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EFFECT OF COMBINED THERAPY WITH IMIDOCARB AND PREDNISOLONE ON HEMATOLOGICAL PARAMETERS IN DOGS INFECTED WITH *BABESIA CANIS*

Nevidnyk-Pravda A. Yu., Ushakova H. O.

Oles Honchar Dnipro National University, Dnipro, Ukraine, e-mail: aaasssaaa079@gmail.com

Summary. *Babesia canis* infection is a significant tick-borne hemoprotozoan disease in dogs, often causing hemolytic anemia and alterations in hematological parameters. This study aimed to evaluate the effect of combined therapy with imidocarb and prednisolone on hematological indices in naturally infected dogs. Thirteen dogs showing initial clinical signs of *B. canis* infection were included in the study. Infection was confirmed via microscopic examination of blood smears. Hematological parameters, including erythrocyte count, hemoglobin concentration, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), leukocyte and platelet counts, and total protein, were measured before and after therapy. Treatment consisted of a single simultaneous administration of imidocarb (7 mg/kg) and prednisolone (2.2 mg/kg) within the first 24 hours after diagnosis. Following therapy, significant improvements were observed in red blood cell count, hemoglobin concentration, hematocrit, platelet count, and leukocyte distribution, indicating partial restoration of erythrocyte mass and enhancement of inflammatory and regenerative responses. MCHC, RDW, and total protein showed minimal changes, but overall trends suggest effective alleviation of hemolytic anemia and stabilization of hematological status. The findings support the use of combined imidocarb and prednisolone therapy as an effective early intervention for dogs naturally infected with *B. canis*

Keywords: hemolytic anemia, tick-borne infections, blood

Introduction. Babesiosis is one of the most common transmissible protozoan diseases of dogs, caused by members of the genus *Babesia*, of which *Babesia canis* is the most clinically significant (Birkenheuer et al., 2020; Bajer et al., 2022). The disease is characterized by damage to erythrocytes, leading to the development of hemolytic anemia, thrombocytopenia, leukocyte changes, and a systemic inflammatory response (Boozer and MacIntire, 2003; Eichenberger et al., 2016). Clinical manifestations vary from mild apathy and fever to severe complications such as shock, multiple organ failure, and death (Solano-Gallego et al., 2016; Strobl et al., 2020).

B. canis is transmitted by the bite of infected ticks, mainly *Dermacentor reticulatus*, whose activity is regulated by seasonal and climatic factors (Kohn et al., 2019; Rubel et al., 2020). Given the expansion of the vector range and changing climatic conditions, the spread of babesiosis among dogs in Europe and other regions shows a tendency to increase, making this disease a pressing problem in veterinary medicine (Bajer et al., 2022; Weingart et al., 2023). This expansion is evidenced by reports of canine babesiosis in previously non-endemic areas, underscoring its emerging status (Pawelczyk et al., 2022). Regional studies in Eastern Europe, such as in Kharkiv Region of Ukraine, have demonstrated high levels of *Ixodes ricinus* tick infestation with *Babesia* spp., with infection rates reaching up to 35.8% in adult ticks and a resulting 36.9% infection rate among dogs following tick bites, highlighting the significant local risk (Sumakova et al., 2025).

Modern treatment of babesiosis is based on the use of antiprotozoal drugs, in particular imidocarb dipropionate, which has demonstrated high efficacy in eradicating the parasite (Penzhorn et al., 1995; Baneth, 2018). While other drugs like doxycycline have been explored for prophylactic purposes, their efficacy in treatment is limited, highlighting the need for effective therapeutic protocols (Vercammen, De Deken and Maes, 1996). However, imidocarb does not always prevent severe hematological disorders and can cause side effects, including hepatotoxicity and nephrotoxicity (Kock and Kelly, 1991; Máthé, Dobos-Kovács and Vörös, 2007). Furthermore, the emergence of drug resistance is a growing concern in the control of protozoan parasites, which could potentially compromise the efficacy of existing treatments (De Koning, 2017). In this regard, researchers suggest a combination therapy that includes glucocorticoids, in particular prednisolone, to reduce the inflammatory response and immunopathological damage to the blood (Schoeman and Herrtage, 2008; Sikorski et al., 2010). Previous experimental and clinical studies have shown that the combination of antiprotozoal treatment and corticosteroids can accelerate the recovery of hematological parameters, such as red blood cell, hemoglobin, and platelet levels, and reduce the risk of complications (Reyers et al., 1998; Brandão, Hagiwara and Myiashiro, 2003; Máthé et al., 2006). The immune response to *B. canis* is complex, and understanding the duration of protective immunity following infection or treatment remains a critical area of investigation (Vercammen, De Deken and Maes, 1997). However, most of the existing data are limited to individual clinical cases or experimental models, and there are not enough systematic studies on the effect of combination therapy on the hematopoietic system of dogs with natural infection with *B. canis*.

