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Serum Cystatin C Concentration as a Marker Acute Renal Dysfunction in Critically Ill Dogs

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Abstract: The objective of this study, was the evaluate sCys-C concentration as a marker of acute renal failure in critically ill dogs. For this purpose, a total of 60 dogs with critically ill were investigated. All cases were selected among critically ill dogs, who were classified into the four groups on the basis of clinical examination, laboratory and radiological and ultrasonographical findings; G1-Control (15 healthy dogs) G2-Multiple trauma (15 dogs); G3-Shock (15 dogs); G4-Urogenital disease (15 dogs). Serum Cys-C was measured by sandwich enzyme immunoassay method using ELISA kit. Serum Cr, sUr and sP concentrations were measured by a photometer using commercially available kits. The mean value of sCys-C was 0.46±0.05 mg L^{-1}, the mean value of sCr was 0.54±0.06 mg dL^{-1}, the mean value of sUr was 13.09±3.92 mg dL^{-1}, the mean value of sP was 3.75±0.24 mg dL^{-1}. The mean value of sCys-C, sCr, sUr and sP values for G1 were statistically different, when compared G3 and G4 ($p<0.05$). There was no statistical difference between G1 and G2.

Key words: Cystatin-C, trauma, urogenital diseases, schock, renal dysfunction, dog

INTRODUCTION

Acute renal failure is characterized by decline of the glomerular filtration rate. Serum creatinine and urea concentrations is widely used biochemical parameter for rapid estimate glomerular filtration rate in veterinary clinical practice. However, the serum creatinine (sCr) and urea (sUr) concentrations can be influenced by some non-renal factors such as protein intake and muscular mass (Randers and Erlandsen, 1999). Different serum markers are required to establish an early and accurate diagnosis of an impaired renal function in critically ill dogs.

Cystatin-C (Cys-C) is a small non-glycosylated 120 amino acid protein in the super family of cysteine proteinase inhibitors (Villa *et al*., 2005). In the kidney, Cys-C is freely filtered through glomerulus, reabsorbed and catabolized in proximal renal tubules (Randers and Erlandsen, 1999; Antognoni *et al*., 2005). Its filtration is unchanged in kidney tubuler diseases where its urinary excretion is increased. Cys-C plasma concentration is thus mainly depent on the glomerular filtration rate and its serum concentration is determined by glomerular filtration (Nilson-Ehle and Grubb, 1994; Randers and Erlandsen, 1999; Braun *et al*., 2002). In human medicine, Cys-C as a marker of glomerular filtration ration is well documented and it is considered to be a better indicator of renal failure than creatinine (Herget-Rosenthal *et al*., 2004; Xia *et al*., 2004; Villa *et al*., 2005). In veterinary medicine, there are a few reports about sCys-C that it is also, the most important serum marker of renal function assessment in dogs (Jensen *et al*., 2001; Almy *et al*., 2002; Braun *et al*., 2002; Antognoni *et al*., 2005, 2007).

The difficulties associated with evaluating and monitoring renal function in critically ill dogs are well known. To the authors' knowledge there is not one report regarding the importance of sCys-C in these patients. The purpose of the present study was to prospectively evaluate sCys-C concentration as a marker of acute renal failure in critically ill dogs.

MATERIALS AND METHODS

In this study, a total of 60 dogs (32 males and 28 females) with critically ill were investigated. The mean age of dogs was 4.76±0.54. All cases were selected among

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critically ill dogs who were classified into the 4 groups on the basis of clinical examination, laboratory and ragiological and ultrasonographical findings; G1-Control (15 healthy dogs) G2-Multiple trauma (20 dogs); G3-Shock (20 dogs); G4-Urogenital disease (20 dogs).

Blood samples were taken from the cephalic vein and centrifuged at 1700 g for 5 min. The sera were collected in plastic tubes and frozen at -20°C until needed for the determination of sCys-C, sCr, sUr and phosphorus (sP). Serum Cys-C was measured by sandwich enzyme immunoassay method using ELISA kit (BioVendor; Human Cystatin C ELISA Cat. No.: RD191009100 Heidelberg, Germany) according to the manufacturers instructions (Risch *et al*., 1999). sCr, sUr and sP concentrations were measured by a photometer (Microlab 200, Merck, Germany) using commercially available kits.

Data are expressed as mean±standard deviation. Relationship between the variables was analyzed using a Tukey's correction. A $p<0.05$ was considered as statistically significant. All statistical analysis were performed using the SPSS 10.0 program.

RESULTS AND DISCUSSION

The 60 dogs were divided into four groups. Their sCys-C, sCr, sUr and sP values are summarized in Table 1.

