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Tei index (myocardial performance index) and cardiac biomarkers in dogs with parvoviral enteritis

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ABSTRACT

Tei index (myocardial performance) and cardiac biomarkers were evaluated in dogs with parvoviral enteritis (PVE). Tei index was calculated as isovolumic contraction time plus isovolumic relaxation time divided by ejection time. Myocardial and skeletal muscle damages were assessed by serum levels of cardiac troponin I (cTnI), creatine (phospho) kinase, lactate dehydrogenase and aspartate aminotransferase. Serum magnesium level was also determined. According to treatment response, dogs were divided into the survivor ($n = 20$) and non-survivor groups ($n = 23$). Seven healthy dogs served as controls. The mean value of the Tei index was higher in non-survivors, compared with survivors ($p < 0.02$) and healthy controls ($p < 0.01$). Serum level of cTnI in non-survivors was higher than that of survivors and controls ($p < 0.05$). Tei index showed the highest sensitivity and specificity to predict mortality. The findings of an elevated Tei index and an increase in serum cTnI are factors associated with a poor prognosis in cases of canine parvovirosis.

1. Introduction

Canine parvovirus (CPV-2) infection causes significant morbidity and mortality in dogs worldwide, despite the presence of vaccine (Hoskins, 1993; Carmichael, 2005). The disease is spread from dog to dog by direct or indirect contact with their faeces. The disease occurs in 3 distinct forms: (1) intestinal form; leucopoenia, vomiting, and severe haemorrhagic diarrhoea in dogs from about 8 weeks of age; (2) cardiac form; nonsuppurative myocarditis and sudden death from respiratory and/or cardiovascular failure in pups 3–8 weeks old; and (3) generalized disease with focal necrosis of many tissues in pups less than 2 weeks old (Lenghaus and Studdert, 1984). During the CPV infection, anaerobic bacteria that normally reside in the intestines can cross into the bloodstream from impaired intestinal mucosa, a process known as translocation, and cause systemic inflammatory response syndrome and sepsis (Turk et al., 1992; Otto et al., 2000; de Laforcade et al., 2003; Prittie, 2004; Otto, 2007; Yilmaz and Senturk, 2007). Myocarditis is reported not only primarily to CPV but also secondarily to sepsis in dogs with PVE (Carpenter et al., 1980; Vortel et al., 1982; Lenghaus and Studdert, 1984; Meunier et al., 1984; Van Rensburg and Meintjes, 1986; Agungpriyono et al., 1999; Atwell and Kelly, 2008).

Cardiac function has been evaluated by several echocardiographic indices (Boon, 1996; Moise and Fox, 1999). Doppler-derived Tei index of myocardial performance that combines systolic and diastolic time intervals has been used a convenient method for evaluation of global ventricular function (Tei, 1995; Arnlov et al., 2005; Teshima et al., 2006, 2007), and reported to be superior to the other echocardiographic indices such as fractional shortening, ejection fraction, and mitral early to late ventricular filling ratio (Tei, 1995; Tei et al., 1995). Also, selected serum biomarkers can provide clinical information about cardiac damage. Cardiac troponin I (cTnI) is considered a definitive biomarker for detection of myocardial damage in humans and dogs (Schober et al., 1999, 2002; Rosalki et al., 2004; Walker, 2006; Babuin and Jaffe, 2005; Apple et al., 2008) and increases in serum cTnI also correlate with morphological changes in the heart (Apple et al., 2008). Use of other classical cardiac biomarkers such as creatine kinase (CK), lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) can be limited due to lack of tissue specificity and sensitivity (Schober et al., 2002; Qi and Sun, 2004; O'Brien, 2008; Franco et al., 2009).

Although the diagnostic use of Tei index and cardiac biomarkers have been studied in cardiac diseases (Tei, 1995; Schober et al., 2002; Rosalki et al., 2004; Ibeth et al., 2005; Sousa et al., 2007), their prognostic importance is seldom investigated in humans, and not known yet in dogs with PVE, as a useful animal model of acute-onset and chronic-progressive cardiomyopathies (Lenghaus

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and Studdert, 1984; Meunier et al., 1984) and sepsis (Turk et al., 1992; de Laforcade et al., 2003; Otto, 2007; Yilmaz and Senturk, 2007). Thus, this study was aimed to study the behaviour and possible prognostic value of Tei index and serum cardiac biomarkers (CK, LDH, AST and cTnI) in CPV-infected dogs, having clinical and haematological criteria of sepsis. Since a considerable number of experimental, epidemiological and clinical studies are now available which point to an important role of magnesium (Mg) in the etiology of myocardial pathology (Chang et al., 1985; Mann et al., 1998; Chakraborti et al., 2002; Soliman et al., 2003), serum Mg level was also investigated in this study.

