Research Article

Relationships Between Symmetric Dimethylarginine (SDMA), Blood Urea Nitrogen and Creatinine Levels in Dogs

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Abstract

Renal failure is a frequently encountered disorder of the dogs and cats. Blood urea and creatinine levels are the conventional diagnostic parameters, but elevate only after advanced stage, so a significant period for the therapy onset is mislayed. Serum symetric dimethly arginine (SDMA) is a spesific and early biomarker of renal insufficiency. The aim of this study is to investigate the state of relationships between SDMA, BUN and creatinine levels in dogs. In the present study, SDMA, BUN and creatinine levels are determined in 50 dogs by ELISA. Obtained results displayed an absence of a correlation, but also indicated renal insufficiency in 14% of the dogs which had none related clinical suffering or laboratory finding. This striking ratio displayes the diagnostic efficiency of SDMA and also emphasizes the requirement of routine SDMA usage in clinical practice on behalf of early diagnosis, theurapeutic success, therapy expanses and animal welfare.

Keywords: Acute Renal Failure, Biomarker, Chronic Renal Failure, Dog

Introduction

Renal failure in dogs is a frequently diagnosed disorder and evaluated in two categories; Acute renal failure (ARF) is defined as reduction in glomerular filtration rate and metabolic and endocrine functions, due to renal damage and if not treated results with chronic renal failure (Shaw & Ihle, 2007). Chronic renal failure (CRF) is a progressive and irreversibl disorder characterized by structural and functional loss of the kidneys (Shaw &Ihle, 2007; Roudebush et al., 2010). The condition may sustain for years before becoming clinically apparent. Reported incidence in geriatric dogs is 10%, where in general pet population is 1-3% (Brown, 2017). CRF is the most frequent renal disorder of dogs (Grouer, 2009; Roudebush et al., 2010; Brown, 2017).

Prognosis of renal failure is largely correlated with the time of diagnosis. Current diagnostic and prognostic parameters are restricted with serum creatinine level, systolic blood pressure, and blood urea level in clinical practice (IRIS, 2018). In fact, these parameters reflect renal damage only on advanced stages. Literature states that serum creatinine level increases after %75 of renal function is lost (Brown, 2017). Last studies demonstrated that, a kidney spesific biomarker, Serum Symmetric Dimethyl Arginine (SDMA) levels determines renal failure much more earlier that serum urea and creatinine levels (Yerramıllı & Jewell, 2014; Hall et al., 2014; Hall et al., 2015; Hall et al.,2016; Nabıty et al., 2016). SDMA is excreted by the kidneys, so precisely reflects glomerular filtration rate, as well is reported to increase even in 25% renal function loss (Yerramıllı & Jewell, 2014; Hall et al., 2014; Hall et al.,2015; Nabıty et al., 2015; Hall et al., 2016).

Furthermore, unlike creatinine level which is in correlation with body weight, SDMA is independent with body condition, so more accurate monitoring of the disease progression can be achieved in CRF, characterized by progressive weight loss (Hall et al., 2015). Therefore, the projection for a sensitive and earlier diagnosis plus accurate monitoring in CRF includes SDMA determination together with systolic blood pressure and serum creatinine level (Yerramıllı et al., 2014; Relford et al., 2016; IRIS, 2018). Reference values for SDMA in healthy dogs are reported (Rentko et al., 2013), but studies focusing on relationship between serum SDMA and urea and creatinine levels are limited. The aim of this study is to determine the SDMA levels in healthy dogs together with urea and creatinine levels, and demonstrate any possible relationships if present.

Materials and methods

Ethical Approval

This study was approved by the Ondokuz Mayıs University Animal Studies Local Ethic Committee with 68489742-604.01.02-E.6791 approval number.

Animals

In the study, 50 dogs from both gender and various ages referring to University Animal Hospital with various complaint were included. Routine clinical examination were performed. Blood specimen for biochemical analyses were collected from the patients and history, age, species, gender and owner information were recorded.

Serum Analysis

Serum specimen were obtained from 5 ml of venous blood after centrifugation for each patient. Routine serum biochemical profile (total protein, globuline, liver and pancreatic enzymes, urea and creatinine levels were analysed with Mindray DS 120 biochemical analyser according to the manufacturers instructions.

