Original Article

Shock status and anti-shock infusion therapy in canine acute spontaneous babesiosis

Oksana Dubova[1*] Lyudmila Kovalova[1] Anatolyi Dubovyi[1] Pavel Kovalov[1] Inna Chala[1]

Abstract

Canine babesiosis is a serious disease that is accompanied by the development of shock. The aim of the work was to establish shock, assess its degree, as well as to conduct a clinical trial of anti-shock infusion therapy. 100 dogs of different breeds, weighing 20–40 kg, aged 2–4 years, were involved. The studies used oscillometry (blood pressure, pulse rate), assessment of vascular-platelet hemostasis (platelet count, spontaneous aggregation ability), coagulogram (prothromine and activated partial thromboplastin time, fibrinogen), enzyme immunoassay (fibrin degradation products and D-dimer), biochemical (soluble fibrin-monomer complexes) and hemodynamic (circulating blood volume, hematocrit) methods of investigation. In dogs with acute babesiosis sub-compensated shock grade II developed. The basis for the diagnosis is a significant decrease in the specific volume of circulating blood (p<0.001) and average blood pressure (p<0.05), an increase in the *Allgöwer's* Shock Index (p<0.05). Disseminated intravascular coagulation develops at the stage of consumption coagulopathy, which is confirmed by an increase in the level of soluble fibrin-monomer complexes (p<0.001), fibrin degradation products and D-dimer (p<0.05), hypofibrinogenemia (p<0.001), multidirectional shifts in activated partial thromboplastin time and prothrombin time tests. This condition is urgent and requires anti-shock therapy.

Infusion therapy with a mixture of solutions of the plasma substitute *Rheopolyglucine* and the disaggregant *Persantine* at a dose of 5 ml (45 mg *Dexrtan* and 2.5 mg *Dipyridamole*) per 1 kg of animal body weight restores researching parameters and indicators for 48 hours. The use of drugs in an infusion mixture is more effective than using them separately.

Keywords: canine babesiosis, sub-compensated shock, DIC-syndrome, *Rheopolyglucine-Novofarm®, Persantine®*, infusion therapy

[1]*Polissia National University, Stary Boulevard, 7, Zhytomyr, Ukraine*
***Correspondence**: oxdubova@gmail.com* (O. Dubova)
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Introduction

Canine babesiosis is a severe blood-protozoal disease (Köster *et al*. 2015; Eichenberger *et al*. 2016; Goddard *et al*. 2016). Pathogens of the disease affect red blood cells. They are distributed all over the world and belong to different species of *Babesia* spp.: large shapes (*B. canis* Piana et Galli-Valeria, 1895, *B. vogeli* Reichenow, 1937, *B. rossi* Nutall, 1910) and small shapes (*B. gibsoni* Patton, 1910, *B.vulpes* Baneth, Florin-Christensen, Cardoso & Schnittger 2015 and other). Different types of *Babesia* spp. have different virulence (Lack *et al*. 2012; Schnittger *et al*. 2012; Köster *et al*. 2015).

The defeat of red blood cells leads to serious consequences for the dog's body. First of all, this is due to oxygen deficiency in various tissues. Further, disorders of hemodynamics, microcirculatory hemorheological properties are involved in the pathogenesis. As the disorders progress, a state of shock occurs (Shah *et al*. 2011; Rafaj *et al*. 2013; Köster *et al*. 2015; Goddard *et al*. 2016; Roopali *et al*. 2018). Shock is always accompanied by disorders of the hemostasis system, which manifest themselves in the form of disseminated intravascular coagulation syndrome (DIC syndrome). Both processes create a "vicious circle" that mutually condition and complicate each other. Eventually the shock becomes irreversible and fatal to the animal's life (Vincent and De Backer 2013; Dubova 2016; Dubova *et al*. 2020).

Given the severity and unpredictability of the development of shock, there is a need for immediate emergency medical intervention and intensive care.

The main means of stabilizing hemodynamics and hemorheology are infusion therapy, as well as drugs that affect the vascular tone and contractile capacity of the myocardium (Leone *et al*. 2015; Lewis *et al*. 2018). The most effective means for infusions to restore hemodynamic parameters are colloidal solutions (Lee and Kim 2013; Langer *et al*. 2014), in particular, *Rheopolyglucine*® (Dextran), an affordable drug and one that is well tolerated by dogs. In addition, it is necessary to introduce disaggregants in order to stop thrombosis in the microcirculation zone of organs and tissues (Liu *et al*. 2013; Balakumar *et al*. 2014). According to the results of clinical work, *Persantine* ® (Dipyridamole) has been proved to be the best disaggregant. This remedy is also widely available and can be used for dogs according to indications.