The mean value of sCys-C was 0.46±0.05 mg L^{-1}, the mean value of sCr was 0.54±0.06 mg dL^{-1}, the mean value of sUr was 13.09±3.92 mg dL^{-1}, the mean value of sP was 3.75±0.24 mg dL^{-1}. The mean value of sCys-C, sCr, sUr and sP values for G1 were statistically different when compared G3 and G4 ($p<0.05$). There was no statistical difference between G1 and G2.

Monitoring renal function is extremely important in the management of critically ill patients. GFR, which can be measured by determining the clearance of various substances, is the gold standard' parameter for monitoring renal function. Renal damage with <75% of non-functional nephrons in dogs may not show increased concentrations of sUr and sCr (Palacio *et al*., 1995). Since, a sUr and sCr are not useful to detect mild renal damage in dogs.

Cys-C is a cysteine protease inhibitor produced by all nucleated cells. It is freely filtered by the glomerulus and is not influenced by non-renal factors such as inflammation or gender. Cys-C production in the body is a stable process that is not influenced by renal conditions, increased protein catabolism, or dietetic factors. Moreover, it does not change with age or muscle mass like creatinine does. Its biochemical characteristics allow free filtration in the renal glomerulus and subsequent metabolism and reabsorption by the proximal tubule.

For these reasons, sCys-C has been suggested to be an ideal endogenous marker of GFR (Risch *et al*., 1999; Herget-Rosenthal *et al*., 2004). Usefulness of sCys-C measurement has been described for early the detection of renal disease in humans (Randers and Erlandsen, 1999; Mares *et al*., 2003; Xia *et al*., 2004). Therefore, some of the extra-renal factors such as melanoma, colon cancer and HIV infections may affect the increase in sCys-C levels in human (Randers and Erlandsen, 1999; Mares *et al*., 2003). There are few studies on dogs with renal diseases among sCys-C, serum creatinine and urea nitrogen comparison. In these studies, sCys-C was found to be a better marker for glomerular filtration rate than creatinine together with urea nitrogen (Jensen *et al*., 2001; Almy *et al*., 2002; Braun *et al*., 2002; Antognoni *et al*., 2005, 2007).

In one study, hypercystatinemia is reported to be indicative progression of the disease as a consequence of an alteration of renal failure (Antognoni *et al*., 2005). In our study was observed that the sCys-C levels in G3 and G4 were significantly higher when compared with the G1. This condition was related to the GFR in critically ill dogs can change rapidly because of, for example, renal hypoperfusion secondary to shock or renal dysfunction. This findings is in agreement with other studies in dogs and humans (Jensen *et al*., 2001; Almy *et al*., 2002; Braun *et al*., 2002; Antognoni *et al*., 2005, 2007; Villa *et al*., 2005).

In this study, the value of sCys-C was higher in G2 than in G1 but not statistically important. It was reported in humans that kidney function was associated with incident hip fracture (Fried *et al*., 2007).

Table 1: Serum concentrations of Cys-C, Cr, Ur and P in critically ill dogs and the controls. Data expressed as Mean±Standard deviation (x±SD)

Groups	Sex of patients (male/female)	sCys-C (mg L^{-1})	sCr (mg dL^{-1})	sUr (mg dL^{-1})	sP (mg dL^{-1})
G1/15	6/9	0.46±0.05	0.54±0.06	13.09±3.92	3.75±0.24
G2/15	7/8	0.64±0.08	0.76±0.07	22.9±4.54	4.46±0.36
G3/15	5/10	0.97±0.09*	1.54±0.08*	56.2±5.67*	6.44±0.45*
G4/15	9/6	1.31±0.12*	2.04±0.09*	86.4±8.85*	7.78±0.98*

*$p<0.05$ statistically significant from G1

In the other study, Villa *et al.* (2005) reported that 10 of 50 patient with multiple trauma had elevated sCys-C values. In agreement with previosly study, in our study, 4 of 15 dogs with multiple trauma had a increased sCys-C values.

CONCLUSION

It was concluded that sCys-C evaluation can be used for early dedection of renal dysfunction in critically ill dogs affected by schock or urogenital disease.

REFERENCES

Almy, F.S., M.M. Christopher, D.P. King and S.A. Brown, 2002. Evaluation of cystatin C as an endogenous marker of glomerular filtration rate in dogs. J. Vet. Intern. Med., 16: 45-51. DOI: 10.1892/0891-6640 (2007)21[936:EOBVOC]2.0.CO;2. PMID: 17939546. URL: http://dx.doi.org/10.1892/0891-6640(2007) 21[936:EOBVOC]2.0.CO:2.