Serum SDMA levels were analysed with Canine symmetric dimethylarginine (SDMA) ELISA Kit (Shanghai YL Biotech Co., Ltd) with ELISA method according to the manufacturers instructions.

Statistical Analysis

In comparision of serum urea, creatinine and SDMA levels descriptive analysis and Tamhane test for relationship were used.

Results

Recorded serum urea, creatinine and SDMA levels of dogs are presented in Table 1, mean and standart deviations of the parameters are presented in Table 2 and correlation between the parameters are presented in Table 3.

Table 1. Serum urea, creatinine and SDMA levels

DOG NO	UREA (mg/dl)	CREA-TININE (mg/dl)	SDMA (nmol/L)	OPTIC DENSITY
1	12,20	0,78	158,93	0,1735
2	41,00	1,59	197,23	0,2012
3	25,90	0,65	160,73	0,1748
4	63,10	1,29	244,79	0,2356
5	116,50	1,00	485,1	0,4094
6	16,20	0,43	133,26	0,1477
7	10,40	0,90	122,84	0,1474
8	33,60	0,39	66,707	0,1068
9	22,90	0,62	229,86	0,2248
10	22,30	0,65	263,18	0,2489
11	73,90	0,78	525,61	0,4387
12	34	0,82	126,44	0,15
13	36,4	0,29	205,94	0,2075
14	18,7	0,57	109,98	0,1381
15	40,9	0,14	126,16	0,1498
16	27,6	0,26	54.125	0,0977
17	41	0,87	158,65	0,1733
18	46,4	0,64	262,91	0,2487
19	55,9	0,63	112,34	0,1398
20	40,7	0,55	288,21	0,267
21	23,2	0,66	787,35	0,639

22	38	0,56	130,45	0,1529
23	32,6	0,96	565,57	0,4676
24	30	0,26	133,35	0,155
25	22	0,22	264,29	0,2479
26	61	0,58	289,18	0,2677
27	35	0,57	120,63	0,1458
28	34	0,55	150,5	0,1674
29	57	0,57	136,12	0,1411
30	55	1,02	150,91	0,1677
31	19	0,09	128,51	0,1515
32	14	0,04	153,26	0,1694
33	27	0,48	147,73	0,1654
34	55	0,17	201,24	0,2041
35	121	1,17	242,44	0,2339
36	72	0,6	180,09	0,1888
37	66	0,14	135,29	0,1564
38	23	0,48	136,12	0,157
39	22	0,22	90,489	0,124
40	14	0,19	184,92	0,1923
41	43	0,39	300,51	0,2759
42	26	0,34	88	0,1222
43	26	0,18	141,9	0,1606
44	41	1	787,35	0,6651
45	25	0,42	323,33	0,2924
46	30	0,51	162,11	0,1758
47	84	0,86	557,83	0,462
48	29	0,6	113,3	0,1405
49	82	0,51	606,5	0,4972
50	18	0,36	251,71	0,2406

Table 2. Mean and standart deviations of serum urea, creatinine and SDMA levelss

	Av.	Std. Dev.	Std. Er.	95% Av. Conf. Interval		Min	Max
				Low Band	High Band		
UREA (mg/dl)	40.0880	24.50451	3.46546	33.1239	47.0521	10.40	121.00
CREA-TININE (mg/dl)	.5710	.32552	.04603	.4785	.6635	.04	1.59
SDMA (nmol/L)	233.879	173.1281	24.48402	184.6769	283.0819	54.13	787.35

Table 3. Relationshıp between serum urea, creatinine and SDMA levels

	Difference between means	*Std. error*	*SDMA*	
			95% Conf. Interval	
			Low Band	*High Band*
UREA (mg/dl)	-193.79*	24.73	-254.8388	-132.7440
CREA-TININE (mg/dl)	-233.31*	24.48	-293.8355	-172.7813

* Significance level p≤0.05

Another remarkable point is in 14% of the dogs (dog 5, 11, 21, 23, 44, 47 and 49) creatinine values were in normal and urea levels -which also may be affected by other interventions- were slightly above the reference levels, SDMA levels indicated renal failure presence.