2. Material and method

2.1. General variables

Dogs with CPV were presented between December 2008 and April 2009 at the Small Animal Clinic of the Faculty of Veterinary Medicine at Uludag University. CPV infection was suspected of compatible clinical and laboratory findings, and then confirmed by a positive result of the commercial Snap CPV antigen test in 43 dogs, of both gender and different breed, less than or equal to 6 months of age suffering from vomiting and bloody diarrhoea. Eleven dogs with PVE had been vaccinated at least once with commercial parvovirus containing vaccine, 5–20 days (11.9 ± 4.7 days) before performing the faecal antigen test. The remaining sick dogs (n = 32) had not been vaccinated previously. The test used in the study (Antigen Rapid CPV Kit, Animal genetics, Inc., Korea) detects a surface protein antigen of CPV (including intact virus particles) shed in the faeces of CPV-infected dogs. This test could not produce positive results as a result of modified live parvovirus vaccines, positive results indicate infection with wild type CPV-2 (Schultz et al., 2008).

Selected clinical (body temperature and heart and respiratory rates) and haematological findings (PCV, total white blood cell and platelet counts) were used to assess the general health status of the animal and to identify the possibility of the existence of systemic inflammatory response syndrome (SIRS) in the patients, as described previously for dogs (de Laforcade et al., 2003; Yilmaz and Senturk, 2007). Dogs were classified as septic if serological confirmation of infection was available and if two or more of the following criteria (SIRS) were met: hypo- or hyper-thermia (temperature <37.8 °C or >39.4 °C, respectively), tachycardia (heart rate >140 bpm), tachypnoea (respiratory rate >30 breaths/min.), leucopoenia (WBC count <5500/μL) or leucocytosis (WBC count >12,500/μL), and thrombocytopoenia (platelet count <180,000/μL). Dogs that fulfilled the criteria for sepsis at admission day were included for this study.

Dogs with PVE were isolated from the other hospitalized patients, and treated as described in our previous study (Yilmaz and Senturk, 2007). Survival rates were recorded, and according to treatment responses, dogs were divided into 2 groups, survivor (n = 20) and non-survivor (n = 23).

Controls animals (n = 7, age matched to dogs with PVE) were selected from dogs brought to our clinics for vaccination, on the basis of normal physical examination results, complete blood count and serum biochemistry profiles.

2.2. Clinical and haematological examinations

Dogs were examined for signalment, history of vaccination, physical and laboratory examinations, quick tests and follow-up information on the outcomes. The body temperature, heart and respiratory rates, mucous membrane colour, capillary refill time, peripheral pulse quality, and hydration and mental status were recorded for each of the animals.

Complete blood cell count was performed by an automated analyser (Celldyn 3500, Abbot).

2.3. Cardiologic examinations

All ECG and echocardiographic examinations were performed in all patients within 1 day of admission.

ECG: Cardiac rhythms were analyzed in dogs in right lateral recumbency, and amplitudes of ECG waves and the durations of intervals were measured on lead II (50 mm/s; 1 cm/mV; Esoate, Italy), as suggested (Miller et al., 1999).

Echocardiography: Each dog was examined in a quiet, darkened and comfortable private room to allow them to relax. Doppler echocardiography was performed using conventional clinical echocardiographic equipment (Caris Plus, Esoate, Italy) with 2.5–7.5-MHz phased array electronic transducers in conscious unsedated dogs. Echocardiograms were reviewed to assess the cardiac geometry and function, as suggested (Boon, 1996; Moise and Fox, 1999). All geometric and functional parameters obtained from echocardiographic measurements in dogs with PVE were compared with those of controls. Systolic time intervals (pre-ejection period [PEP], ET, PEP/ET ratio, and mitral early to late ventricular filling [E/A] ratio) were measured using the method referred by others (Boon, 1996; Moise and Fox, 1999). Velocity of circumferential fiber shortening (vcf) was calculated by an accepted formula: LV internal dimension at diastole minus LV internal dimension at systole divided by LV internal dimension at diastole multiply ET, as suggested (Boon, 1996).

Tei index (myocardial performance index): From the transmitral pulsed Doppler, the time interval between the end of mitral filling and the onset of mitral filling was determined (“a”). From transaortic pulsed Doppler, the time interval from the beginning of aortic flow to the end of aortic flow was determined (“b” or LVET).

The IMP can be calculated as IMP = (a–b)/b

To determine the IRT, the time from the R wave to the end of aortic flow was subtracted from the R wave to the onset of mitral flow interval. As “a–b” represents total isovolumic time, the ICT is the difference between IRT and “a–b” (Tei, 1995; Lavine, 2006). Tei index was calculated three times consecutively and used its arithmetic mean for each dog.

2.4. Cardiac and muscle damage biomarkers

cTnI was determined by the DPC Immulite. This assay has been previously validated showing satisfactory imprecision values (Apple et al., 2008). CK, LDH, AST and magnesium were analyzed using an automated analyser (Olympus A400) and commercial reagents (Olympus LTD.).

2.5. Statistical analysis

All data were normalized by logarithmic transformation before analysis. Student t test was used to compare the differences in age and body weight between healthy controls and dogs with PVE. Concentrations of serum markers and cardiologic examination results among groups were analyzed by one-way analysis of variance. The Tukey test was used for all pair-wise comparisons of the mean responses with the different groups. Pearson correlation coefficient (r) was used to analyse the degree of associations among Tei index and cardiac biomarkers and results of cardiologic examination. Receiver operation characteristics (ROC) curve analysis was used for the determination of a prognostic cut-off value for the best differentiation between survivors and non-survivors (SPSS Inc). For all comparisons, values of $P < 0.05$ were considered significant, and all data were expressed as mean ± standard deviation.