in the antioxidant activity of blood serum in the experimental chickens may be associated with antioxidant homeostasis restoration after the extreme stress factor. Additionally, the chickens showed a post-treatment tendency to a decrease in all previously described lipid peroxidation products versus their baseline concentration (pre-treatment).

It is important to note the influence of hormonal status on the antioxidant system activity of the body. Thus, thyroid hormones have antioxidant activity due to phenolic groups in their molecules [49]. This may be partly due to inhibited excessive intensification of lipid peroxidation in the chickens during treatment.

An analysis of mineral metabolism parameters allows us to observe a slight upward trend in the phosphorus concentration in the birds' blood. Thus, before treatment, and 10 and 20 days after the triple administration, this microelement values in the chickens' blood were 2.16 ± 0.02 mmol/L versus 2.24 ± 0.03 mmol/L in the control, 2.31 ± 0.03 mmol/L versus 2.24 ± 0.03 mmol/L in the control, and 2.29±0.02 mmol/L versus 2.34±0.02 mmol/L

in the control, respectively. Additionally, no significant changes were found in the discussed microelement as compared with the control values. The differences between the groups for calcium concentration in the chickens' blood were insignificant and unreliable.

The chickens' body in the recovery phase after pathologies of various nature needs additional energy resources [41]. A stabilized level of tissue oxygenation can be observed in the chickens, which is confirmed by normalized red blood parameters, decreased lactate dehydrogenase and, accordingly, decreased proportion of oxygen-free glycolysis. The intensified energy metabolism [8, 5, 50], as well as the redistributed energy resources due to stress response decrement in the experimental chickens allows optimizing their physiological and biochemical status, particularly, activating and expanding adaptive and compensatory capabilities of the organism. Obviously, the activation of the thyroid gland depends on these changes in energy metabolism. The above changes in the physiological and biochemical status in the experimental chickens are probably associated with possible involvement of Butaphosphan in phosphorylation reactions needed for the synthesis of nucleotides, in particular those related to macroergs (ATP and GTP) [5, 8, 9, 51] and the activation of some metabolic substrates (glucose, glycerol, etc.). The stated above obviously determines its biostimulating properties and involvement in a number of the described positive biological effects.

Pronounced changes in homeostatic parameters in the chickens during dermanyssosis treatment with a combined drug containing Butaphosphan create prerequisites for boosted recovery of the organism. The stated above was also reflected in other studies [30, 50].

Table

Morphophysiological, and physiological and biochemical blood parameters of the Hy-Line chickens, (n=10)

Indicator	Study Period	Experimental group	Control group
Morphophysiological blood values			
Erythrocytes, $\times 10^{12}$/L	Pre-Treatment	2.30 ± 0.05***	2.71 ± 0.06
	10 days after triple treatment	2.60 ± 0.05	2.80 ± 0.07
	20 days after triple treatment	2.80 ± 0.04	2.75 ± 0.05
Hemoglobin, g/L	Pre-Treatment	106.60 ± 1.72***	124.30 ± 1.28
	10 days after triple treatment	115.40 ±1.45***	123.60 ±0.43
	20 days after triple treatment	125.0 ± 0.37	125.50 ± 0.65
Leucocytes, $\times 10^{9}$/L	Pre-Treatment	16.10 ± 0.48**	20.40 ± 0.65
	10 days after triple treatment	19.30 ± 0.58	19.80 ± 0.77
	20 days after triple treatment	20.30 ± 0.63	19.20 ± 0.79
Leucogram, %			
Eosinophiles, %	Pre-Treatment	1.90 ± 0.31***	6.80 ± 0.25
	10 days after triple treatment	5.50 ± 0.34*	6.80 ± 0.29
	20 days after triple treatment	7.0 ± 0.33	7.30 ± 0.26

