VETERINARSKI ARHIV 84 (6), 575-589, 2014

The concentrations of the inflammatory markers the amino-terminal portion of C-type pronatriuretic peptide and procalcitonin in canine babesiosis caused by *Babesia canis*

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BRKLJAČIĆ, M., M. TORTI, J. PLEADIN, V. MRLJAK, I. ŠMIT, I. KIŠ, I. MAYER, M. CRNOGAJ, V. MATIJATKO: The concentrations of the inflammatory markers the amino-terminal portion of C-type pronatriuretic peptide and procalcitonin in canine babesiosis caused by *Babesia canis*. Vet. arhiv 84, 575-589, 2014.

ABSTRACT

Canine babesiosis is a multisystemic protozoan disease, considered as sepsis with a wide range of clinical signs, which can result in various outcomes, from mild to fatal. In veterinary medicine there are still no specific biomarkers for sepsis, therefore the aim of this study was to investigate markers widely used in human medicine, but poorly in veterinary medicine and never in canine babesiosis. Ninety-seven dogs were included in this study, among which 72 were diagnosed for babesiosis and 25 were healthy and used as the control group. Concentrations of procalcitonin (PCT) and the amino-terminal portion of C-type pronatriuretic peptide (NT-pCNP) were determined for each dog. There was a significant difference in PCT concentrations between the healthy and the babesiosis group before and after the antibabesial treatment, but there were no significant differences between the dogs that survived and the dogs that died. In contrast, there was no significant difference in NT-pCNP concentrations between the healthy and babesiosis groups before and after the antibabesial treatment, but there were significant differences between the dogs that survived and the dogs that died. It may be concluded that as in human medicine, PCT is most probably a good marker for both detection and grading of SIRS complications developed only in bacterial induced systemic infections, whereas NT-pCNP can be considered a good prognostic pro-inflammatory marker of outcome in canine babesiosis.

Key words: babesiosis, dog, inflammatory marker, C-type pronatriuretic peptide, procalcitonin, outcome

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ISSN 0372-5480
Printed in Croatia

Introduction

Canine babesiosis is a multisystemic protozoan and potentially fatal disease. Dogs can be infected with a wide range of *Babesia* species (BECK i sur., 2009). The vast majority of canine babesiosis in Croatia is caused by *B. canis* (BECK et al., 2009; BRKLJAČIĆ et al., 2010) and it has a wide range of clinical signs, which can result in various outcomes, from mild to fatal (MATIJATKO et al., 2010; MATIJATKO et al., 2012).

The differences in clinical manifestations of babesiosis appear to be the result of the interplay of the parasite-host interactions. A hypothesis that may explain all the different manifestations of the disease is that systemic inflammatory response syndrome (SIRS) and subsequent multiple organ dysfunction syndrome (MODS) provide the underlying pathophysiologic mechanism within which apparently unrelated aspects of babesiosis form a predictable pattern (SCHETTERS et al., 2009). The host response to the infection is a complex process and the pro-inflammatory state of the acute phase response also initiates anti-inflammatory mediators. The extent of the pro- and anti-inflammatory events should be balanced and proportional to the insult (ABBAS et al., 2000).

In veterinary medicine there are still no specific biomarkers for sepsis and therefore many studies are in progress with the goal of finding a reliable diagnostic and prognostic marker of sepsis in various animal species (MATIJATKO et al., 2007; DeCLUE et al., 2011; BRKLJAČIĆ, 2012). In canine babesiosis various biomarkers have already been studied, namely acute phase proteins in cases of canine babesiosis caused by *B. canis* (MATIJATKO et al., 2007) and *B. rossi* (KOSTER et al., 2009). More recently, cytokines were investigated as markers in canine babesiosis (MAYER, 2012).