The aim of the work is the clinical and physiological justification of the development of shock, as well as the use of solutions of plasma substitutes and disaggregants in antishock therapy in canine acute spontaneous babesiosis and a comparative assessment of their use in combination and separately.

Materials and Methods

Ethics Statement: The studies were approved by the Ethics Committee of the Faculty of Veterinary Medicine, Polissia National University (approval number: 2019-07-14).

Animals: Healthy dogs (n=100) and dogs with acute spontaneous babesiosis (n=100), aged 2–4 years, body weight 20–40 kg were chosen for this investigation. The investigated group consisted of sick dogs. The control group – clinically healthy dogs (no clinical signs of any disease; no history of contact with ixodic ticks; no pathogen was detected in the stained blood smears; hematological parameters were within the normal reference range).

Clinical and microscopic studies. Clinical studies were made by general methods of clinical research. The basis for the diagnosis of babesiosis was the determination of the pathogen in the study of thin blood smears stained with Giemsa (Satpathy *et al*. 2014). The causative pathogen was identified as large *Babesia* spp. (Lack *et al*. 2012; Schnittger *et al*. 2012; Köster *et al*. 2015). Specific typing of *Babesia* was not performed.

Studies of vascular platelet hemostasis. Blood sampling for the study was performed by *Vena saphena antebrachii* of the right limb. The use of a 3.8% sodium citrate solution in a ratio of 1:10 was necessary for the correct assessment of the hemostasis system (Barkagan and Momot 2008). The number of platelets and hematocrits were determined using a Mindray BC-3600 hematology analyser (Mindray Medical Rus Co. Ltd, Russian Federation). Testing of the vascular-platelet link of hemostasis was performed by evaluating the spontaneous platelets aggregation ability (spPAC) by shaking according to N. I. Tarasova (Barkagan and Momot 2008; Panzer and Jilma 2011) with a determination of the number of platelets.

Oscillometric measurement of blood pressure and calculation of its indexes. The blood pressure indicators are systolic blood pressure (Sys), diastolic blood pressure (Dia) and pulse (P). Blood pressure was measured using a PetMap graphic II (CardioCommand, USA) veterinary blood pressure monitor (sys, dia, P). The estimated indicators are mean arterial pressure (MAP) calculated by the formula (1) and Allgöwer's Shock Index (ASI) calculated by the formula (2) (Nathan *et al*. 2016; Dubova *et al*. 2018):

$$MAP = \frac{(Sys - Dia)}{3} + Dia \quad (1),$$

MAP – mean arterial pressure, mm Hg;
Sys – systolic blood pressure, mm Hg;
Dia – diastolic blood pressure, mm Hg.

$$ASI = {}^{P}/_{Sys} \quad (2),$$

ASI – Allgöwer's shock index;
P – pulse rate, beats per minute;
Sys – systolic blood pressure, mm Hg.

Assessment of hemodynamic parameters. Hemodynamic parameters included the determination of circulating blood volume (CBV) and its components, as well as the calculation of specific circulating blood volume SCBV (ml/kg) using the T-1824 blue Evans dye dilution method (Loginova *et al.* 2016; Yao *et al.* 2018). Blood loss volume (BLV) was determined using the *Moore*'s hematocrit method according to formula (3) (Schorn 2010; Timerbulatov *et al*. 2012; Pacagnella *et al*. 2013; Lopez-Picado *et al*. 2017):

$$BLV = CBV_{norm} \times \frac{(Ht_{norm} - Ht_{research})}{Ht_{norm}} \quad (3),$$

BLV – blood loss volume, ml;

CBV – circulating blood volume normal, ml;

Ht_{norm} – hematocrit value normal, L/L;

$Ht_{research}$ – hematocrit value of the animals' research group, L/L.

Assessment of markers of DIC syndrome. The content of soluble fibrin-monomeric complex (SFMC) was determined by a quantitative variant of the ortho-phenanthroline method (Barkagan and Momot 2008; Rafaj *et al*. 2013; Panteleev *et al*. 2015). The fibrinogen level was assessed by the Claus clotting method using a coagulometer ACL TOP 350 CTS (Instrumental Laboratory, USA) (Rafaj *et al*. 2013; Wiseman *et al*. 2013; Roshal and Gil 2019)**.** The content of fibrin degradation products (FDP) and F-dimmer was determined by solid-phase enzyme immunoassay (Rafaj *et al*. 2013; Gil 2019). Prothrombin time (PT) and activated partial thromboplastin time (APTT) were measured using a coagulometer ACL TOP 350 CTS (Instrumental Laboratory, USA) (Roshal 2013a; Roshal 2013b; Panteleev *et al*. 2015).