Therefore, evaluating the effect of combination therapy with imidocarb and prednisolone on

hematological parameters in dogs infected with *B. canis* is of utmost importance to optimize the treatment strategy, reduce the risk of complications, and increase the survival of the animals.

B. canis infection is a significant tick-borne hemoprotozoan disease in dogs, frequently causing hemolytic anemia and alterations in hematological parameters. Previous investigations have documented pronounced reductions in red blood cell count, hemoglobin concentration, and hematocrit in infected canines, reflecting severe anemia due to parasite-driven hemolysis (Boozer and MacIntire, 2003; Bajer et al., 2022). The prevalence and clinical significance of this disease are recognized not only in Europe but also in other parts of the world, as highlighted in regional reviews (Panti-May and Rodríguez-Vivas, 2020). Studies from endemic regions, such as Ukraine, report a high incidence of the disease following tick exposure, with over 46% of dogs developing babesiosis after being bitten by an infected tick, underscoring the substantial burden of the disease in these areas (Sumakova et al., 2025). Studies evaluating therapeutic approaches, particularly the administration of imidocarb, have reported partial restoration of erythrocyte mass and initiation of erythropoietic regeneration (Máthé et al., 2006; Máthé, Dobos-Kovács and Vörös, 2007; Baneth, 2018).

Mild declines in total protein levels have been associated with subtle disturbances in protein metabolism, possibly linked to inflammatory processes and tissue healing (Birkenheuer et al., 2020). Hematological indices such as mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW) in previous studies have demonstrated a microcytic pattern with minimal changes in hemoglobin per erythrocyte, suggesting early regenerative activity and limited variability in red cell size (Onishi et al., 1993; Brandão, Hagiwara and Myiashiro, 2003).

Red blood cell alterations reported in the literature indicate that *Babesia* infection triggers both direct hemolytic effects and compensatory erythropoietic responses. Pre-treatment microcytosis and slightly reduced MCHC may reflect iron redistribution and hindered hemoglobin production due to infection-associated inflammation (Máthé et al., 2006; Birkenheuer, 2021). Gradual restoration of MCV and MCHC following effective therapy has been documented, indicating recovery of erythropoiesis after parasite clearance.

Thrombocytopenia is consistently observed in *Babesia*-infected dogs, reflecting platelet depletion through immune-mediated destruction, splenic sequestration, and direct parasitic effects on megakaryocytes (Scheepers et al., 2011; Strobl et al., 2020). Studies have shown partial restoration of platelet counts following antiparasitic therapy, highlighting the benefit of early intervention.

Leukocyte dynamics in canine babesiosis have also been described, with initial leukopenia and post-treatment neutrophilia accompanied by persistent lymphopenia, reflecting ongoing inflammation and modulation of the immune response (Wykes et al., 2014; Eichenberger et al., 2016; Solano-Gallego et al., 2016). Serial monitoring of these parameters has been emphasized as valuable for prognostic evaluation and guiding supportive care (Solano-Gallego et al., 2016; Weingart et al., 2023).

Finally, regional differences in *Babesia* species and vector ecology have been reported to influence the severity and pattern of hematological alterations, underlining the importance of local epidemiological knowledge in clinical management (Rubel et al., 2020; Bajer et al., 2022). Collectively, these studies underscore the complexity of hematological responses in canine babesiosis and the critical role of prompt and targeted therapeutic interventions (Penzhorn et al., 1995; Baneth, 2018; Weingart et al., 2023).

This study **aimed** to evaluate the effect of combined therapy with imidocarb and prednisolone on hematological indices in naturally infected dogs. To achieve this aim, 13 dogs naturally infected with *B. canis* were included in the study. The following tasks were set: to confirm infection by microscopic examination of blood smears; to study the dynamics of hematological parameters, including erythrocyte count, hemoglobin concentration, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), leukocyte and platelet counts, and total protein; to evaluate the effect of combined therapy with imidocarb (7 mg/kg) and prednisolone (2.2 mg/kg) on these hematological parameters.