Procalcitonin (PCT) is a biochemical peptide precursor of hormone calcitonin, and is considered to be the best prognostic marker used to monitor the clinical course and progression of various inflammatory states in humans, especially in cases of SIRS, sepsis and MODS (MEISNER et al., 1999). High concentrations of PCT were detected in patients with malaria, a disease with extremely similar pathogenesis to canine babesiosis. Furthermore, a correlation between concentrations of PCT and the severity of the disease has also been noted (DAVIS et al., 1994; AL-NAWAS and SHAH, 1997; HESSELINK, 2009). PCT is an excellent marker for distinguishing SIRS from sepsis and it has several advantages compared to human C-reactive protein (CRP). Most important of all, PCT has wide range reactivity, which results in a significant rise in its plasma concentrations in severe forms of MODS, as well as in serious systemic inflammations (MEISNER et al., 1999). Therefore, in human medicine PCT is a better and much more precise marker than CRP, whose concentrations usually reach maximum values even in mild or moderate grades of inflammation (MEISNER et al., 1999).

C-type natriuretic peptide (CNP) is expressed primarily by the vascular endothelium and macrophages in response to several stimuli, such as tumour necrosis factor (TNF),

interleukin-1β (IL-1β), or transforming growth factor-β (TGF-β), which are known to play a role in the pathogenesis of sepsis. Furthermore, it has been proven that microbial products directly stimulate production of CNP (SUGA et al., 1993). Therefore, CNP is an interesting biomarker for sepsis, but with questionable clinical use because of its poor stability in peripheral blood (DEL RY et al., 2011).

Recent identification of the amino-terminal (NT) portion of proCNP (pCNP), together with assay development, compensates for all the missing features of CNP, and because of its practical potential it represents a new method for evaluating CNP production. NT-pCNP is a reliable marker of CNP biosynthesis, because they are both produced as well as secreted in equimolar amounts (DEL RY et al., 2011). Compared with CNP, NT-pCNP is a larger molecule with a longer half-life in circulation and does not correlate with other natriuretic peptides, so this all together makes it exploitative for clinical purposes (PRICKET et al., 2001).

The majority of studied biomarkers appeared to be good in differentiating dogs infected with *Babesia* sp. from healthy dogs, but they were unable to predict the outcome of the disease. To our knowledge, both PCT and NT-pCNP have not yet been investigated in canine babesiosis. Therefore, the aim of this study was to investigate these two markers (PCT and NT-pCNP), widely used in human medicine, but sporadically in veterinary medicine, and never in canine babesiosis.

Materials and methods

Ninety-seven dogs were included in this study. Among those, seventy-two had babesiosis, diagnosed at the Clinic for Internal Diseases, Faculty of Veterinary Medicine University of Zagreb. The remaining twenty-five dogs were admitted to the same Clinic either for a routine yearly examination (15 of them) or for antibabesial drug administration (10 of them). In ten of them imidocarb dipropionate (Imizol®, Schering-Plough, Essex Animal Health, Friesoythe, Germany) was administrated for prophylactic purposes (6.6 mg/kg subcutaneously) at the owner's request. Since babesiosis is a very frequent disease in Croatia, despite the numerous tick preventative treatments, many dogs are still being infected with babesiosis, so their owners sometimes request this kind of prophylaxis. Healthy dogs (with clinical and laboratory findings within reference ranges) admitted for a routine yearly check-up, together with dogs preventively treated with Imizol® (also with clinical and laboratory findings in reference ranges), were included in this study as a healthy control group, in order to investigate whether the antibabesial drug has an impact on investigated parameters.

After the first physical examination, samples of blood were taken from v. cephalica antebrachii in EDTA-containing tubes, as well as in tubes without any additive.

Dogs with babesiosis and healthy dogs treated with antibabesial drug were sampled twice, upon admission and 24 hours after antibabesial treatment. Fifteen healthy dogs who were not treated with Imizol® were sampled only once. Haematology and biochemistry profiles, as well as the concentrations of PCT and NT-pCNP, were determined for each dog.