Clinical trial of infusion therapy methods. Animals with babesiosis were treated according to the traditional protocol using the antiprotozoal drug Pyro-stop® (NPO Api-San LLC, Russian Federation), as well as means of pathogenetic and symptomatic therapy. To test antishock infusion media, 2 groups of dogs with acute spontaneous babesiosis of 40 animals each were formed.

Antishock therapy for animals of the first group was carried out using solution infusions *Rheopolyglucine-Novofarm*® (Dextran) (production of Novofarm-Biosynthesis LLC, Ukraine) in a dose of 5 ml (50 mg) per 1 kg of body weight per day for 3 days. Intramuscularly, *Persantine*® (Dipyridamole) solution (manufactured by Boehringer Ingelheim International, GmbH, Germany) was administered in 2 stages at a dose of 0.5 ml (2.5 mg) per 1 kg of body weight per day for 3 days. For animals of the second group, an infusion of a mixture of *Rheopolyglucine-Novofarm*® and *Persantine*® solutions was performed in a ratio of 90:10 at a dose of 5 ml (45 mg of Dextran and 2.5 mg of Dipyridamole) per 1 kg of dog body weight once a day for 3 days. The choice of dose was due to the optimal effect on the processes of disaggregation in the microcirculatory bed in conditions of the development of conditions that threatened the life of the animal (Barkagan 2005; Barkagan and Momot 2008; Annane *et al*. 2013; Monteiro 2017; Allahham *et al*. 2021).

The dynamics of changes in the studied indicators were evaluated every 24 hours. When creating a mixture of infusion solutions, attention was paid to changes in the qualitative parameters of the solution: changes in the density of the solution, its transparency, precipitation or the development of opalescence were not established. When carrying out infusions of a mixture of solutions, manifestations of allergic reactions were not established. To control blood pressure during the introduction of infusion media, measurements were carried out every three hours.

Statistical analysis. Statistical processing of the results was carried out using Statistica 13.3 IT Application. The Fisher distribution (ANOVA) was used to determine the statistically significant effect on the studied indicators. The reliability of the data obtained was evaluated by the Fisher F-criterion at a confidence level of $p<0.05$.

Results

In the season of tick activity, the incidence of dogs with babesiosis can reach 35–40% (according to our clinic). All animals whose owners contacted the clinic had a history of contact with ixodes ticks *Dermacentor reticulatus* Fabricius, 1794, and *Ixodes ricinus* Linnaeus, 1759. Clinical signs determine the severity of the disease: fever (100%), anemia of visible mucous membranes (90%), which often turned into jaundice (45%), hemoglobinuria (80%), vomiting with yellow-red bile (15%), tachycardia and tachypnea (100%). In some cases, clouding of consciousness, a soporotic state, lesions of the nervous system in the form of discoordination were recorded.

The basis for the diagnosis was the determination of pathogens in fixed blood smears stained by the Giemsa method. The intensity of parasitemia was 10–12% of the affected blood cells.

The oscillometric measurement of blood pressure and its indices became the basis for assessing the hemodynamic state of sick dogs, which is primarily able to determine the state of shock (Table 1).

Calculated indicators of mean blood pressure were significantly reduced by 1.46 times, the pulse was significantly accelerated and the *Allgöwer's* Shock Index was increased by 2.5 times.

Significant changes were found in hemodynamic parameters (Table 2).

Indicators of Ht, CBV, SCBV, % of CBV from body weight were reduced statistically significantly.

In sick dogs, blood loss was established - an average of 1790 ml (36%).

Significant changes were found in the vascular-platelet link of hemostasis (Table 3).

Reliable indicators of thrombocytopenia, as well as an increase in spPAC, were determined.

Markers of DIC syndrome as an integral companion of the state of shock have been established (Bhagavan and Ha 2011; Dubova 2016; Levi 2018; Saini and Dunn 2019; Dubova *et al*. 2020) (Table 4).

There was a significant increase in the level of SFMC by 10 times, FDP by 4.5 times, D-dimer by 4 times, significant hypofibrinogenemia (by 7.4 times). Coagulation tests showed multidirectional shifts: APTT was shortened, while PT was significantly elongated.

The therapeutic efficacy of the applied infusion media was evaluated in dynamics, the results are presented in Tables 5 and Figures 1–4.

The indicators of MAP and ASI in the dynamics of infusion therapy changed in the direction of physiological parameters. In group II animals, the indicator reached the control level after 48 hours, and in group I – after 72 hours (Fig 1, 2).

SCBV and Ht indicators changed in the direction of physiological synchronously in both study groups. After 72 hours in both groups, the SCBV index did not differ from that in the control group. The hematocrit value reached reference values after 48 hours (Fig. 3).

The parameters of the vascular-platelet hemostasis link changed in the direction of physiological values (Fig. 4).

The increase in the number of platelets was more pronounced in group II, where the indicator reached the control level after 48 hours. Similar changes were noted in the spPAC indicator, which reached the control level after 48 hours in group II.