Materials and methods. A clinical study on the effect of combined therapy with imidocarb and prednisolone on hematological parameters in dogs infected with *B. canis* was conducted. The study included 13 dogs that exhibited the first signs of *B. canis* infection at the time of the initial veterinary consultation, which was confirmed by the results of blood smear analysis. This diagnostic method, involving the microscopic identification of intraerythrocytic parasites on stained blood smears, is a well-established and reliable technique for confirming acute *Babesia* infection, as utilized in other regional studies (Sumakova et al., 2025). The study was carried out from February to April 2024 at the Veterinary Complex 'Peredovyi' in Dnipro (Amur-Nizhnyodniprovsky District). The animals represented various age groups, breeds, and sexes. Dogs with diagnosed concomitant diseases or with incomplete or unreliable laboratory data were excluded from the study. Detection of *B. canis* parasites in erythrocytes was performed using thin blood smears stained with fast-acting LEUCODIF 200 dye (Erba Lachema, Czech Republic), followed by examination under 100× magnification using an optical microscope Leica DM4 (Germany) (Fig. 1). Intraerythrocytic forms of the parasite were identified and documented.

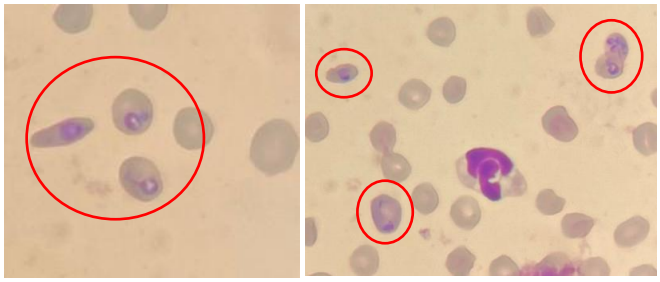

Figure 1. Blood smear from dogs infected with *B. canis* (Leucodiff stain, ×100 oil immersion, NA 1.25). Intraerythrocytic forms of the parasite are clearly visible and indicated with a red circle.

For hematological analysis, blood samples were collected from the cephalic or saphenous vein into EDTA-containing tubes. The following parameters were measured: erythrocyte count, hemoglobin concentration, leukocyte count, platelet count, mean corpuscular hemoglobin concentration (MCHC), erythrocyte distribution width (RDW), total protein, and hematocrit. These parameters were analyzed using an automatic hematological analyzer MicroCC-20 Plus (HTI, USA). Quantitative assessment of segmented neutrophils and lymphocytes was performed by microscopic counting on stained blood smears.

The main period of treatment was the first 24 hours, during which dogs received combined therapy with imidopyran (Arterium, Ukraine, 7 mg/kg) and prednisolone (Darnitsa, Ukraine, 2.2 mg/kg) administered simultaneously. Clinical signs and hematological parameters were monitored at baseline, during treatment, and after completion of therapy.

Animal handling and all procedures were performed following the recommendations of the 'European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes' (CE, 1986) and Council Directive 2010/63/EU (CEC, 2010), and under Art. 26 of the Law of Ukraine No. 3447-IV of 21.02.2006 'About protection of animals from cruel treatment' (VRU, 2006) and basic bioethical principles (Simmonds, 2017). Under the current procedure, the research program was reviewed and approved by the Bioethics Committee of the Veterinary Complex 'Peredovyi' (Dnipro, Ukraine).

A range of statistical methods was applied to evaluate hematological changes associated with the combined therapy. Descriptive statistics were calculated to determine mean, median, mode, standard deviation, and variance for both the control group and the treated group. Differences in mean values were analyzed using the Student's *t*-test, and analysis of variance (ANOVA) was applied to compare mean values across different time points and groups (Van Emden, 2019).

Results and discussion. Key hematological parameters were analyzed in dogs at three stages: clinically healthy (control group), before treatment, and after treatment of babesiosis.

In infected dogs, the RBC (Fig. 2a) count was significantly reduced before treatment to $3.59 \pm 0.37 \times 10^6$/μL ($P < 0.0001$; $F = 0.0107$), indicating pronounced anemia due to parasite-induced hemolysis. Following therapy, the RBC partially recovered to $4.20 \pm 0.27 \times 10^6$/μL ($P = 0.0001$ compared to pre-treatment; $F = 0.2763$), reflecting improvement in hematological status.