Babesiosis was confirmed by demonstration of the parasite in blood smears stained with May-Grünwald/Giemsa solutions. All the dogs suffering from babesiosis were treated with 6.6 mg/kg of Imizol® just after establishing the diagnosis, together with supportive therapy in those who needed it (crystalloid and colloid fluid therapy, transfusion, antimicrobial drugs etc.).

DNA was extracted from 200 µL of EDTA-treated blood using the DNeasy® Blood and Tissue Kit (Qiagen, Hilden, Germany) according to the manufacturer's instructions in an automatic system for DNA isolation, QIACube® (Qiagen, Hilden, Germany). Amplification of a fragment (~560 bp) of the 18s rRNA gene was obtained using two pairs of primers according to HERWALDT et al. (2003) in nested PCR.

Amplification of longer fragment (1715 bp) was obtained with the forward primer CRYPTO F 5'-AACCTGGTTGATCCTGCCAGTAGTCAT-3' and the reverse primer CRYPTO G 5'-GAATGATCCTTCCGCAGGTTCACCTAC-3'. Amplified DNA was subjected to capillary electrophoresis by QIAExcel (Qiagen, Hilden, Germany) and viewed under UV light. PCR products were purified using a ExoSAP-IT® CLEAN UP (USB, USA) according to the manufacturer's instructions and fully sequenced using an ABI PRISM® BigDyeTM Terminator system and GeneAmp® PCR 2400 (PE Biosystems, USA) with forward primer BAB F 5'- CCCTTCATCGGTGGTAACTT-3' and reverse primer BAB R 5'-GTGGCCACCACTCCCGTGCC-3'. Sequences were assembled using Lasergene® software (DNASTAR, Madison WI, USA) together with the pertaining SeqManTM and EditSeqTM software. Obtained sequences were compared within the Gen Bank procurable sequences in order to identify the *Babesia* species.

Haematology profile was performed using a Horiba ABX Hematology Analyser (Diagnostics, Montpellier, France), while biochemistry profile was performed using an Olympus AU 600 Analyser with original reagents (Olympus Diagnostica GMBH, Hamburg, Germany).

Concentrations of PCT was obtained by the ELISA method using Canine Procalcitonin, PCT ELISA Kit (Wuhan EIAab Science Co. Ltd., China) and the automatic machine ChemWell 2910 (Awareness Technology Inc., USA) by measuring absorbance after adding stop-solution at 450 nm.

Concentrations of NT-pCNP were obtained by the ELISA method using an NT-proCNP kit (Biomedica, Austria) and automatic machine ChemWell 2910 (Awareness Technology Inc., USA) by measuring absorbencies after adding stop-solution at 450

nm. The NT-proCNP assay utilises a highly purified polyclonal sheep antibody directed against aminoacids 1-19 and 30-50 of human NT-proCNP (96% homologous with canine proCNP (http://www.ncbi.nlm.nih.gov/genome/guide/dog; http://blast.ncbi.nlm.nih.gov/Blast.cgi). This kit has already been used in detecting NT-proCNP in dogs (DECLUE et al., 2011).

Statistical analysis. Descriptive statistics was performed according to the usual statistical methods and normality was tested by means of the Kolmogorov-Smirnov test. No distributions were normal so we used the Sign test to test differences between the same animals on two consequent days and the Kruskal-Wallis test to test differences within the same variable but between different groups, according to the severity of the disease (healthy, babesiosis survivors and babesiosis non-survivors). The level of significance was set at $P<0.05$. Correlations between investigated parameters were tested by Spearman rank order (level of significance was set at $P<0.05$). All statistical analyses were performed using the statistical software program Statistica (Statistica 8 for Windows, StatSoft Inc.).

Results

Dogs presented to the Clinic for Internal Diseases of the Faculty of Veterinary Medicine, University of Zagreb, between January 2009 and January 2011 were included in this study and babesiosis was diagnosed in seventy-two dogs during the study period. Among them there were 52 males and 20 females, aged from 6 months to 10 years and of different breeds including mixed breed dogs (n = 26).

