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RESEARCH NOTE

Increased serum urea to creatinine ratio and its negative correlation with arterial pressure in canine babesiosis

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Abstract

The increase of the serum urea to creatinine ratio (UCR) was observed in dogs infected with *Babesia canis*. Previous studies have suggested that decrease of blood pressure can be one of the reasons for this phenomenon. In this work statistically significant increase of the UCR was observed in dogs with babesiosis. Comparison of the UCR between 23 azotaemic dogs and 25 non-azotaemic dogs infected with *Babesia canis* showed statistically significantly higher mean of the UCR in azotaemic dogs. Correlations between UCR and systolic, diastolic and mean arterial pressure (SAP, DAP and MAP) in 48 dogs infected with *B. canis* were negative (UCR and SAP : $r = -0.3909$; UCR and DAP: $r = -0.3182$; UCR and MAP: $r = -0.3682$) and statistically significant ($p < 0.05$). This result may indicate contribution of hypotension in the increase of the UCR in canine babesiosis. However, the correlations were not high, and there was no statistically significant correlation between UCR and arterial pressures in azotaemic dogs. Thus, it seems that decrease of blood pressure in dogs with babesiosis explains only partially the cause of increased UCR in infected dogs. The other authors suggested hyperureagenesis and myocardial injury as a potential reason for the increased UCR in canine babesiosis. Thus, further studies are needed to determine causes of increased UCR in dogs with babesiosis, especially on the connection between UCR changes and the concentrations of plasma cardiac troponins and ammonia, and the occurrence of occult blood on fecal examination.

Keywords

Azotaemia, *Babesia canis*, blood pressure, canine babesiosis, serum urea to creatinine ratio

Babesiosis is a disease caused by the infection with parasites of the genus *Babesia*. Acute renal failure is observed in dogs infected with *Babesia canis*, *B. rossi*, *B. vogeli* or *B. gibsoni* (Defauw *et al.* 2012, Matijatko *et al.* 2012, Schoeman 2009). Amongst these species *B. rossi* is the most virulent and *B. vogeli* has the lowest pathogenicity (Schoeman 2009). Serum urea to creatinine ratio (UCR) is one of tools used in the differentiation between pre-renal and renal azotaemia in human medicine. Higher UCR was observed in humans with pre-renal azotaemia in comparison with patients with acute renal failure (Morgan *et al.* 1977). The increase of the UCR was detected in dogs infected with *B. rossi* in South Africa (Lobetti 2012). De Scally *et al.* (2006) suggested that increase of this parameter in canine babesiosis may result from hypotension the latter reported in canine babesiosis (Jacobson *et al.* 2000, Zygner and Gójska-Zygner 2014).

The current work is a continuation of previous research on the correlation between decreased blood pressure and azotaemia in dogs with babesiosis (Zygner and Gójska-Zygner 2014). In this study the authors have compared the UCR in dogs infected with *B. canis* and investigated the connection between the value of the UCR and systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and mean arterial pressure (MAP) in infected dogs.

In previous study (Zygner and Gójska-Zygner 2014), samples of the blood and serum were collected from 48 dogs infected with *B. canis* (group A) and 33 healthy dogs as a control group (group B). All blood samples were collected before any treatment during the first visit in the clinic. The results of that study showed lower blood pressures (SAP, DAP and MAP) in infected dogs in comparison to healthy dogs, and negative correlations between blood pressures (SAP, DAP and MAP) and

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serum concentrations of urea and creatinine in infected dogs (Zygner and Gójska-Zygner 2014). The values of statistics with ranges for blood pressures and serum urea and creatinine concentrations were presented in the previous work (Zygner and Gójska-Zygner 2014). Concentrations of serum urea and creatinine were determined (in mg/dL for both parameters) using a clinical chemistry analyser (XL 640, Erba Mannheim, Germany). Dogs with both serum urea and creatinine concentrations above reference intervals were considered azotaemic. Group A was subdivided into 2 subgroups: 23 azotaemic dogs (A1) and 25 non-azotaemic dogs (A2). Infection in group A was diagnosed by blood smear examination stained with Giemsa and confirmed by the PCR method. Blood pressures (SAP, DAP and MAP; three readings in each dog) were measured (in mmHg) in all dogs using non-invasive oscillometric technique (Cardell veterinary monitor 9405, Midmark, USA) during the first visit in the Multiwet clinic (in the same room) before blood sample collection and treatment. The results were analysed using program Statistica 10. Shapiro–Wilk's W test was used for the estimation of normality in the distributions of UCR, SAP, DAP and MAP values in groups A and B, and subgroups A1 and A2. Levene's test for homogeneity of variances in groups with normal distribution was used. Mann-Whitney U test (lack of normal distribution in at least one of 2 compared groups) was used to compare the values of the UCR between groups A and B. Cochran–Cox test (t-test with a separate estimation of variances; normal distributions in both groups and difference between variances) was used to compare the values of the UCR between subgroups A1 and A2. Spearman's rank correlations between the values of UCR and SAP, DAP and MAP in group A, between the values of the UCR and SAP in subgroups A1 and A2, and between the UCR values and DAP values in subgroup A1 were calculated. Pearson's correlations between the values of the UCR and MAP in subgroups A1 and A2, and between the values of the UCR and DAP in subgroup A2 were calculated. The value of $p < 0.05$ was considered significant.