Hemoglobin levels (Fig. 2b) also decreased markedly before treatment to 83.42 ± 2.96 g/L ($P < 0.0001$; $F = 0.0250$) and rose to 90.77 ± 3.38 g/L after therapy ($P < 0.0001$; $F = 0.6554$), indicating partial restoration of oxygen-carrying capacity.

Hematocrit (Fig. 2c) followed a similar trend, dropping to 22.54 ± 1.45% before treatment ($P < 0.0001$; $F = 0.0955$) and increasing to 26.92 ± 1.42% after therapy ($P < 0.0001$; $F = 0.9457$), demonstrating improvement in erythrocyte volume fraction.

In infected dogs, the mean total protein level (Fig. 3) was slightly reduced before treatment at 65.59 ± 2.26 g/L ($P = 0.1300$; $F = 0.1845$) and decreased further to 63.06 ± 1.55 g/L after therapy ($P = 0.0038$; $F = 0.2081$), suggesting mild alterations in protein metabolism during infection.

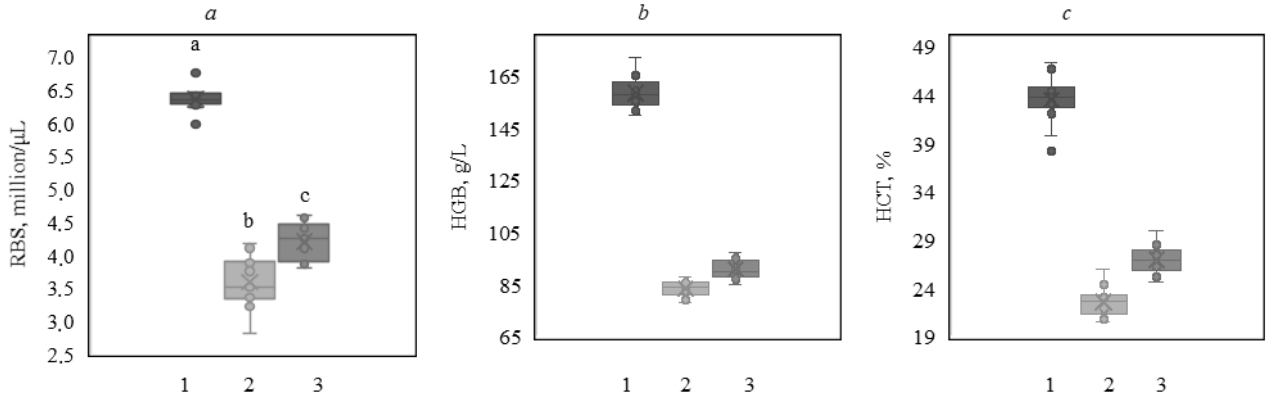

Figure 2. Comparative analysis of erythrocyte indices in dogs: (*a*) red blood cell count, (*b*) hemoglobin concentration, and (*c*) hematocrit values (x ± SD, n = 13): 1 — clinically healthy control dogs, 2 — infected dogs before therapy, 3 — infected dogs after therapy; ^{a,b,c} — mean values with unlike letters were significantly different between the groups ($P < 0.05$).

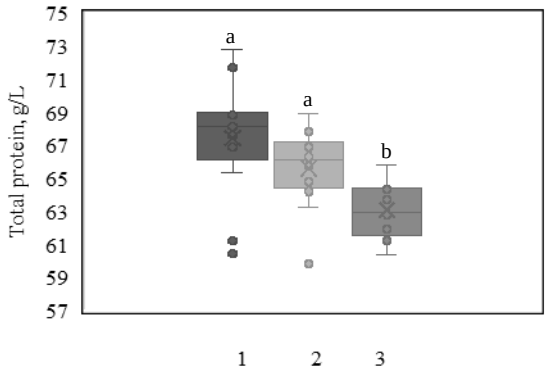

Figure 3. Serum total protein concentrations in control dogs and in animals with babesiosis prior to and following treatment (x ± SD, n = 13): 1 — clinically healthy control dogs, 2 — infected dogs before therapy, 3 — infected dogs after therapy; [a,b,c] — mean values with unlike letters were significantly different between the groups (P < 0.05).