Markers of DIC syndrome after 72 hours synchronously reached physiological values in both groups of animals. Since the difference between the indicators in both groups was unreliable, they were combined into a single group to demonstrate the result (Table 5).

Thus, as a result of the infusion therapy carried out in order to eliminate the shock state of dogs with babesiosis, the studied indicators changed to the level of reference indicators of the control group, but in group II the changes occurred 24 hours faster, thereby speeding up the recovery processes of the studied parameters.

Table 1 Indicators of arterial pressure and its indices in dogs under acute spontaneous babesiosis, n=100, M±m

Indicators	Investigated group	Control group
Sys, mmHg	82.7 ± 2.6 *	134.4 ± 4.8
Dia, mmHg	66.6 ± 2.9 *	89.6 ± 4.2
P, bpm	126 ± 6.7 *	82 ± 6.4
MAP, mmHg	71.9 ± 3.7 *	105.4 ± 4.3
ASI	1.52 ± 0.38 *	0.61 ± 0.08

* Difference between groups is significant (p<0.05).

Table 2 Hemodynamic indicators of dogs under acute spontaneous babesiosis, n=100, M±m

Indicators	Investigated group	Control group
Ht, L / L	0.28 ± 0.04 ***	0.438 ± 0.03
CBV, mL	3170 ± 165 ***	4940 ± 94
SCBV, mL / kg	79.3 ± 5.2 ***	123,3 ± 6.8
% of CBV from body weight	7.9 ± 0.4 ***	12.3 ± 0.4

*** Difference between groups is significant (p<0.001).

Table 3 The state of vascular-platelet hemostasis in dogs under acute spontaneous babesiosis, n=100, M±m

Indicators	Investigated group	Control group
Platelets, 10^9 / L	175.4 ± 24.7 ***	302.3 ± 16.3
spPAC, %	54.4 ± 4.3 ***	16.8 ± 1.7

*** Difference between groups is significant (p<0.001).

Table 4 Markers of intravascular coagulation in dogs under acute spontaneous babesiosis, n=100, M±m

Indicators	Investigated group	Control group
SFMC, g / L	0.32 ± 0.017 ***	0.03 ± 0.002
FDP, g / L	0.36 ± 0.07 ***	0.078 ± 0.01
D-dimer, µg / L	0.68 ± 0.1 ***	0.17 ± 0.018
Fibrinogen, g / L	0.36 ± 0.07 ***	2.65 ± 0.19
APTT, sec	37.4 ± 4.4	46 ± 5.2
PT, sec	30.4 ± 2.2 ***	20.2 ± 2.1

*** Difference between groups is significant (p<0.001).

Table 5 Changes in markers of DIC syndrome during infusion therapy, n=80, M±m

Indicators	Before therapy	After therapy
SFMC, g / L	0.3 ± 0.02 ***	0.027 ± 0.002
FDP, g / L	0.41 ± 0.08 ***	0.069 ± 0.008
D-dimer, µg / L	0.66 ± 0.08 ***	0.15 ± 0.008
Fibrinogen, g / L	0.43 ± 0.06 ***	3.12 ± 0.16
APTT, sec	34.4 ± 3.7	42 ± 3.2
PT, sec	31.8 ± 1.5 ***	20 ± 1.6