Continued Table

Monocytes, %	Pre-Treatment	4.10 ± 0.28**	5.70 ± 0.21
	10 days after triple treatment	5.40 ± 0.31	6.10 ± 0.38
	20 days after triple treatment	6.50 ± 0.48	5.90 ± 0.43
Basophiles, %	Pre-Treatment	1.20 ± 0.29*	2.10 ± 0.23
	10 days after triple treatment	1.30 ± 0.26	1.90 ± 0,23
	20 days after triple treatment	1.80 ± 0.25	1.70 ± 0.21
Lymphocytes, %	Pre-Treatment	67.80 ± 0.57***	58.30 ± 0.47
	10 days after triple treatment	58.10 ± 0.31	57.0 ± 0.70
	20 days after triple treatment	58.30 ± 0.80	57.60 ± 0.78
Pseudoeosinophiles, %	Pre-Treatment	25.0 ± 0.37**	27.10 ± 0.38
	10 days after triple treatment	29.70 ± 0.72	28.20 ± 0.42
	20 days after triple treatment	26.40 ± 0.45	27.50 ± 0.40
Physiological and biochemical blood parameters			
Total Protein, g/L	Pre-Treatment	42.14 ± 0.33***	48.40 ± 0.59
	10 days after triple treatment	44.06 ± 0.37***	48.80 ± 0.47
	20 days after triple treatment	48.97 ± 0.54	49.93 ± 0.55
Albumins, g/L	Pre-Treatment	19.05 ± 0.48***	25.87 ± 0.39
	10 days after triple treatment	23.42 ± 0.22***	25.96 ± 0.32
	20 days after triple treatment	25.95 ± 0.27	26.47 ± 0.35
Globulins, g/L	Pre-Treatment	23.09 ± 0.32	22.53 ± 0.26
	10 days after triple treatment	20.64 ± 0.18***	22.84 ± 0.23
	20 days after triple treatment	23.02 ± 0.31	23.46 ± 0.23
Alanine Aminotransferase, U/L	Pre-Treatment	12.17 ± 0.44***	16.22 ± 0.60
	10 days after triple treatment	15.89 ± 0.45	15.32 ± 0.37
	20 days after triple treatment	18.11 ± 0.31**	16.20 ± 0.35
Aspartate Aminotransferase, U/L	Pre-Treatment	170.47 ± 3.25**	191.83 ± 3.92
	10 days after triple treatment	190.04 ± 4.29	197.63 ±3.29
	20 days after triple treatment	195.40 ± 2.85	191.84 ±3.57
Alkaline Phosphatase, U/L	Pre-Treatment	534.38 ± 14.33	548.68 ± 18.78
	10 days after triple treatment	556.65 ± 13.35	537.48 ± 16.32
	20 days after triple treatment	575.01 ± 12.98	538.45 ± 12.10
Creatinine, μmol/L	Pre-Treatment	41.85 ± 0.80**	36.57 ± 0.70
	10 days after triple treatment	37.20 ± 1.01	35.01 ± 0.97
	20 days after triple treatment	35.66 ± 0.84	37.02 ± 1.02
Creatinphosphokinase, U/L	Pre-Treatment	2187.71 ± 51.70*	1971.53±59.35
	10 days after triple treatment	2022.70 ± 56.80	1875.65±63.23
	20 days after triple treatment	1758.10 ± 51.19	1801.79±45.18
Cholesterol, mmol/L	Pre-Treatment	2.38 ± 0.08***	3.35±0.10
	10 days after triple treatment	2.80 ± 0.08**	3.29 ± 0.08

Continued Table

	20 days after triple treatment	3.18 ± 0.05	3.37 ± 0.07
Triglycerids, mmol/L	Pre-Treatment	4.89 ± 0.06***	6.27 ± 0.12
	10 days after triple treatment	5.64 ± 0.11***	6.41 ± 0.09
	20 days after triple treatment	6.40 ± 0.09	6.36 ± 0.10
Lipase, U/L	Pre-Treatment	20.75 ± 1.0**	16.56 ± 0.67
	10 days after triple treatment	15.64 ± 0.80	14.32 ± 0.55
	20 days after triple treatment	16.39 ± 0.63	14.97 ± 0.66
Antioxidant Activity in Blood Serum, %	Pre-Treatment	48.40 ± 1.25**	59.10 ± 1.73
	10 days after triple treatment	60.10 ± 0.90	57.90 ± 0.98
	20 days after triple treatment	56.0 ± 1.12	59.0 ± 1.20
Lipids Containing Isolated Double Bonds, relative units	Pre-Treatment	4.46 ± 0.17***	1.97 ± 0.17
	10 days after triple treatment	3.40 ± 0.15***	2.13 ± 0.13
	20 days after triple treatment	2.19 ± 0.10	1.90 ± 0.11
Diene Conjugates, relative units	Pre-Treatment	2.76 ± 0.08***	1.33 ± 0.17
	10 days after triple treatment	2.02 ± 0.14**	1.41 ± 0.09
	20 days after triple treatment	1.63 ± 0.08	1.51 ± 0.13
Triene Conjugates, relative units	Pre-Treatment	1.65 ± 0.12***	0.70 ± 0.10
	10 days after triple treatment	0.77 ± 0.09	0.81 ± 0.11
	20 days after triple treatment	0.67 ± 0.06	0.80 ± 0.08
Oxodiene Conjugates, relative units	Pre-Treatment	1.30 ± 0.09**	0.78 ± 0.09
	10 days after triple treatment	0.63 ± 0.05	0.80 ± 0.09
	20 days after triple treatment	0.88 ± 0.06	0.75 ± 0.08
Schiff's Base, relative units	Pre-Treatment	1.23 ± 0.08***	0.50 ± 0.07
	10 days after triple treatment	0.86 ± 0.07*	0.58 ± 0.07
	20 days after triple treatment	0.55 ± 0.05	0.49 ± 0.07
Glucose, mmol/L	Pre-Treatment	14.82 ± 0.33*	13.65 ± 0.28
	10 days after triple treatment	14.66 ± 0.24*	13.54 ± 0.26
	20 days after triple treatment	15.02 ± 0.16**	13.89 ±0.18
α-Amylase, U/L	Pre-Treatment	250.54 ± 13.04**	178.91 ± 7.05
	10 days after triple treatment	255.88 ± 11.47***	183.30 ± 6.29
	20 days after triple treatment	241.91 ± 7.43**	189.43 ± 6.60
Lactate Dehydrogenase, U/L	Pre-Treatment	1524.99 ± 62.68***	1053.47±50.45
	10 days after triple treatment	1071.71 ± 51.48	1048.82±50.71
	20 days after triple treatment	1043.04 ± 43.30	1078.04±50.21
Gamma Glutaminetransferase, U/L	Pre-Treatment	16.11 ± 0.42	17.02 ± 0.53
	10 days after triple treatment	17.07 ± 0.42	16.49 ± 0.38
	20 days after triple treatment	17.13 ± 0.63	16.41 ± 0.41
Calcium, mmol/L	Pre-Treatment	2.71 ± 0.04	2.85 ± 0.06
	10 days after triple treatment	2.81 ± 0.06	2.91 ± 0.03