In infected dogs, MCV (Fig. 4a) decreased to 63.45 ± 2.49 fL before treatment (P = 0.0178; F = 0.4335) and slightly increased to 64.69 ± 2.59 fL after therapy (P = 0.2423; F = 0.8904), indicating microcytic erythrocytes and an early regenerative response.

MCHC (Fig. 4b) remained relatively stable, measuring 36.21 ± 5.58 g/dL before treatment and 35.72 ± 6.81 g/dL after therapy (P > 0.05), suggesting limited changes in hemoglobin concentration per erythrocyte. RDW (Fig. 4c) showed minimal variation, with values of 15.99 ± 1.04% before treatment and 15.67 ± 1.05% after therapy (P > 0.05), indicating little change in erythrocyte size distribution.

In infected dogs, platelet count (Fig. 5) dropped sharply to 38.23 ± 6.20×10³/μL before treatment (P < 0.0001; F = 0.0000) and partially recovered to 65.15 ± 4.80×10³/μL after therapy (P < 0.0001; F = 0.3370), highlighting severe thrombocytopenia during acute infection and improvement following treatment.

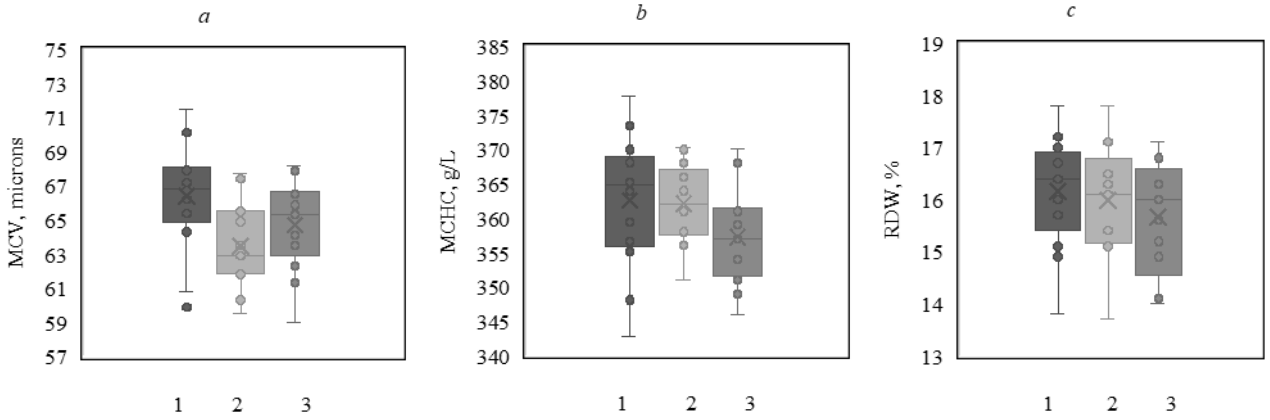

Figure 4. Erythrocyte indices in dogs naturally infected with *B. canis*: (*a*) mean corpuscular volume (MCV), (*b*) mean corpuscular hemoglobin concentration (MCHC), and (*c*) red cell distribution width (RDW) (x ± SD, n = 13): 1 — clinically healthy control dogs, 2 — infected dogs before therapy, 3 — infected dogs after therapy; [a,b,c] — mean values with unlike letters were significantly different between the groups (P < 0.05).

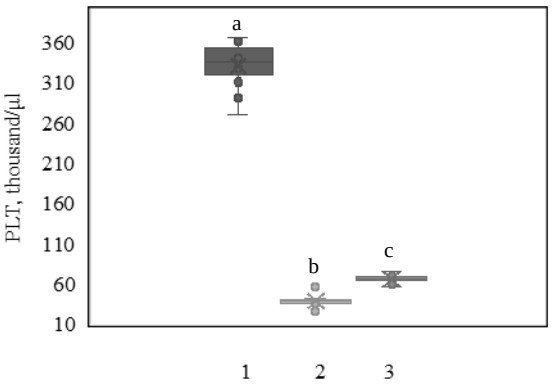

Figure 5. Platelet counts (PLT) in control dogs and in dogs infected with *B. canis* before and after treatment (x ± SD, n = 13): 1 — clinically healthy control dogs, 2 — infected dogs before therapy, 3 — infected dogs after therapy; [a,b,c] — mean values with unlike letters were significantly different between the groups (P < 0.05).

In infected dogs, WBC count (Fig. 6a) decreased to 7.08 ± 0.60×10³/μL before treatment (P < 0.0001; F = 0.0676) and increased to 11.68 ± 0.79×10³/μL after therapy (P < 0.0001; F = 0.6319).

