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Strong monovalent electrolyte imbalances in serum of dogs infected with *Babesia canis*

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ABSTRACT

Canine babesiosis is a systemic tick-borne protozoan disease caused by infection with parasites of the genus *Babesia*. Acid–base disorders and ion imbalances have been described in dogs infected with *Babesia rossi* in South Africa. In this paper, the authors describe changes to monovalent ion concentrations and calculated parameters of monovalent ions in 70 dogs naturally infected with *B. canis*, a species occurring in Europe. Hyponatraemia, hypokalaemia, hyperchloraemia, decrease of chloride gap, strong ion gap, difference between sodium and chloride concentrations, and an increase of chloride-to-sodium and sodium-to-potassium ratios were the most prevalent changes. Hyponatraemia, hypokalaemia and hyperchloraemia were detected less frequently than in dogs infected with *B. rossi*, but the severity of these changes were similar. Comparison of monovalent ion concentrations in azotaemic and non-azotaemic, and anaemic and non-anaemic dogs infected with *B. canis* showed that azotaemic dogs had significantly lower sodium concentrations. The results of this study indicate a possible development of hyperchloraemic acidosis and the probable contribution of aldosterone in the development of hypokalaemia. However, further study on blood gas, aldosterone, and antidiuretic hormone in dogs infected with *B. canis* is needed.

Introduction

Canine babesiosis is a protozoan disease caused by infection with tick-borne parasites of the genus *Babesia*. There are 5 species of this genus that infect dogs, i.e., *B. canis*, *B. vogeli*, *B. rossi*, *B. gibsoni*, and *B. conradae*. The 3 former species are large forms and the 2 latter species are small forms of *Babesia*. The most severe form of babesiosis is caused by infection with *B. rossi*, while *B. vogeli* is considered the least pathogenic (Irwin, 2009). Among canine *Babesia* species, only *B. canis* has been detected in dogs in Poland (Adaszek and Winiarczyk, 2008; Welc-Falęciak et al., 2009; Zygner et al., 2009). This species causes moderate to severe forms of canine babesiosis (Irwin, 2009).

The prevalence of canine babesiosis caused by *B. rossi* in South Africa, where *Haemaphysalis elliptica* (the only known vector of *B. rossi*; formerly misidentified as *H. leachi*) were the most common tick species infesting dogs, was about 12% in sick dogs presented to the Onderstepoort Veterinary Academic Hospital. Infection with *B. rossi* leads to acute forms of the disease in dogs, and mortality rates in South Africa amounted to 12%. However, wild canids in Africa infected with this pathogen did not develop clinical signs of the disease (Penzhorn, 2011). Penzhorn (2011) hypothesized that domestic dogs, as exotic animals to Africa, are more susceptible to infection with *B. rossi* (African canine *Babesia* species) than African wild canids. According to Penzhorn (2011), domestic dogs had not sufficient time to adapt to *B. rossi* infection. In Europe, in areas endemic for *Dermacentor reticulatus* ticks (the main vector of *B. canis*), DNA of *B. canis* was detected in 4.6–27.8% of dogs presented to veterinary clinics (Duh et al., 2004; Torina and Caracappa, 2006; Zygner et al., 2009). Although canine babesiosis caused by *B. canis*, when compared to the 2 other large *Babesia* species, is considered to be of intermediate severity, subclinical infection with *B. canis* was detected in dogs in one study in Poland (Welc-Falęciak et al., 2009).

Schetters et al. (1997) observed differences between the levels of parasitaemia between dogs infected with *B. rossi* (parasitaemia higher than 1%) and *B. canis* (parasitaemia lower than 1%) and a correlation with anaemia and severity of the disease. Moreover, some complications of the disease caused by *B. rossi*, such as hypoglycaemia, hyperlactataemia, and rapid intravascular haemolysis, have been associated with disease severity (Jacobson, 2006). Böhm et al. (2006) also showed that high parasitaemia was significantly

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associated with mortality in dogs infected with *B. rossi*. In dogs infected with *B. canis*, the level of parasitaemia is significantly lower (Schetters et al., 1997). Thus, the level of parasitaemia seems to be one of the reasons for the much more severe course of the disease caused by *B. rossi* in dogs. However, in dogs infected with *B. canis* there has been no correlation observed between levels of parasitaemia and the severity of the disease and anaemia (Schetters et al., 1997; Furlanello et al., 2005; Zygner et al., 2011).

The severity of the disease depends on the *Babesia* species and also on the immune status of the host (Schoeman, 2009). The immunological response, and probably, overproduction of TNFα, which is observed in bovine, human, and mouse babesiosis and in similar diseases, i.e., human and mouse malaria (Clark and Jacobson, 1998; Clark et al., 2004; Kontaş and Salmanoğlu, 2006), leading to hypotension, hypoxia, and septic shock, plays the most important role in the pathogenesis of canine babesiosis. Immunopathological mechanisms during the course of the disease result in systemic inflammatory response syndrome, multiple organ dysfunction syndrome, haemolysis, and other complications (Jacobson, 2006; Matijatko et al., 2009; Máthé et al., 2006). Injury of the liver, kidney, lungs, pancreas, heart, and brain has been described during the course of canine babesiosis. Clinical signs of the disease include: fever, anorexia, apathy, oliguria, haemoglobinuria, vomiting and diarrhoea, dehydration and hypotension, icterus, pale mucous membranes, splenomegaly, and dyspnea (Jacobson, 2006; Máthé et al., 2006). These complications lead to acid–base disturbances and changes in monovalent ion concentrations in the serum of affected dogs (Leisewitz et al., 2001). However, study of serum electrolyte concentrations have been performed only in dogs infected with *B. rossi*. The fact that renal injury, hypotension, and consequently haemodilution, is also observed in dogs infected with *B. canis* suggests that hyponatraemia, hypokalaemia, and hyperchloraemia should also be present in these dogs (Máthé et al., 2006; Matijatko et al., 2009; Schetters et al., 2009). These changes may not only result from haemodilution and/or renal insufficiency, but also from acid–base disturbances (DiBartola, 2006a; DiBartola and De Morais, 2006; Leisewitz et al., 2001).