Antognoni, M.T., D. Siepi, F. Porciello and G. Fruganti, 2005. Use of serum cystatin C determination as a marker of renal function in the dog. Vet. Res. Commun., 29: 265-267. DOI: 10.1007/s11259-005-0058-5. INSPEC: 16244971. http://dx.doi.org/10.1007/s 11259-005-0058-5.

Antognoni, M.T., D. Siepi, F. Porciello, F. Rueca and G. Fruganti, 2007. Serum cystatin C evaluation in dogs affected by different diseases associated or not with renal insufficiency. Vet. Res. Commun., 31: 269-271. DOI: 10.1007/s11259-007-0044-1. INSPEC: 17682892. http://dx.doi.org/10.1007/s11259-007-0044-1.

Braun, J.P., A. Perxachs, D. Pechereau and De La Farge, 2002. Plasma cystatin C in the dog: Reference values and variations with renal failure. Comp. Clin. Pathol., 11: 44-49. DOI: 10.1007/s580-002-8081-2. http:// dx.doi.org/10.1007/s580-002-8081-2.

Fried, L.F., M.L. Biggs, M.G. Shlipak, S. Seliger, B. Kestenbaum, C. Stehman-Breen, D. Siscovick, T. Harris, J. Cauley, A.B. Newman and J. Robbins, 2007. Association of kidney function with incident hip fracture in older adults. J. Am. Soc. Nephrol., 18: 282-286. DOI: 10.1681/ASN.2006050546. PMID: 17167115. http://dx.doi.org/10.1681/ASN. 2006050546.

Herget-Rosenthal, S., G. Marggraf, J. Hüsing, F. Göring, F. Pietruck, O. Janssen, T. Philipp and A. Kribben, 2004. Early detection of acute renal failure by serum cystatin C. Kidney Int., 66: 1115-1122. DOI: 10.1111/j. 1523-1755.2004.00861.x. PMID: 15327406. http://dx. doi.org/10.1111/j.1523-1755.2004.00861.x.

Jensen, A.L., M. Bomholt and L. Moe, 2001. Preliminary evaluation of a particle-enhanced turbidimetric immunoassay (PETIA) for the determination of serum cystatin C-like immunoreactivity in dogs. Vet. Clin. Pathol., 30: 86-90. DOI: 10.1111/j.1939-165X.2001. tb00263.x.PMID:1202432.http://dx.doi.org/10.1111/j. 1939-165X.2001.tb00263.x.

Mares, J., D. Stejskal, J. Vavrouskova, K. Urbanek, R. Herzig and P. Hlustik, 2003. Use of cystatin C determination in clinical diagnostics. Biomed Papers, 147: 177-180. PMID: 15037900. http://publib.upol.cz/~obd/fulltext/Biomed/2003/ 2/177.pdf.

Nilson-Ehle, P. and A. Grubb, 1994. New markers fort he determination of GFR: Iohexol clearance and cystatin C serum concentration. Kidney Int. Suppl., 47: 17-19. PMID: 7869664.

Palacio, J., F. Liste and M. Gascon, 1995. Urinary protein/creatinine ratio in the evaluation of renal failure in canine leishmaniasis. Vet. Res., 37: 389-395. PMID: 8644438.

Randers, E. and E.J. Erlandsen, 1999. Serum cystatin C as endogenous marker of the renal function-A Rew. Clin. Chem. Lab. Med., 37: 389-395. DOI: 10.1515/CCLM. 1999.064. http://10.1515/CCLM.1999.064.

Risch, L., A. Blumberg and A. Huber, 1999. Rapid and accurate assessment of glomerular filtration rate in patients with renal transplants using serum cystatin C. Nephrol Dial Transplant., 14: 1991-1996. DOI:10.1093/ndt/14.8.1991.http://dx.doi.org/10.1093/ ndt/14.8.1991<http://dx.DOI.org/10.1093/ndt%2F 14.8.1991.

Villa, P., M. Jiménez, M.C. Soriano, J. Manzanares and P. Casasnovas, 2005. Serum cystatin C concentration as a marker of acute renal dysfunction in critically ill patients. Crit Care, 9: 139-143. PMID: 15774046.

Xia, L.H., X.G. Bing and X.T. An, 2004. Serum cystatin C assay for detection of early renal impairment in diabetic patients. J. Clin. Lab. Anal., 18: 31-35. DOI: 10.1002/jcla.20005. http://dx.doi.org/10.1002/ jcla.20005.