EURASIAN JOURNAL OF HEALTH SCIENCES
ISSN 2651-3501

Eurasian JHS 2019;2(4(suppl)):179-181

Research Article/
Araştırma Makalesi

Correspondence: Yeliz KAYA
E-mail: yelizkaya06@gmail.com

Symmetric Dimethylarginine (SDMA): A Novel Kidney Biomarker

Neslihan TAŞCENE[1], Yeliz KAYA[2], Tevhide SEL[2]

[1] Foot and Mouth Disease Institute, Republic of Turkey Ministry of Agriculture and Forestry, Ankara, TURKEY

[2] Department of Biochemistry, Faculty of Veterinary Medicine, Ankara University, Ankara, TURKEY

ABSTRACT

Chronic Kidney Disease is an important disease mainly in elderly and some breed cats. The duration of clinical findings in renal failure is not sufficient for early diagnosis. The kidney is an organ that can stabilize itself and continue to function until it loses 75% of its function. Unfortunately emergence of clinical findings is only possible at this time and this is the most important factor that makes treatment difficult. Creatinine has an more important place in the diagnosis of renal failure than urea but rise in blood occurs when 75% of kidney function is lost. Therefore, creatinine is not an adjunct parameter in early diagnosis. There is a new biomarker that has just begun to be discovered and is included in the studies for early diagnosis: Symmetric Dimethylarginine (SDMA). SDMA and kidney function are highly correlated. SDMA is a methylated arginine amino acid. SDMA is excreted by the kidneys. In this study, blood results of cats diagnosed with chronic renal failure were compared. Also, SDMA and creatinine were compared in some patients and their effects on diagnosis were considered. SDMA, creatinine and BUN values were measured in a blood sample taken from a 10 year old hybrid female cat. SDMA value (15 µg / dL) was high, creatinine (2.2 mg / dL) and BUN (23 mg / dL) values were within normal ranges. This shows us that kidney function is still working, and renal insufficiency is at an early stage. According to the results, the increase in creatinine is correlated with SDMA. As SDMA increases, the loss of renal function increases as a percentage and leads to an increase in creatinine over time. More detailed information can be gathered on the role of SDMA and creatinine in early diagnosis and its relationship with kidney.

Key words: Chronic Renal Failure, Creatinine, SDMA.

Simetrik Dimetilarjinin (SDMA): Yeni Bir Böbrek Biyobelirteci

ÖZET

KBY başlıca yaşlı ve bazı ırk kediler olmak üzere tüm hayvanlarda önemli bir hastalıktır. Böbrek yetersizliğinde klinik bulguların ortaya çıkış süresi erken tanı için yeterli değildir. Böbrek kendini dengeleyebilen ve işlevinin %75'ini kaybedene kadar görevini yerine getirmeye devam edebilen bir organ olduğu için klinik bulguların ortaya çıkması da ancak bu zamanda mümkündür. Maalesef bu durum tedaviyi zorlaştıran en önemli etkendir. Kreatinin Böbrek yetmezliği tanısında üreden bile daha önemli bir yere sahiptir; fakat kanda yükselmesi ancak böbrek fonksiyonunun %75'inin kaybolmasında ortaya çıkmaktadır. Dolayısıyla Kreatinin erken tanıda yardımcı bir parametre değildir. Yeni yeni keşfedilmeye başlanan ve çalışmalarda erken tanı için yer verilen yeni bir biyobelirteç mevcuttur: Simetrik Dimetilarjinin (SDMA). SDMA ve böbrek fonksiyonu yüksek korelasyon içindedir. SDMA bir metillenmiş arginin amino asididir. SDMA böbrekler tarafından atılır. Bu çalışmada kronik böbrek yetmezliği tanısı konmuş kedilere ait kan sonuçları karşılaştırılmıştır ve bazı hastalarda SDMA ile kreatinin karşılaştırılarak tanıdaki etkileri göz önünde bulundurulmuştur. 10 yaşında melez dişi bir kediden alınan kan örneğinde SDMA, kreatinin ve BUN değerlerine bakılmıştır. SDMA değeri 15 µg/dL yani yüksek kreatinin (2.2 mg/dL) ve BUN (23 mg/dL) değerleri ise normal aralıklarda çıkmıştır. Bu bize Böbrek fonksiyonlarının çalıştığını ancak böbrek yetersizliğinin başlangıç aşamasında olduğunu göstermektedir. Burdan çıkarılabilecek sonuca göre SDMA ile Kreatinin artışı korelasyon içindedir ve SDMA yükseldikçe böbrek fonksiyonundaki kayıplar yüzde olarak artmaktadır ve zamanla Kreatininde yükselmesine neden olmaktadır. Daha ayrıntılı çalışmalar yaparak SDMA ile Kreatininin erken tanıdaki rolü ve böbrekle ilişkisi hakkında bilgi toplanabilir.

Anahtar kelimeler: Kreatinin, Kronik Böbrek Yetmezliği, SDMA.

INTRODUCTION

Chronic renal failure is an irreversible and progressive disease (Adalati et al. 2003). It is a disease caused by decreased glomerular filtration rate. When the glomerular filtration rate decreases to 35-50 ml/min, clinical symptoms begin to appear. Uremic syndrome begins when GFR decreases below 20-25 ml / min and end stage renal disease occurs when GFR decreases to 5-10 ml / min(Tanriverdi et al. 2010). The clinical manifestation of Chronic Renal Failure can be confused with other diseases. General symptoms include polyuria, polydipsia, vomiting, lethargy, weight loss, and loss of appetite (Relford et al. 2016). Important parameters in Chronic Kidney Diseases are: Urea, Creatinine, BUN (Blood urea nitrogen), Total Protein, Phosphorus, Calcium and SDMA (Symmetric Dimethylarginine) (Smeltzer and Bare 2000).

