P-54

Evaluation of physiological biomarkers as predictive factors and prognosis markers of kidney injury in dogs naturally infected with *Leishmania infantum*

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Background

In South America, especially in Brazil, the agent of zoonotic visceral leishmaniasis affects different species of animals, with a high infection rate in dogs [1]. Kidney function is one of the main impairments among the clinical changes observed in infected animals [2]. Clinical characteristics may vary from an apparent healthy state to severe illness and death, depending on the immune response triggered by the patient [3]. Therefore, early diagnosis of kidney injury is extremely important to improve the patient's prognosis. This study aimed to evaluate physiological biomarkers as predictive factors of kidney injury and prognostic markers for the evolution of the infection in dogs naturally infected by *L. infantum*.

Materials and methods

Medical records of 59 dogs of different breeds, ages, and sexes, infected by *L. infantum* were evaluated at a Veterinary Hospital in Belo Horizonte, Minas Gerais, Brazil. The dogs were classified in the stages suggested by LeishVet, 2011 [4] and had to be under treatment with immunotherapy [5] as suggested by Brasileish, 2019 [6]. Medical records should present parasite examinations for *Leishmania sp.* by direct or molecular identification or titration above 1:160 in the Indirect Fluorescent Antibody Test (IFAT) or sample value four times higher than the cutoff point in the Enzyme-Linked Immunosorbent Assay (ELISA). Dogs that showed signs of dehydration, episodes of vomiting, diarrhea, inappetence, or lower urinary tract disease were excluded from the study. In Trial 0 (T0), we evaluated red blood cells, leukocytes, platelet count, hematocrit, total plasma proteins, plasma globulins (determined by subtracting albumin from total protein), plasma albumin, serum creatinine, serum urea, serum phosphorus, serum symmetrical dimethyl arginine (SDMA), urinalysis, urinary density, urinary protein creatinine ratio (UPC), urinary creatinine, urinary protein, and systemic blood pressure. Six months after T0, 24 dogs returned for clinical and laboratory evaluation. The second medical record analysis was identified as Trial 1. The twenty-four dogs were evaluated through the same exams performed at T0.

Results

Of the thirty-three dogs classified IIa and IIb stages [4] evaluated at T0, on thirteen (39%), UPC was the first biomarker to assess kidney injury to present values above the reference values. SDMA was the first biomarker evaluated to present values above the reference in 6% of the dogs. SDMA and UPC levels increased simultaneously in two dogs (6 %) classified [4] IIa and IIb stages. The correlation of biomarkers evaluated at T0 and T1 (Table 1), platelets (T0) showed a negative correlation with UPC and phosphorus at T1. Urinary density (T0) and UPC (T1) showed a strong negative correlation. Leukocytes (T0) had a moderate correlation with urea (T1). Phosphorus (T0) had a moderate correlation with urinary protein (T1).

Urinary creatinine protein ratio demonstrated advantages compared to the symmetric serum dimethyl arginine for the assessment of renal injury at the time points studied. Furthermore, both analytes did not show significance as a predictive factor or as a prognostic marker in dogs with canine leishmaniosis evaluated in this study.

Table 1: Correlations between the biomarkers studied at T0 and T1 that showed statistically significant.

Biomarker	Trial 0	Biomarker	Trial 1	Correlation	*P*
Urinary Creatinine	T0	Urinary Density	T1	0,73	0,003
Plasma Globulin	T0	Leukocytes	T1	0,48	0,019
Urinary Creatinine	T0	Urinary Protein	T1	-0,71	0,023
Platelets	T0	UPC	T1	-0,69	0,023
Platelets	T0	Urinary Protein	T1	-0,69	0,026
Total Plasma Proterin	T0	Plasma Globulin	T1	0,45	0,027
Urinary Density	T0	UPC	T1	-0,69	0,027
SDMA	T0	Urinary Creatinine	T1	0,68	0,029
Urinary Creatinine	T0	UPC	T1	-0,68	0,03
Leukocytes	T0	Urea	T1	-0,44	0,031
Total Plasma Protein	T0	Leukocytes	T1	0,43	0,031
Platelets	T0	Leukocytes	T1	-0,43	0,036
Phosphorus	T0	Urinary Protein	T1	0,66	0,036
HC	T0	Total Plasma Proterin	T1	-0,42	0,043
Urinary Protein	T0	UPC	T1	0,65	0,043
Platelets	T0	Phosphorus	T1	-0,41	0,048
Systemic Blood Pressure	T0	Leukocytes	T1	0,41	0,049

Conclusions

Platelets were the main physiological biomarker demonstrating value as prognostic markers and predictive factors for kidney injury, showing a significant correlation with biomarkers of kidney injury such as serum phosphorus and urinary protein creatinine ratio. The level of leukocytes, hematocrit, urinary density, and systemic blood pressure also showed significant values as predictive factors for kidney damage and as a prognostic markers in dogs naturally infected by *L. infantum*.

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