*** Difference between groups is significant (p<0.001).

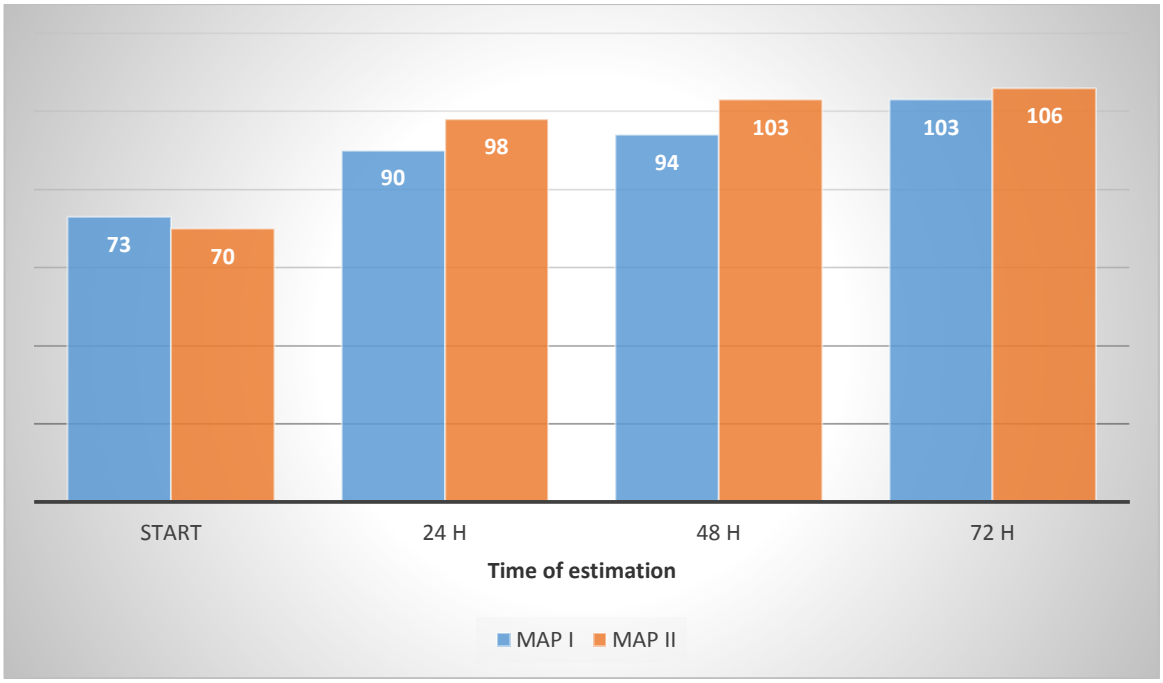

Figure 1 Dynamic changes in MAP (mm Hg) during infusion therapy

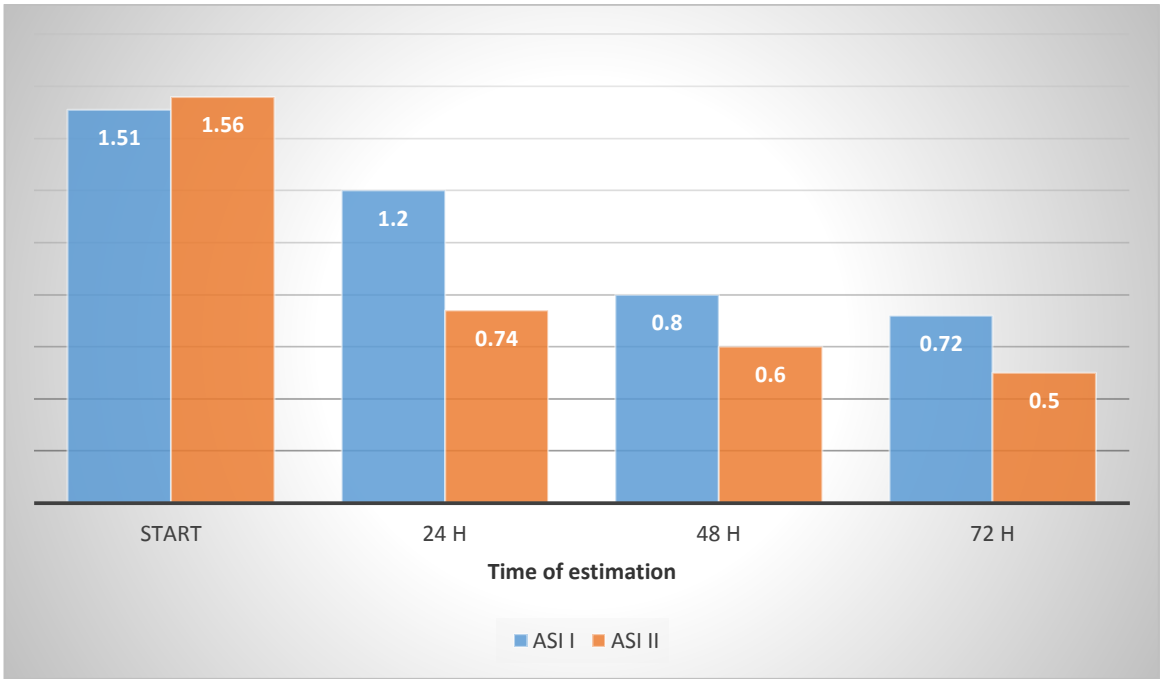

Figure 2 Dynamic changes in ASI during infusion therapy

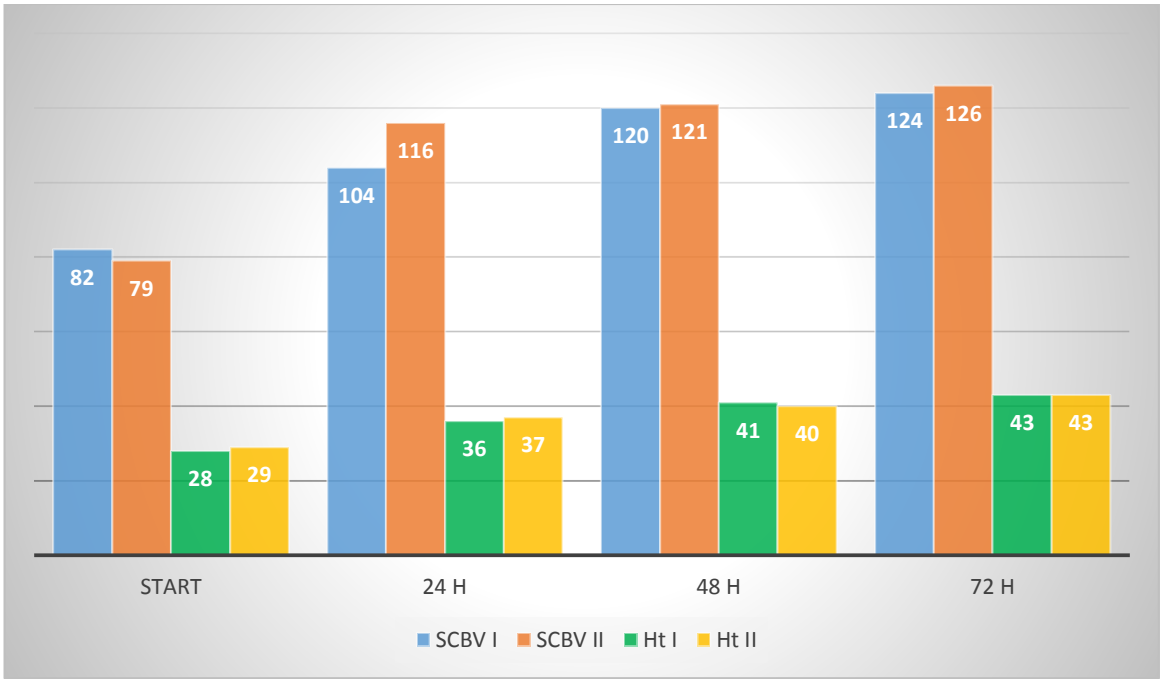

Figure 3 Dynamic changes of SCBV (ml/kg) ta Ht (%)* during infusion therapy
*The Ht indicator is presented in % for the convenience of demonstrating changes

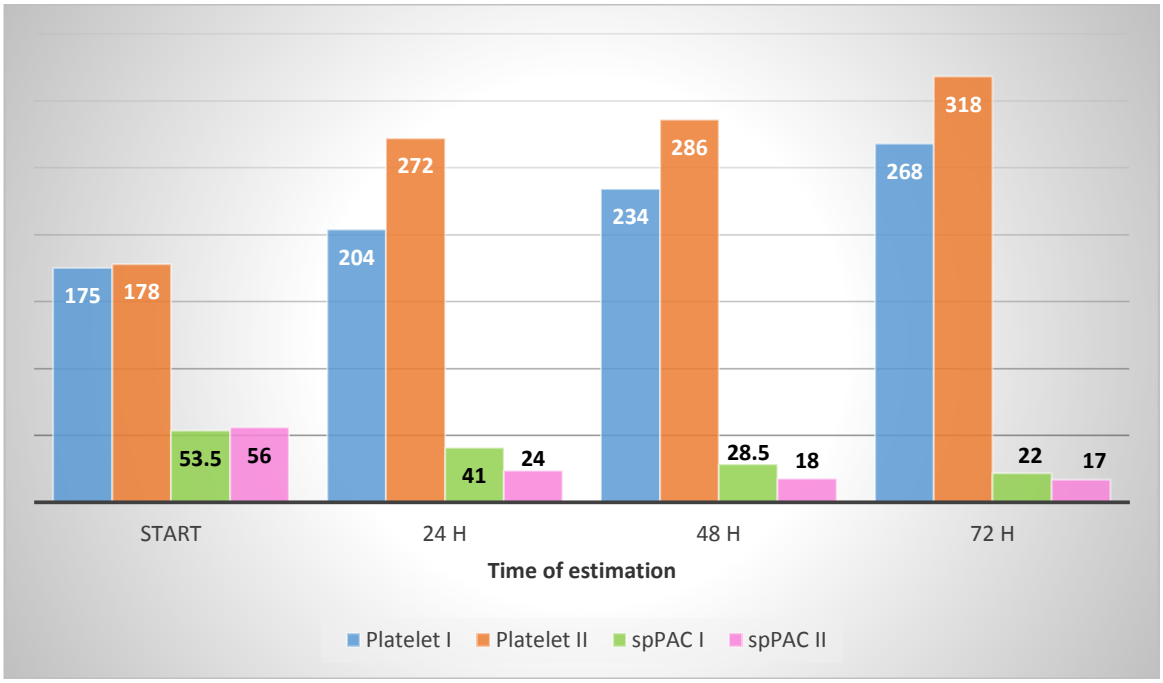

Figure 4 Dynamic changes in platelet count (109 / L) and spPAC (%) during infusion therapy.s

Discussion

Acute spontaneous babesiosis is the main seasonal disease during the ixodic tick activity season. The chain of pathological processes that develops with babesiosis is due to the influence of the pathogen on the dog's body (Lack *et al*. 2012; Schnittger *et al*. 2012; Köster *et al*. 2015; Eichenberger *et al*. 2016; Goddard *et al*. 2016; Solano-Gallego *et al*.).