Microscopic evaluation of blood smears demonstrated the presence of large (3-5μm), pyriform parasites, namely *B. canis* in erythrocytes of all 72 sick dogs. Sequence analysis confirmed the presence of *B. canis* in all 72 samples tested.

Since there were no significant statistical differences between the two subgroups of healthy dogs (namely those who were pretreated with an antibabesial drug and those who were not), they were joined and observed as one control group (n = 25).

On the day of admission, all the dogs with babesiosis included in this study presented with one or more of the following clinical signs: depression (70/72), anorexia (71/72), pale mucous membranes (44/72), fever (40/72), splenomegaly (35/72) and dark coloured urine (29/72). Among the dogs studied, 4 dogs died and 68 dogs survived babesiosis, so the mortality rate was 5.8%.

On the day of admission, white blood cell count (WBC), platelet count (PLT) and haematocrit (HCT) were significantly lower ($P<0.01$) in dogs with babesiosis compared to the control group. The mean white blood cell count was significantly lower before antibabesial treatment and significantly higher after antibabesial treatment in the babesiosis group, compared to the group of healthy dogs. The mean platelet count showed

Table 1. Biochemical parameters (median ± 2 standard deviations) in healthy dogs and dogs with babesiosis before antibabesial treatment (BT) and after antibabesial treatment (AT).

	Blood urea nitrogen (mmol/L)		Creatinine (μmol/L)		Total proteins (g/L)		Albumin (g/L)		Glucose (mmol/L)		Bilirubin (mmol/L)		Alkaline phosphatase (U/L)	
	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT	BT	AT
Healthy	5.2 ± 2.8	5.2 ± 2.8	91 ± 64.8	93 ± 68.2	66 ± 8.4	69 ± 6.4	28 ± 4.2	29 ± 3.8	5.8 ± 1.1	5.9 ± 1.3	6.1 ± 2.7	6.3 ± 2.4	54 ± 38.2	58 41±6
Babesiosis (survivours)	6.0 ± 11.4	6.5 ± 8.6	87 95.4	88 ± 94.7	58 ± 14.9	55 ± 12.6	26 ± 6.4	25 ± 7.4	5.4 ± 2.2	5.4 ± 1.6	8.8 ± 80.8	6.8 170.6	111 279.2	120 495.4
Babesiosis (non survivours)	47 ± 16.6	64.1 ± 33.1	431 384.8	684 566.4	57 ± 19	36 ± 6	27 ± 7	17 ± 3.0	4,5 ± 0.9	6.2 ± 0.6	295.2 484.8	736.7 324.5	99 ± 27	228 ± 120
Reference ranges	3.3 - 8.3		44 - 140		55 - 75		26 - 33		3.6 - 6.5		0.0 - 8.6		20 - 156	

Reference ranges according to Diagnostic Laboratory of the Clinic for Internal Diseases, Facutly of Veterinary Medicine University of Zagreb

an upward trend from the first day to the second day. There were no significant differences in the studied hematological parameters between the dogs with babesiosis that survived compared to the dogs that died.

Total protein, albumin and blood glucose concentrations and alkaline phosphatase activity were significantly different (P<0.05) in dogs with babesiosis in comparison to the healthy group (Table 1).

Blood urea nitrogen, creatinine and total bilirubin concentrations and alkaline phosphatase activity were significantly different (P<0.05) in dogs that died versus those that survived babesiosis (Table 1).