Shapiro–Wilk's W-test for normality in the values of UCR showed a lack of normal distribution in group A ($N = 48$, $W = 0.8895$, $p = 0.0003$). The distribution of the UCR values was normal in group B ($N = 33$, $W = 0.9875$, $p = 0.9618$), and subgroups A1 ($N = 23$, $W = 0.9408$, $p = 0.1868$) and A2 ($N = 25$, $W = 0.9712$, $p = 0.6751$). Levene's test for homogeneity of variances with normal distribution of the UCR values in subgroups A1 and A2 showed non-homogeneous variances ($F = 13.9925$, $p = 0.0005$). The distribution of the SAP and DAP in group A was not normal (SAP: $N = 48$, $W = 0.9479$, $p = 0.0331$; DAP: $N = 48$, $W = 0.9511$, $p = 0.0445$) and

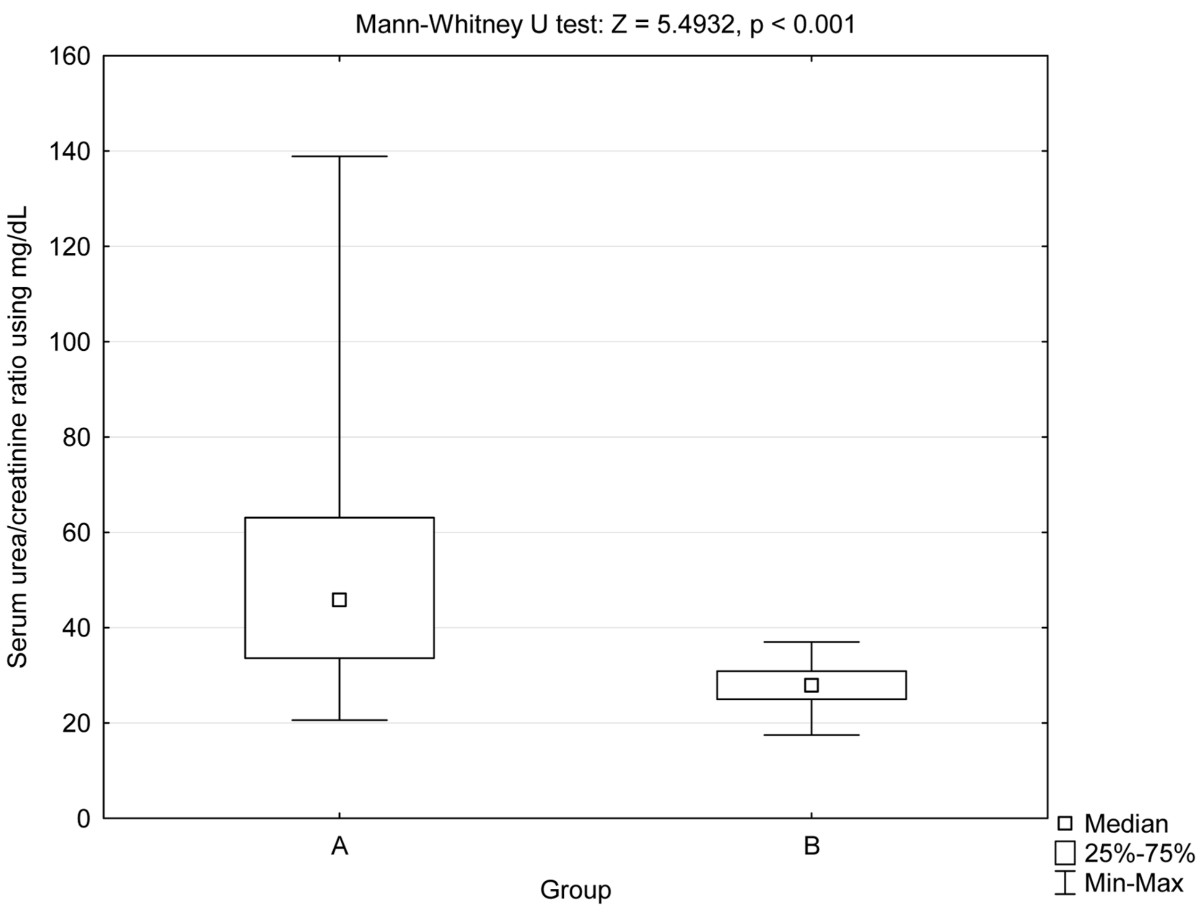

Fig.1. Comparison of serum urea to creatinine ratio between 48 dogs infected with *B. canis* (group A) and 33 healthy dogs (group B).