In our previously published works (Dubova 2016; Dubova et al. 2020), it was shown that the activity of the pathogen is powerful enough to cause complications, the main one being acquired hemostasiopathy - DIC syndrome, which is pathogenetically closely related to the development of shock (Köster *et al*. 2015; Dubova 2016; Levi 2018; Saini and Dunn 2019; Dubova *et al*. 2020).

The symptoms noted in dogs determined multiple organ pathology. Fever, anemia followed by jaundice, tachycardia and tachypnea, vomiting with red bile indicate intoxication syndrome involving the liver and the development of hepatitis with hepatobiliary insufficiency. Hemoglobinuria characterizes the development of nephrotic syndrome with the phenomena of acute glomerulonephritis and renal failure (Köster *et al*. 2015; Solano-Gallego *et al*. 2016; Levi 2018).

The defeat of the nervous system in the form of clouding of consciousness, discoordination characterizes the destructive effect of hypoxia and intoxication caused by the destruction of red blood cells and the toxic influence of pathogens (Köster *et al*. 2015; Levi 2018).

Severe lesions of the body, which led to a fatal outcome, were accompanied by the development of bleeding and edema. Such signs characterize the DIC syndrome of the fibrinolysis stage and the terminal phase of shock (Vincent and De Backer 2013; Levi 2018).

Thus, acute spontaneous babesiosis develops acute multiple organ pathology and intoxication syndrome due to the development of shock and DIC syndrome.

Oscillometric studies have established significantly reduced MAP and accelerated P, obviously as compensation for the drop in the hemodynamic potential of blood flow. As a result, the ASI index increased by 2.5 times, determining the transition of the shock of the II degree of subcompensated to the shock of the III degree of decompensated by its magnitude (Nathan *et al*. 2016; Lopez-Picado *et al*. 2017).

Hemodynamic parameters of Ht, CBV, SCBV, % of blood from body weight were significantly reduced by 1.5 times. The blood loss determined in sick animals was 36%, which determined the shock of the II degree – subcompensated, but with a pronounced tendency to decompensation (Schorn 2010; Timerbulatov *et al*. 2012; Nathan *et al*. 2016; Lopez-Picado *et al*. 2017).

Thus, oscillometric and hemodynamic parameters are closely correlated with each other. A drop in BCV is the cause of a decrease in tissue blood supply and extensive cellular dysfunction. It is the decrease in tissue perfusion that is the equivalent of a state of shock (Vincent and De Backer 2013; Nathan *et al*. 2016).

Hemorheological disorders are especially dangerous with consequences in the field of microcirculation of organs and tissues leading to ischemic lesion, as well as the risk of bleeding at the level of the microcirculatory bed (Wiseman *et al*. 2013; Gil 2019; Tyutyumova *et al*. 2019). Thrombocytopenia and a marked increase in the spontaneous aggregation ability of platelets were found. A decrease in platelets in circulation indicated their release into blood clots – "consumption thrombocytopenia". Such a symptom is part of the DIC syndrome, which, together with the state of shock, forms a "vicious circle" (Bhagavan and Ha 2011; Dubova 2016; Levi 2018; Saini and Dunn 2019).

The development of DIC syndrome is confirmed by special markers of the process: an increase in the level of SFMC, FDP, D-dimer against the background of reliable hypofibrinogenemia (Bhagavan and Ha 2011; Wiseman *et al*. 2013; Gil 2019; Roshal and Gil 2019; Saini and Dunn 2019; Tyutyumova 2019; Dubova *et al*. 2020). Multidirectional shifts in the coagulation tests of APTT and PT characterize the stage of "consumption coagulopathy" of the DIC syndrome (Levi 2018, Saini and Dunn 2019).

Thus, based on the data obtained, the condition of dogs with acute spontaneous babesiosis is characterized as stage II shock, subcompensated, with a tendency to decompensation, against the background of the stage of coagulopathy and DIC syndrome.

Given the threat of an increase in the process, the severe prognostic status of the shock state, there is a need for urgent intensive care measures. The primary task is to restore adequate tissue perfusion and the volume of circulating blood in the shortest possible time, which is vital. Such an event is infusion therapy with plasma replacement solutions (Langer *et al*. 2014; Hahn 2017; Lewis *et al*. 2018).