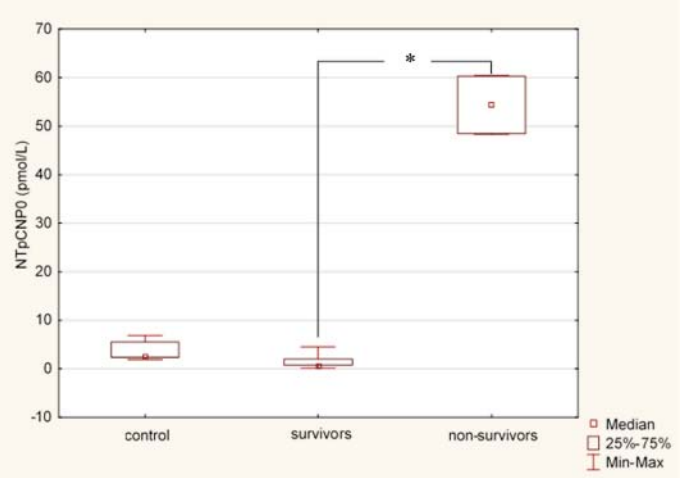

Fig. 1. NT-pCNP concentration (pmol/L) in control group, canine babesiosis survivors group and canine babesiosis non-survivors group before antibabesial treatment (NTpCNP0). *Indicates a significant difference (P<0.05) by the Kruskal-Wallis test. The plots show the median (square within box), 25th and 75th percentiles (box), and range (whiskers).

Table 2. Correlations of investigated parameters with the outcome of babesiosis. (Spearman Rank Order - result was considered as significant for P<0.05).

Investigated parameter	Negative outcome
NT-pCNP before antibabesial treatment	P<0.01; R = 0.991
NT-pCNP after antibabesial treatment	P<0.01; R = 0.888
PCT before antibabesial treatment	P<0.01; R = -0.06
PCT after antibabesial treatment	P<0.01; R = -0.05

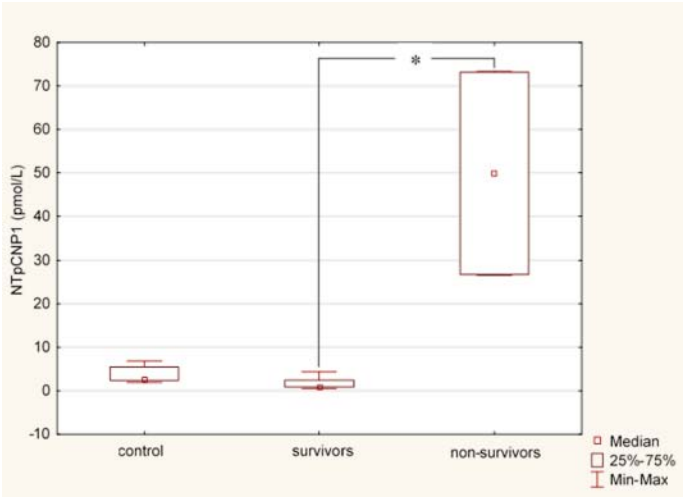

Fig. 2. NT-pCNP concentration (pmol/L) in control group, canine babesiosis survivors group and canine babesiosis non-survivors group after antibabesial treatment (NTpCNP1). *Indicates a significant difference (P<0,05) by the Kruskal-Wallis test. The plots show the median (square within box), 25th and 75th percentiles (box), and range (whiskers).

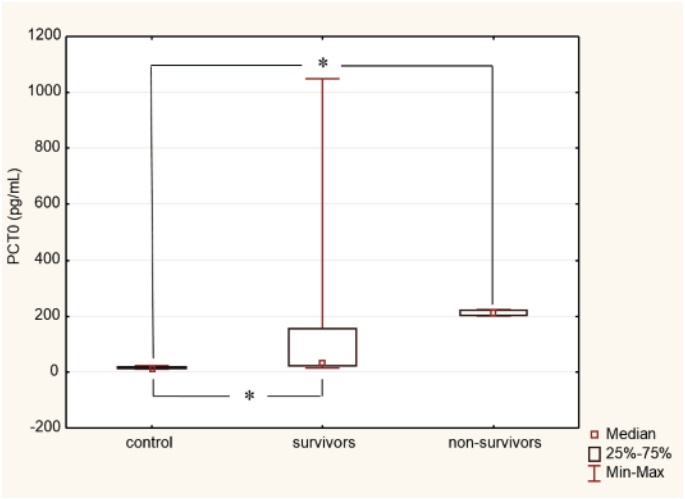

Fig. 3. PCT concentration (pg/mL) in control group, canine babesiosis survivors group and canine babesiosis non-survivors group before antibabesial treatment (PTC0). *Indicates a significant difference (P<0,05) by the Kruskal-Wallis test. The plots show the median (square within box), 25th and 75th percentiles (box), and range (whiskers).