the distribution of the MAP in group A was normal ($N = 48$, $W = 0.9602$, $p = 0.1025$). The distribution of the SAP and DAP in subgroup A1 was not normal (SAP: $N = 23$, $W = 0.8991$, $p = 0.0243$; DAP: $N = 23$, $W = 0.8680$, $p = 0.0059$) and the distribution of the MAP in subgroup A1 was normal ($N = 23$, $W = 0.9507$, $p = 0.3032$). The distribution of the SAP was not normal in subgroup A2 ($N = 25$, $W = 0.8941$, $p = 0.0136$) and the distribution of the DAP and MAP in subgroup A2 was normal (DAP: $N = 25$, $W = 0.9698$, $p = 0.6411$; MAP: $N = 25$, $W = 0.9302$, $p = 0.0877$).

Medians of the UCR (using mg/dL) in groups A and B amounted to $M_A = 45.85$ (25th% – 75th%: 33.6 – 63.1; Min. – Max.: 20.6 – 138.9) and $M_B = 27.9$ (25th% – 75th%: 25 – 30.9; Min. – Max.: 17.5 – 37), respectively. Comparison of the UCR values between group A and B showed statistically significantly higher median in group A (Fig. 1). Means of the UCR (using mg/dL) in subgroups A1 and A2 amounted to $\bar{x}_{A1} \pm S.D._{A1} = 70.3 \pm 24.3$ (Min. – Max.: 27.7 – 138.9) and $\bar{x}_{A2} \pm S.D._{A2} = 35.044 \pm 8.2$ (Min. – Max.: 20.6 – 52.5), respectively. Comparison of the UCR values between subgroup A1 and A2 showed statistically significantly higher mean in subgroup A1 (Fig. 2). Correlations between UCR and SAP, DAP and MAP in 48 dogs infected with *B. canis* (group A) were negative and statistically significant (Table I). There were no correlations between UCR and blood pressures (SAP, DAP and MAP) in subgroups A1 and A2 (Table I).

A significantly higher serum UCR in infected dogs probably resulted from pre-renal azotaemia what was suggested in previous studies (De Scally *et al.* 2006). Moreover, Lobetti (2012) showed that haemolysis had no influence by interference in analysis of creatinine concentration on the increase of the UCR in dogs infected with *B. rossi*. The current study showed statistically significant negative correlations between UCR and blood pressures in infected dogs. This result may indicate contribution of hypotension in increase of UCR in dogs with babesiosis, what was suspected by De Scally *et al.* (2006) in previous study. However, the correlations observed in dogs from group A were not high. Moreover, there were no statistically significant correlations between UCR and blood pressures in azotaemic dogs infected with *B. canis*. Thus, it seems that decrease of blood pressure in dogs with babesiosis explains only partially the cause of increased UCR in infected dogs, and there should be other reasons for this phenomenon. De Scally *et al.* (2006) and Lobetti (2012) suggested hyperureagenesis resulted from ammonia loading as a result of haemolysis or gastrointestinal haemorrhage as an explanation