The objectives of this study were to evaluate strong monovalent electrolyte changes in the serum of dogs infected with *B. canis* (formerly *B. canis canis*) and to assess association of these changes with azotaemia and anaemia. The obtained results allowed for comparisons to be drawn with a similar study on dogs infected with *B. rossi* (formerly *B. canis rossi*) conducted by Leisewitz et al. (2001).

Materials and methods

Study design

From March 2009 to June 2011, 70 samples of whole blood and serum from dogs infected with large *Babesia* were collected (group A). All infected dogs had been presented to the Center of Small Animal Health Clinic Multiwet in Warsaw with clinical signs of babesiosis. Observed clinical signs in these dogs were as follows: lethargy, decreased appetite, fever or decreased temperature, pale mucous membranes, dehydration, vomiting, diarrhoea, and dark-brown urine. Clinical examination included: temperature measurement, cardiac and pulmonary auscultation, assessment of the pulse quality, mucous membranes examination, abdominal and superficial lymph nodes palpation, and estimation of dehydration percentage. Hydration status estimation was based on the skin turgor, mucous membrane moisture, capillary refill time, position of the eyes in their orbits, heart rate, and character of the pulse according to Silverstein (2009). All dogs had acute severe babesiosis and required hospitalization. Infection with parasites of the genus *Babesia* was initially diagnosed by capillary blood smear examination stained with Giemsa. In all these cases, large babesiae were detected. Blood samples were collected prior to treatment, within 1–3 days of disease commencement. The first day of disease was considered as the first day the dog presented with lethargy. Exclusion criteria were as follows: any drug therapy in the preceding 4 weeks (including dogs misdiagnosed with babesiosis), known concurrent disease or infection, history of travelling abroad in the preceding one year, and detected lipaemia. Haemolysis was not considered as an exclusion criterion because of its minimal influence on monovalent electrolyte changes, especially potassium, in dogs (Stockham and Scott, 2008). The inclusion criteria were: diagnosis of babesiosis and collection of blood samples for analysis prior to treatment.

Twenty clinically healthy dogs (10 males and 10 females; 3 beagles, 5 German shepherds, 4 Labradors, 8 mixed-breed dogs; 2–5 years and 7 months of age) were used as the control group (group B). These dogs were brought to the veterinary clinic for vaccination against rabies, or canine distemper, parvovirus, and infectious canine hepatitis. The dogs were examined, and all had good appetites, were in good condition, and had no clinical signs of any disease. Samples of whole blood and serum from these dogs were also collected.

Serum and blood analysis

Ethylenediamine tetraacetic acid (EDTA) was used as an anticoagulant. Serum was obtained by the centrifugation of blood samples without an anticoagulant. Sodium (Na^+), potassium (K^+), and chloride (Cl^-) concentrations in serum samples were determined by a clinical chemistry analyser (Rapidchem 744, Siemens Healthcare Diagnostics). Obtained results allowed calculation of parameters such as corrected chloride concentration ($[Cl^-]$ corr. = ($[Cl^-]$ in dog × 146/$[Na^+]$ in dog)]; where 146 is the normal mean sodium concentration in dogs), chloride gap ($[Cl^-]$gap = 110 − $[Cl^-]$corrected; where 110 is the normal mean chloride concentration in dogs), the difference between sodium and chloride concentrations ($[Na^+] - [Cl^-]$), chloride-to-sodium ratio ($[Cl^-]/[Na^+]$), sodium-to-potassium ratio ($[Na^+]/[K^+]$), and strong ion gap (SIG = $[Na^+] + [K^+] - [Cl^-]$), according to De Morais and Leisewitz (2006), and De Morais and Constable (2006). These parameters were calculated for various reasons. Corrected chloride concentration was calculated because chloride concentration may be affected by water balance (thus, sodium concentration changes, too). Chloride parameters (such as: $[Cl^-]$gap, $[Na^+] - [Cl^-]$, and $[Cl^-]/[Na^+]$) were calculated in order to estimate the contribution of chloride in base excess, and SIG changes indicate changes in unmeasured strong ions (e.g. lactate). Effective extracellular fluid osmolality (ECF) was calculated according to Wellman et al. (2006) using the formula:

$$\text{Eff. ECF Osm.} = 2 \times [Na^+]\,(\text{mEq/L}) + \frac{[\text{glucose}\,(\text{mg/dL})]}{18}$$

where milliequivalent weight is millimolecular weight multiplied by the valence; mEq/L = mmol/L × valence.

Blood urea and creatinine concentrations in serum samples, albumin and glucose concentrations, and in healthy dogs liver enzyme activities, were determined by a clinical chemistry analyser (XL 640, Erba Mannheim, Germany). Dogs with both blood urea and creatinine concentrations above reference intervals were considered as azotaemic, as according to Chew et al. (2011). Complete blood counts (CBC) were determined by an automatic haematological analyser (Diatron®, Abacus). Red blood cell morphology and leukocyte count were performed with a microscope using peripheral blood smears stained with Giemsa. Dogs with at least 2 out of 3 parameters below reference intervals were considered as anaemic (haematocrit lower than 0.37 L/L, red blood cell count lower than