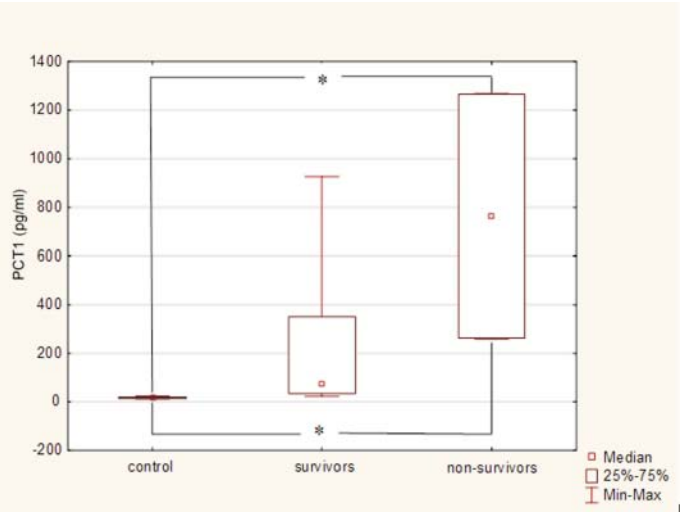

Fig. 4. PCT concentration (pg/mL) in control group, canine babesiosis survivor group and canine babesiosis non-survivors group after antibabesial treatment. * Indicates a significant difference (P<0,05) by the Kruskal-Wallis test. The plots show the median (square within box), 25th and 75th percentiles (box), and range (whiskers).

There was no significant difference in NT-pCNP concentrations between the healthy and babesiosis groups (both survivors and non-survivors) before and after the antibabesial treatment. However, there were significant differences before as well as after the antibabesial treatment in NT-pCNP concentrations between the dogs that survived and the dogs that died (Fig. 1 and Fig. 2).

In contrast, there was a significant difference in PCT concentrations between the healthy and the babesiosis groups (both survivors and non-survivors) before and after the antibabesial treatment, but there were no significant differences before, as well as after the antibabesial treatment in PCT concentrations between the dogs that survived and the dogs that died (Fig. 3 and Fig. 4).

A statistically significant positive correlation was established between both NT-pCNP and PCT concentrations and negative outcome before and after antibabesial treatment (Table 2). There was no statistically significant correlation between NTpCNP and PCT before antibabesial treatment (R = -0.09, P>0.05) or after antibabesial treatment (R = -0.077, P>0.05) in both groups of babesiosis (survivors and non-survivors).

Discussion

Canine babesiosis is an economically important and potentially life-threatening disease which has worldwide distribution, with numerous cases reported throughout the United States, South Africa, Asia and Europe (ANDERSON et al., 1980; LOBETTI, 1998; ZAHLER et al., 2000; CACCIO et al., 2002), and which involves several pathophysiological mechanisms that are still not completely understood (JACOBSON and CLARK, 1994; BOOZER and MACINTIRE, 2003). Until now, *Babesia canis, B. vogeli, Theileria annae, Theileria equi, B. cabali* and *B. gibsoni* have been isolated from dogs in Croatia, with *B. canis* being the most frequent cause of canine babesiosis in Croatia (BECK et al., 2009).

This study included a large number of dogs of more than 30 breeds. Based on hospital records, the breed distribution roughly represents the popularity of breeds in Croatia. Also, in this study there were 52 males and 20 females. This ratio between male and female dogs with babesiosis could be explained by the predominance of male dogs in Croatia, together with the fact that males are usually prone to wandering which increases their exposure to ticks.

