SHORT COMMUNICATION

Symmetric Dimethylarginine (SDMA) as Biomarker of Chronic Kidney Diseases in Dogs

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Abstract

Chronic renal failure is the loss of the ability of kidneys to excrete waste products, concentrate urine, electrolytes and fluid balance leading to retention of creatinine, urea and other metabolic waste products in the body. The present study was planned to evaluate and correlate Symmetric Dimethylarginine (SDMA) with the severity of chronic kidney disease (CKD) and with BUN and creatinine in dogs. Twenty four dogs presented at Veterinary Clinical Complex of LLUVAS, Hisar (India), diagnosed to be suffering from renal failure on the basis of history, clinical signs and ultrasonographic findings were included in the study. The dogs were divided into three categories (atypical, mild and severe) based on the duration of presentation of cases after emergence of the clinical signs. Six apparently healthy dogs were taken for comparsion with affected ones. Serum from all the affected and apparently healthy animals was used to evaluate SDMA using ELISA kits, whereas BUN and creatinine were determined using biochemistry autoanalyzer. SDMA was significantly (20-fold) elevated in dogs suffering from renal failure as compared to the control group. Significant ($p<0.01$) positive correlations of SDMA with BUN and serum creatinine were found in all three categories of dogs indicating that serum SDMA can be a biomarker for detection of CKD earlier than does measurement of serum creatinine in dogs.

Key words: Biomarker, BUN, Chronic renal failure, Creatinine, Dogs, SDMA.

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Introduction

Renal failure is the clinical syndrome that occurs when the kidneys are no longer able to maintain their regulatory, excretory and endocrine function, which results in retention of nitrogenous solutes and derangement of fluid, electrolyte and acid base balance. Renal failure is one of the common diseases encountered in dogs and it is one of the major causes of death in young (acute renal failure) and older (chronic renal failure) dogs (Kraje, 2002). Chronic kidney disease (CKD) is common cause of morbidity and mortality in dogs. Renal failure in dogs is diagnosed on the basis of structural damage to the kidneys and decreased renal function or both. Now a day's a non-invasive method of detection of disease and process of underlying disease is required. An ideal biomarker to detect kidney disease would be specific, able to detect both AKI (acute kidney injury) and CKD, sensitive for detecting early disease, capable of documenting extent or severity of disease, monitoring disease progression, and predictive of clinical outcome. Routinely used biomarkers like serum creatinine and blood urea nitrogen (BUN) are not specific or sensitive in diagnosis of disease in early stages. Symmetric Dimethylarginine (SDMA) rises at 40% renal damage as compared to creatinine which increases at 75% kidney damage (Nabity et al., 2015). SDMA is mainly filtered out from the kidneys so considered an accurate and sensitive biomarker for estimating glomerular filtration rate (GFR) and assessing renal dysfunction in dogs. Therefore, the present study was planned to evaluate the serum level and correlation of SDMA with the severity of chronic kidney disease and to relate it with BUN & serum creatinine in dog.

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Materials and Methods

The investigation was carried out on 24 dogs presented at Veterinary Clinical Complex, Lala Lajpat Rai University of Veterinary and Animal Sciences (LUVAS), Hisar, India diagnosed to be suffering from renal failure on the basis of history, clinical signs and ultrasonographic findings. All the dogs were divided into three categories atypical, mild (illness less than 10 days) and severe (n=5, 6 and 13, resp) based on the duration of presentation of cases after emergence of the clinical signs. Serum from affected animals and six apparently healthy animals was used to evaluate SDMA using ELISA kits.

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SDMA was estimated using Canine Symmetric Dimethylarginine ELISA kit procured from Bioassay Technology Laboratory as per the manufacturer's instructions. BUN and serum creatinine were estimated using a biochemistry autoanalyzer. Correlation of serum SDMA with BUN and serum creatinine was determined using appropriate statistical software and test.

Results and Discussion

The results of the present study on biomarker and their correlation are presented in Tables 1 and 2.

The data showed that SDMA level in dogs suffering from renal failure was found to be elevated by 20-folds (268±49 µg/dL) as compared to control healthy group of dogs (13±5 µg/dL). The two other biomarkers BUN and Creatinine also were raised significantly ($p<0.05$) during renal failure. Significant difference was observed in mean values between two groups. Very similar results have been reported earlier in CKD affected and healthy dogs by many researchers (Nabity *et al*., 2015; Hall *et al.,* 2016; Dahlem *et al.,* 2017; Kim *et al*., 2020). The values of SDMA paralleled the progression of renal disease in dogs and was strongly correlated with GFR. As in progressive kidney disease GFR is decreased, it leads to the increase in values of SDMA. Le Sueur *et al.* (2019) and Joshi (2021 recorded increased SDMA value in canine chronic renal failure cases. SDMA is eliminated primarily by glomerular filtration and there is no tubular reabsorption or secretion. Therefore, it is used as GFR marker (Ernst *et al*., 2018).

Relationship between SDMA and that of BUN and creatinine was determined in three different groups of dogs. Significant ($p<0.05$) positive correlations were observed between SDMA values and serum creatinine values in group I - atypical CKD (r=0.877), group II - mild CKD (r=0.840), and group III - severe CKD (r=.0.640). The correlations between SDMA and BUN were highly positive, but statistically non- significant in three groups (r=0.698, 0.710, and 0.291, respectively). Significant ($p<0.01$) positive correlations were also observed between BUN and creatinine levels in all three groups of atypical, mild (<10 days) and severe (>10 days duration) CKD cases (r=0.914, 0.693 and 0.841, respectively, Table 2). Results of present study were in accordance with the findings of Nabity *et al*. (2015) indicating significant correlation between creatinine and SDMA. They showed SDMA level to be strongly correlated with GFR. Serum SDMA and creatinine concentrations were linearly and significantly related to glomerular filtration rate. Further the association of all three elements, serum SDMA, BUN and creatinine, was negligible with cystatin C levels in mild cases of CKD (r= 0.064, 0.257 and -0.180, respectively) in our study.

The results in the present study indicate that serum SDMA concentration may be a promising renal prognostic marker in dogs. Using serum SDMA as a biomarker for CKD allows earlier detection of kidney dysfunction in dogs than does measurement of serum creatinine. Earlier detection might be desirable for initiating renoprotective interventions that slow progression of kidney disease.

Table 1: Mean (± SE) values of SDMA, BUN and Creatinine in dogs suffering from renal failure and control

	Renal failure	Control
SDMA(µg/dL)	268±49*	13±5
BUN (mg/dL)	237±29.5	13.6±2.20
Creatinine (mg/dL)	7.31±1.02	0.95±0.02

*($p<0.05$)

Table 2: Correlation between serum biomarkers

Atypical CKD group	**BUN**	**Serum creatinine**	**SDMA**
BUN	1	0.914*	0.698
Serum creatinine	0.914*	1	0.877*
SDMA	0.698	0.877*	1
Mild CKD group	**BUN**	**Serum creatinine**	**SDMA**
BUN	1	0.693	0.71
Serum creatinine	0.693	1	0.840*
SDMA	0.71	0.840*	1
Severe CKD group	**BUN**	**Serum creatinine**	**SDMA**
BUN	1	0.841**	0.291
Serum creatinine	0.841**	1	0.640*
SDMA	0.291	0.640*	1

*($p<0.05$), **($p<0.01$)

In conclusion, SDMA was found to be 20-fold elevated in CKD dogs and appeared to be a more reliable indicator of decreased GFR than creatinine in patients and it increases before creatinine in many dogs with chronic kidney diseases, hence may be used routinely as biomarker of CKD.

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