Continued Table

	20 days after triple treatment	2.89 ± 0.08	2.98 ± 0.04
Phosphorus, mmol/L	Pre-Treatment	2.16 ± 0.02	2.24 ± 0.03
	10 days after triple treatment	2.31 ± 0.03	2.24 ± 0.03
	20 days after triple treatment	2.29 ±0.02	2.34 ± 0.02
Cortisol, mcg/dL	Pre-Treatment	0.75 ± 0.02***	0.38 ± 0.03
	10 days after triple treatment	0.43 ± 0.02**	0.31 ± 0.02
	20 days after triple treatment	0.28 ± 0.02	0.27 ± 0.02
Free Triiodothyronine, pmol/L	Pre-Treatment	5.91 ±0.33**	8.50 ± 0.40
	10 days after triple treatment	9.39 ± 0.35*	8.37 ± 0.34
	20 days after triple treatment	9.67 ± 0.60	8.65 ± 0.35

Note: *, P<0.05; **, P<0.01; ***, P<0.001

We previously showed studies on deacarization of poultry buildings with chickens present using a synthetic pyrethroid-based drug. At the same time, a partial restoration was found for the physiological and biochemical status of chickens after dermanyssosis [41]. Considering the foregoing in the presented study, it can be noted that there is a clear trend towards stabilization of all said homeostatic parameters in the experimental chickens associated with combined Iverbutan. Its action is validated by the elimination of an aggressive haematophagous ectoparasite and by pronounced biostimulating properties of Butaphosphan. Additionally, the latter is needed to prevent free-radical-initiated abnormalities, to optimize metabolic processes, including those associated with energy synthesis, and to prevent hypoxic states. At the same time, we cannot rule out the influence of age and puberty in replacement stock birds on metabolism intensity during recovery after the disease.

CONCLUSIONS

The research has shown that the oral drug Iverbutan is highly effective (95.5 %) in controlling the poultry red mite. During the use of the drug Butaphosphan, a tendency was detected to harmonization of physiological and biochemical processes and activity of functional systems in the chickens, which may be due to its implemented biostimulating properties for sanogenesis mechanisms (adaptation, compensation, and protection).

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Индюхова Е. Н. Физиолого-биохимические механизмы восстановления организма кур на фоне лечения дерманиссиоза комбинированным препаратом Ивербутан / Индюхова Е. Н., Арисов М. В., Максимов В. И., Азарнова Т. О. // Ученые записки Крымского федерального университета им. В. И. Вернадского. Биология, химия. – 2022. – Т. 8 (74), №4. – С. 82–96.

Изучение особенностей реализации физиолого-биохимических механизмов восстановления организма животных на фоне лечения эктопаразитозов является актуальным направлением современной физиологии, в комплексе с биохимией и паразитологией. У цыплят при дерманиссиозе установлено существенное нарушение гомеостаза, что обусловлено чрезмерной интенсификацией процессов липопероксидации на фоне истощения антиокислительной активности сыворотки крови, изменениями в эндокринной системе, глубокими перестройками обменных процессов, а также в системе крови. Установлена высокая терапевтическая эффективность препарата на основе ивермектина и бутафосфана – 95,5 %. При его выпаивании у цыплят отмечена нормализация всех заявленных показателей крови в достаточно короткие сроки. Применение биостимулятора не только расширяет спектр, но и повышает эффективность реализации адаптивно-компенсаторных возможностей организма цыплят на фоне лечения.

Ключевые слова: механизмы восстановления, гомеостаз, стресс-фактор, ивермектин, бутафосфан, цыплята.