Segmented neutrophils (Fig. 6b) rose from 60.66 ± 1.88% before treatment to 73.66 ± 1.63% after therapy (P < 0.0001; F = 0.0688), indicating an ongoing inflammatory response.

Lymphocytes (Fig. 6c) decreased from 28.45 ± 1.27% before treatment to 25.68 ± 1.27% after therapy (P < 0.0001; F = 0.4798), reflecting shifts in leukocyte populations during infection and recovery.

These findings are largely consistent with previously published studies on canine babesiosis. Similar improvements in red blood cell count, hemoglobin concentration, hematocrit, and platelet levels following combined therapy with antiprotozoal drugs and corticosteroids have been reported by Máthé et al. (2006), Brandão, Hagiwara and Myiashiro (2003), and

Reyers et al. (1998), indicating that early intervention with imidocarb and prednisolone effectively supports hematological recovery. The observed stability in MCHC and RDW aligns with the findings of Onishi et al. (1993) and Birkenheuer (2021), suggesting that regenerative erythropoiesis restores red cell mass without marked alterations in cell size or hemoglobin concentration per erythrocyte. Additionally, the partial restoration of leukocyte counts and neutrophil predominance after treatment corresponds with the immune modulation patterns described by Solano-Gallego et al. (2016) and Eichenberger et al. (2016). Overall, our results reinforce the evidence that combination therapy not only alleviates hemolytic anemia but also helps normalize inflammatory and immune responses in dogs naturally infected with *B. canis*.

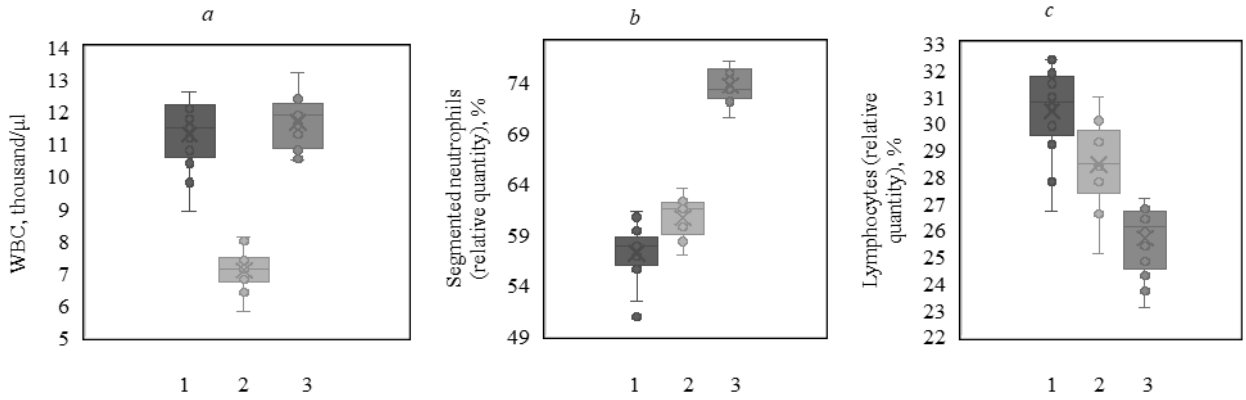

Figure 6. (*a*) Total white blood cell counts (WBC), (*b*) Relative segmented neutrophils, and (*c*) Lymphocyte proportions in control dogs and dogs infected with *B. canis* before and after treatment (x ± SD, n = 13): 1 — clinically healthy control dogs, 2 — infected dogs before therapy, 3 — infected dogs after therapy; ^{a,b,c} — mean values with unlike letters were significantly different between the groups ($P < 0.05$).

Conclusions. Within the first 24 hours of combined therapy with imidopyran (7 mg/kg) and prednisolone (2.2 mg/kg), infected dogs showed early signs of hematological and biochemical recovery. Compared to pre-treatment values, there was a notable increase in platelet and white blood cell counts, as well as the beginning of regenerative changes in erythrocytes. Despite these improvements, some parameters, including lymphocyte percentages and total protein levels, remained below those of clinically healthy controls, indicating ongoing systemic effects of infection. These findings demonstrate that prompt administration of imidopyran and prednisolone can rapidly mitigate acute manifestations of babesiosis, although continued monitoring is essential to ensure complete recovery.

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