Considering the fact that sepsis is defined as SIRS that can be attributed to a confirmed bacterial, viral, fungal or protozoal infection, canine babesiosis, like human *Plasmodium falciparum* malaria can be classified as protozoal sepsis (BONE et al., 1992; JACOBSON et al. 2002; MATIJATKO et al., 2009). SIRS that precedes MODS is caused by excessive release of inflammatory mediators (LOBETTI, 2000).

It is important to be aware that SIRS is an extremely complex phenomenon, and that numerous pro-inflammatory and anti-inflammatory mediators play an important role in its development. Furthermore, their mutual balance is of utmost importance for the outcome of the inflammation, so dysbalance of these mediators results in development of multiple complications, which cannot be viewed as individual occurrences caused by a single event. Thus, development of complications is initiated by numerous factors, so when a complication occurs it is likely that development of several more will follow, which will result in MODS. Since MODS significantly influences the outcome of canine babesiosis (MATIJATKO et al., 2007; MATIJATKO et al. 2009), early recognition of its development, and monitoring its course are crucial.

Since there are many different forms of all kinds of severe diseases that are clinically indistinguishable, high-quality biomarkers for diagnosis and prognosis of canine sepsis are of utmost importance and still searched for (DeCLUE et al., 2011).

Erythrocyte sedimentation rate (ESR) has been routinely used as a non-specific marker in the diagnosis of infections in human medicine (SOX and LIANG, 1986; GABAY and KUSHNER, 1999) since an accelerated ESR is caused by an increased concentration of acute phase proteins, especially fibrinogen (RUHENSTROTH-BAUER et al., 1990). However, the results obtained with the ESR test should be interpreted cautiously because

a reduced haematocrit can increase the ESR. Therefore, it cannot be considered to be an optimal laboratory test for monitoring a haemolytic disease such as canine babesiosis (MATIJATKO et al., 2007). Regarding other haematological tests, the WBC was not demonstrated to be adequate in detecting and monitoring canine babesiosis since it had very low sensitivity (MATIJATKO et al., 2007). Canine babesiosis caused by *B. canis* produces an acute phase response with increased concentrations of acute phase proteins. CRP and SAA demonstrated higher sensitivity in detecting canine babesiosis than traditional inflammatory markers, such as WBC and ESR. Sequential measurement of C-reactive protein and serum amyloid A concentrations proved valuable in monitoring response to antibabesial treatment in uncomplicated canine babesiosis (MATIJATKO et al., 2007). However, CRP concentrations showed no significant difference between uncomplicated and complicated babesiosis and therefore it did not prove useful in predicting the outcome (KOSTER et al., 2009).

NT-pCNP is considered a useful sepsis biomarker in human medicine (PRICKET et al., 2001). It is presumed that NT-pCNP could be important in innate immune response to infection because of its ability to exhibit antimicrobial activity by inhibiting microbial growth, as well as modifying the pathogenicity of microorganisms (VERON et al., 2008). KOCH et al. (2010) investigated the NT-pCNP concentration values in severely ill, both septic and non-septic people, as well as in healthy ones, and noted a large difference between these groups. They also concluded that a decrease in NT-pCNP concentration is usually correlated to a good outcome.

A clinical study conducted on dogs that developed only SIRS and dogs that developed sepsis as a sequel to SIRS, showed that measurement of NT-pCNP concentrations could have great potential in differentiating canine SIRS from sepsis, except in septic peritonitis (DeCLUE et al., 2011). The authors of the aforementioned study did not find NT-pCNP concentrations as a good outcome-predicting marker, since there were no significant differences in NT-pCNP concentrations of dogs that survived compared to dogs that died. In contrast, in our study, the highest concentrations of NT-pCNP were obtained in non-survivors, and were statistically significantly higher than in survivors, but we did not observed significant differences in NT-pCNP concentrations between the dogs with babesiosis and healthy controls. Considering these results, measuring of NT-pCNP concentrations should be thoroughly investigated because high concentrations of NT-pCNP measured in dogs with babesiosis could be in close positive correlation with mortality.