Discussion

Current research indicates that SDMA, a kidney spesific biomarker, diagnoses renal failure much earlier than serum urea and creatinine biomarkers. (Hall et al., 2014; Yerramıllı & Jewell, 2014; Hall et al., 2015; Nabıty et al., 2015; Hall et al., 2016). SDMA is in correlation with the stage of renal failure in dogs and reflects renal function lost and determines the degree of functional failure much more earlier than serum creatinine level and glomerular filtration late (Nabity et al., 2015). Some authors state that creatinine level start to elevate only after 50% renal function lost (Grouer, 2009). Consequently, monitorization of SDMA level together with systolic blood pressure and creatinine levels will bring up a sensitive, precise and accurate CRF follow-up (Rentko et al., 2013; Yerramıllı et al., 2014; Relford et al., 2016). Similarly, in the present study, in 14% of the dogs with acceptable values of urea and creatinine, high SDMA levels were determined indicating renal failure.

Methyl arginine is a product of protein methylisation and has three types; monomethyl arginine, asymmetric dimethyl arginine (ADMA) and SDMA (Bedford & Rıchard, 2005). In men, ADMA enzimatically metabolizes with dimethylarginine dimethylaminohydrolase, but SDMA is ≥90% excreted from kidneys. (Kıelsteın et al., 2002; Schwedhelm & Boger, 2011). L-argininine oral supplementation does not affect SDMA concentration (Rytlewskı et al., 2005).

SDMA is elevated even in 25-30% renal function lost (Hall et al., 2014; Yerramıllı & Jewell, 2014; Hall et al., 2015; Nabıty et al., 2015; Hall et al., 2016). It is reported that SDMA elevated 17 months before creatinine elevation when glomerular filtration rate was 40% in cats with renal failure, furhermore SDMA showed 100% sensitivity with 91% spesivity where creatinine showed 17% sensitivity (Hall et al., 2014). In dogs with renal failure, it was reported that SDMA indicated renal failure 9.5 months before creatinine (Nabıty et al., 2015).

On the contrary to creatinine and urea, SDMA has no correlation with body weight, so the misleading effects of age related muscle degeneration together with the weight loss in CRF prevalent for creatinine are annihilated (Hall et al., 2015). Similarly in the present study, within reference limit creatinine levels were determined in dogs with high SDMA levels.

Reference interval for SDMA is determined as ≥14 µg/dL (413.85 nmol/L) (IRIS, 2018). This interval is considered in the present study and a remarkable fact was, none of the SDMA results were around the reference limits; values were high and indicative or were below the limits avoiding any doubtful results. Although sample size was relatively restricted in the present study, these results suggest that the interval is reasonably confidental.

Variations in SDMA levels with different disorders were investigated in men. Slight elevations in cardiovascular disorders (Meınıtzer et al., 2011), acute inflammatory response (Blackwell et al., 2011), essential hypertension (Wang et al., 2009), diabetes (Krzyzanowska et al., 2007) and inflammatory bowel disease (Owczarek et al., 2010), but a statistical significance was not determined. In the present study all dogs had a clinical complaint and some sort of a disorder, but no relationship was determined between these disorders and SDMA levels.

No correlation between SDMA levels and age, race, gender or diet in dogs were reported (Moesgaard et al., 2007; Hall et al., 2015). Concordantly, in the present study dogs were various age, gender, race and were on different diets, but no relationship between these parameters was observed.

In the present study, there was no correlation between dogs urea, creatinine and SDMA levels, but in 14% of the subjects in which no clinical or laboratory indicator of renal disease including urea and creatinine elevations were present, high SDMA levels were observed indicating the existence of renal disease. These subjects would not been diagnosed as renal failure in conventional procedure, but they were immediately started therapy in the light of high SDMA levels.

These striking result demonstrates the diagnostic efficiency of SDMA marker and underlines the essentialness of this biomarker in clinical practice regarding early diagnosis, theraupetic success and animal welfare.

In conclusion, involvement of SDMA biomarker in conventional diagnostic procedure will provide early diagnosis and advanced therapeutic success in renal failure in dogs.

Conflicts of Interest

The authors declare that there is no conflict of interest for this study.

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