Colloidal solutions are the most effective for achieving these goals. *Rheopolyglucine*, a 10% colloidal solution of dextran ($C_6H_{10}O_5$) with a molecular weight of 30000–40000, was used in our studies. The animals of the two experimental groups were also administered *Persantine* as a vasodilator and antiplatelet agent capable of influencing the aggregation properties of platelets and erythrocytes, as well as having a vasodilating effect, especially at the level of microcirculation vessels of organs. The I investigated group of animals received the drug intramuscularly and the II group – intravenously mixed with *Rheopolyglucine* in a ratio of 10:90, respectively The doses of the drugs used were calculated taking into account the mutual potentiation of the antiaggregational effect of both drugs in the mixture (Barkagan 2005; Barkagan and Momot 2008; Liu *et al*. 2013; Wang *et al*. 2018; Wang *et al*. 2019).

According to the instructions for the preparation, the compatibility of infusion media during mixing was tested experimentally. Reactions from the mixture of *Rheopolyglucine* and *Persantine* preparations in the form of a change in the structure of the solution had not been established. Allergic reactions to the introduction of the mixture in sick dogs were not observed. Taking into account the potential of the action of both drugs and the possibility of hypotension, regular monitoring of blood pressure was carried out.

The results obtained during a clinical trial of different methods of drug administration showed that a mixture of colloidal solution *Rheopolyglucine* and vasodilator-disaggregant *Persantine* showed the best results in restoring hemodynamic and hemorheological parameters, which reached physiological indicators 48 hours after the start of treatment. At the same time, the separate administration of drugs also made it possible to achieve the restoration of parameters but a day later. Only hemodynamic parameters of Ht and SCBV were restored synchronously with both drug regimens.

Colloidal solution *Rheopolyglucine* is not a complete blood substitute as it is not able to carry oxygen but is able to normalize BCV (Annane *et al*. 2013; Hahn 2017; Lee and Kim 2013; Monteiro 2017). It is especially important to restore blood flow in areas of microcirculation (Vincent and De Backer 2013), in which colloidal solutions have an undoubted advantage in contrast to infusion solutions of other groups (Lee and Kim 2013; Langer *et al*. 2014). Since it is this solution that is important for the restoration of hemodynamic parameters, in both groups there is almost the same degree of restoration of the parameters of the volume of circulating blood. The mechanism of its action is realized largely due to the large molecular weight. Due to this, fluid returns from

interstitial edema to the bloodstream (Lee and Kim 2013). In addition, due to the viscosity of the solution, the effect of lubricating the endothelium of the vessel and restoring its elasticity is created (Lee and Kim 2013).

The use of vasodilators and antiplatelet agents is necessary to stop thrombosis as one of the components of the DIC syndrome (Bhagavan and Ha 2011; Liu *et al*. 2013; Wang *et al*. 2018; Wang *et al*. 2019), which is an element of the vicious circle of shock. *Persantine* and other Dipyridamole-based drugs are widely used in humane medicine to achieve these goals. The combined use of *Rheopolyglucine* and *Persantine* mutually potentiates the effect of vasodilation and disaggregation (Annane *et al*. 2013; Wang *et al*. 2018; Allahham *et al*. 2021), therefore, in our clinical trials, we achieved the effect a day earlier than with separate administration of drugs. Due to the effect of disaggregation of dipyridamole, blood clots were reduced directly in the bloodstream at the level of microcirculation (Liu *et al*. 2013). Due to the restoration of the biophysical parameters of the vascular endothelium, the consumption of shaped blood elements (platelets, erythrocytes) stops (Annane *et al*. 2013; Liu *et al*. 2013). The spontaneous aggregation ability of platelets returns to physiological values. The platelet content in the blood is normalized. This condition contributes to the restoration of tissue perfusion and the elimination of shock (Annane 2013; Allahham *et al*. 2021).

Since the first link of hemostasis - vascular-platelet - is restored to physiological values, respectively, the stimulation of the blood coagulation process stops (Gil 2019; Tyutyumova *et al*. 2019). The markers of the DIC syndrome return to the reference values, thus determining the cessation of the development of hemostasiopathy - DIC syndrome as one of the participants in the vicious circle of shock.

Based on the above, the advantage of using a mixture of colloidal solution *Rheopolyglucine* and vasodilator-disaggregant *Persantine* for accelerated and adequate recovery of animals that have suffered grade II shock with a pronounced tendency to grade III as a result of complications of acute spontaneous babesiosis of dogs is obvious. In severe pathological processes, such as shock and DIC syndrome, the time factor for the elimination of these processes and their consequences plays an extremely important role.

Conflict of interest: The authors declare that there is no conflict of interest related to this article.

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