PCT is considered to be an excellent marker of sepsis in human medicine (DAVIS et al., 1994; AL-NAWAS and SHAH 1997; MEISNER, 2000). It is important to note that concentrations of PCT in less severe forms of disease are not so high, but they are higher than in healthy ones. Only a few studies of PCT concentrations in dogs have been

published so far. To our knowledge, there have been only two studies in which canine PCT concentrations were obtained by chemiluminescence assay using LUMItest PCT reagens (BRAHMS Diagnostica GmbH, Hennigsdorf/Berlin, Germany). In one of these studies, it was noticed that there was a significant difference in PCT concentrations between the dogs that developed SIRS and those that did not, but still there was no difference between septic and non-septic dogs (GIUNTI et al., 2006). In another study, by MATIJATKO (2003) there were no significant differences between PCT concentrations in healthy dogs versus dogs with babesiosis. In our study there were no significant differences in PCT concentrations between dogs who survived babesiosis and dogs that died due to babesiosis, but there was a statistically significant difference between PCT concentrations in healthy dogs and dogs with babesiosis (both survivors and non-survivors).

Regarding these results PCT should be considered to be a useful marker in differentiating healthy dogs from dogs with babesiosis, but should not be considered as a good prognostic marker of the outcome of canine babesiosis. On the basis of the aforementioned findings, it can be concluded that PCT is a good marker for differentiation of healthy dogs and dogs that have babesiosis, but it has not proven to be a good prognostic marker and as such cannot be used to predict the outcome of canine babesiosis.

Considering correlations between investigated parameters and the outcome (Table 1) it can be concluded that NT-pCNP is inverse to PCT, and is a good prognostic proinflammatory marker of outcome in canine babesiosis.

Acknowledgements

This research was supported partially by the Ministry of Science, Education and Sports of the Republic of Croatia (Project No. 053-0532266-2220).

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Received: 31 October 2013
Accepted: 11 July 2014

BRKLJAČIĆ, M., M. TORTI, J. PLEADIN, V. MRLJAK, I. ŠMIT, I. KIŠ, I. MAYER, M. CRNOGAJ, V. MATIJATKO: Koncentracije upalnih biljega amino-terminalnog okrajka C-tip pronatrijuretičkog peptida i prokalcitonina u babeziozi pasa uzrokovanoj protozoonom *Babesia canis*. Vet. arhiv 84, 575-589, 2014.

SAŽETAK

Babezioza pasa je multisistemska protozojska sepsa sa širokim rasponom kliničkih znakova od blagih do onih sa smrtnim ishodom. U veterinarskoj medicini još uvijek nisu pronađeni specifični biomarkeri sepse pa je stoga cilj ovog istraživanja bio ispitati markere koji se obilno koriste u humanoj medicini, ali su slabo istraženi u veterinarskoj medicini, a nikada kod babezioze pasa. U ovo istraživanje bilo je uključeno 97 pasa od kojih je u 72 psa dijagnosticirana babezioza dok je preostalih 25 bilo zdravo i korišteno kao kontrolna skupina. Kod svakog psa određene su koncentracije prokalcitonina (PCT) i aminoterminalnog dijela C-tip pronatrijuretičkog peptida (NT-pCNP). Zabilježena je statistički značajna razlika u koncentraciji PCT-a između zdravih pasa i bolesnih pasa prije i nakon antibabezijske terapije, no nije bilo statistički značajne razlike između preživjelih i uginulih. Naprotiv, nije zabilježena statistički značajna razlika u koncentraciji NT-pCNP-a između zdravih i bolesnih pasa, ali je nađena statistički značajna razlika između preživjelih i uginulih. Zaključno, PCT se kao i u humanoj medicini vjerojatno može smatrati dobrim markerom za otkrivanje i stupnjevanje SIRS-a samo u bakterijskim infekcijama, dok se NT-pCNP pokazao kao dobar prognostički marker ishoda babezioze pasa.

Ključne riječi: babezioza, pas, upalni marker, NT-pCNP, prokalcitonin, ishod