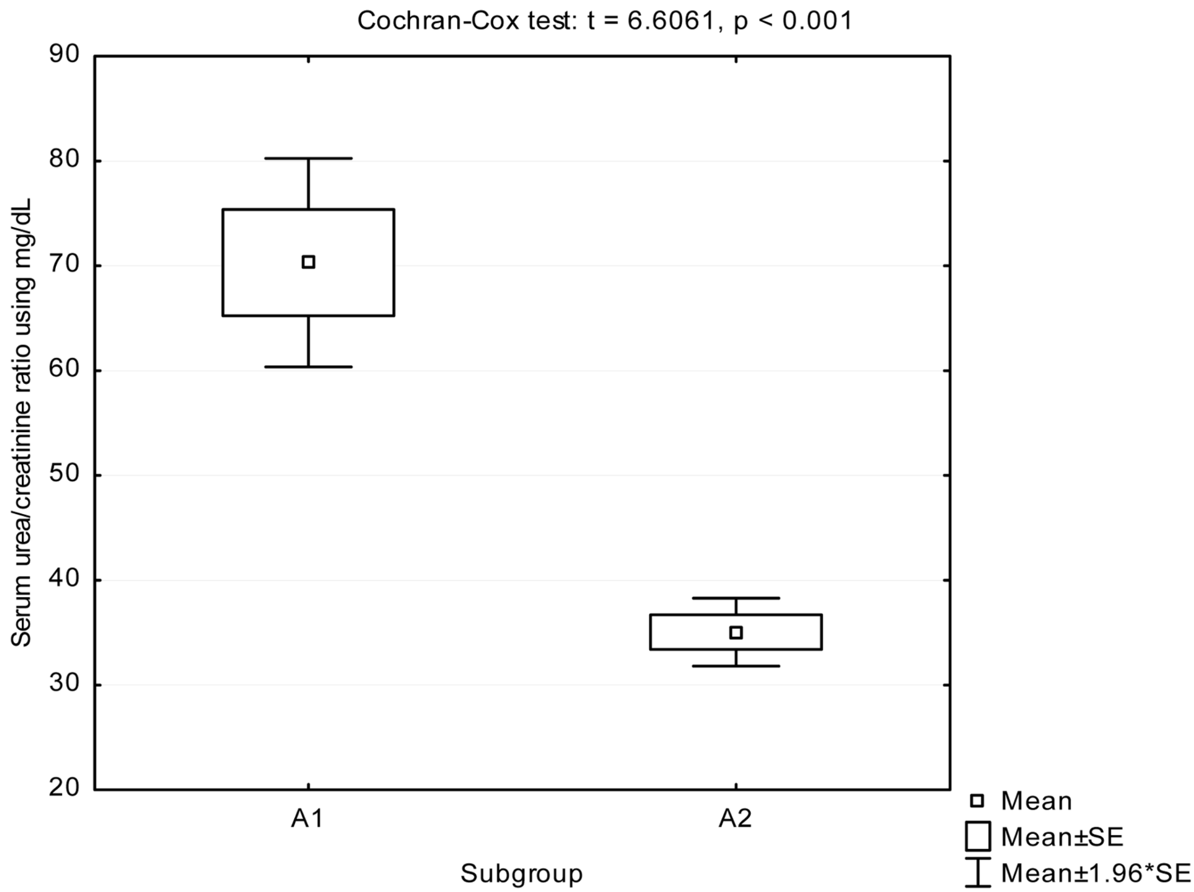

Fig. 2. Comparison of serum urea to creatinine ratio between 23 azotaemic dogs infected with *B. canis* (subgroup A1) and 25 non-azotaemic dogs infected with *B. canis* (subgroup A2)

Table I. Correlations between serum urea to creatinine ratio and arterial pressures in group A and subgroups A1 and A2

Correlation		Group or Subgroup	*r*	*p*	*N*
UCR	SAP	A	–0.3909 (S)	0.006*	48
		A1	–0.2185 (S)	0.316	23
		A2	–0.0509 (S)	0.809	25
	DAP	A	–0.3182 (S)	0.027*	48
		A1	–0.0712 (S)	0.747	23
		A2	–0.0946 (P)	0.653	25
	MAP	A	–0.3682 (S)	0.010*	48
		A1	–0.1447 (P)	0.510	23
		A2	–0.1895 (P)	0.364	25

A1 – subgroup of azotaemic dogs infected with *B. canis*, A2 – subgroup of non-azotaemic dogs infected with *B. canis*, UCR – serum urea to creatinine ratio, SAP – systolic arterial pressure, DAP – diastolic arterial pressure, MAP – mean arterial pressure, *r* –Spearman's (S) or Pearson's (P) correlation coefficient, *p* – a value of *p*, *N* – number of dogs, * – statistically significant result.

for the increase of UCR in canine babesiosis. Lobetti (2012) also suggested that observed in canine babesiosis cardiac injury (Dvir *et al.* 2004, Lobetti *et al.* 2002) may contribute in the increase of UCR in infected dogs.

Lack of correlations between the UCR and blood pressures in azotaemic dogs may also result from the fact that part of these dogs had probably renal azotaemia, what was observed in previous works (Defauw *et al.* 2012, Zygner *et al.* 2013). Thus, significantly higher increase of serum creatinine concentration in comparison to increase of urea concentration in dogs with acute renal failure may cause decrease of the UCR value.

Further studies are needed to determine causes of increased UCR in dogs with babesiosis, especially on the connection between UCR changes and the concentrations of plasma cardiac troponins and ammonia, and the occurrence of occult blood in fecal examination.

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