Creatinine is an important kidney parameter related to GFR. However, it is not 100% reliable in renal function because it is affected by both protein intake and muscle mass(Braun et al. 2008). Creatinine level decreases with age. SDMA level increases only due to GFR reduction. For example, there is a 50% decrease in GFR versus an increase in serum creatinine level from 0.7 to 1.4 mg/dl. In a study with cats blood results for SDMA was found increased, 8 months earlier than creatinine(Grauer et al. 2016). Creatinine begins to increase only when 75% of renal function disappears, whereas SDMA increases only in 20% loss of function(Relford et al. 2016; Nabity et al. 2015).

SDMA is a methylated arginine amino acid. SDMA is derived from intranuclear methylation of L-arginine residues and released into the cytoplasm after proteolysis. SDMA is excreted by the kidneys. Methylation of arginine residues is catalyzed by an enzyme group called protein arginine N-methyl transferases(Kielstein et al. 2006). SDMA has a small molecular size like 202 g/mol and because of its small size SDMA is a good kidney biomarker because it has a positive charge and be filtered by glomerular filtration. SDMA has an extensive renal clearance and that is a point too, to be a good kidney biomarker (Kielstein et al. 2006; Glorieux et al. 2016).

MATERIALS AND METHODS

In this study, blood results from cats diagnosed with kidney disease were compared and creatinine and SDMA values were determined. Blood results were obtained from a veterinary clinic in Ankara. Blood samples from 8 cats are available. In 3 of these, both SDMA and Creatinine levels could be compared. Serum SDMA levels were not evaluated in the remaining 5 cats. 6 parameters were measured in blood serum samples. These are: Creatinine, BUN, Total Protein, phosphorus, calcium and SDMA. Parameters were measured in autoanalysers. Blood was taken from some patients twice: before and after treatment.

RESULTS

Patient 1: The first visit to the clinic was on June the 13, 2019. The cat had a weight loss and The cat was brought to the clinic with complaints of appetite and weight loss. After the blood analyse the cat was diagnosed with CKD. At the first blood analyses Creatinine levels: 4,4 mg/dL (H), Total Protein levels: 9,5 g/dl (H), BUN levels: 53,6 mg/dl (H) were high and Phosphorus levels: 3,4 mg/dl (N) was normal. After clinical treatment on July the 29 the blood was checked for a second time and Creatinine levels decrease to 2,8 mg/dl, BUN levels decrease to 38 mg/dl and phosphorus levels increase to 4,7 mg/dl. The increase in phosphorus levels may be due to food intake due to increased appetite.

Patient 2: In April a cat came to the clinic with serious weight loss and anorexia. After Blood analysis it was diagnosed with CKD and clinical treatment began. Creatinine levels: 3,6 mg/dl, BUN: 64,8 mg/dl and Phosphorus: >15 mg/dl were too high and unfortunately this old cat passed away after 3 days.

Patient 3: This case was slightly different because in this case the cat was a young British shorthair and the blood results at first analysis were too high but only after 2 days at the second check blood reults gone better. Creatinine levels decreased from 20,7 mg/dl to 15,1 mg/dl and BUN levels were higher than 140 mg/dl and it could not be measured. The first check was on august 29, 2019 and second check was on august the 31.

Patient 4: A 14 years old Persian cat with 2 weeks anorexia came to the clinic and the first blood results on May the 6, 2019 are; Creatinine 3,1 mg/dl (H) and BUN 41,1 mg/dl (H). After

treatment on May the 27 Creatinine levels decreased to 2,4 mg/dl and BUN levels decreased to 26,8 mg/dl.

Patient 5: A 10 years old cat with anorexia and vomiting came to the clinic on September 29 and blood serum was taken to check. Creatinine levels: 3,4 mg/dl (H), BUN levels: 119 mg/dl (H), Total Protein levels: 4,9 g/dl (L) and Phosphorus levels: 8,6 mg/dl (H). Based on these values, chronic kidney disease was diagnosed. Unfortunately we lost this patient during the treatment process.

Patient 6: This case is an important case because in this case we can see the difference in early diagnosis between SDMA and Creatinine. This patient is a 10 years old mixed female cat. The blood results on February the 27 are; Creatinine (2,2 mg/dl), BUN (23 mg/dl), Total Protein (7,9 g/dl), Phosphorus (4,3 mg/dl) and Calcium (10,3 mg/dl) are in normal ranges only SDMA levels are high (15 µg/dl). The normal ranges for SDMA are 0 to 14 µg/dl. This is a new increase in SDMA, so we can say that this is an early diagnosis. If we make an estimate for better understanding, it is likely that in this case the kidneys have lost only a small part of its function and are now at the stage of recovery.

Patient 7: A 10 years old sterile female munchkin cat visit the clinic fort he first time on July the 19, 2019. At the first blood results Creatinine levels were too high to measure. SDMA levels were 83 µg/dl, BUN levels were higher than 130 mg/dl Total Protein (9,6 mg/dl) and Phosphorus levels (higher than 16,1 mg/dl) were too high too. Only Calcium levels were in normal ranges (9,6 mg/dl). Here in this case we can see that this is not an early diagnosis because of the values in Creatinine and BUN.

Patient 8: This is a different case because of the cat. This cat has come to the clinic with a very bad general situation. The first blood check was on July the 8, 2019 and Creatinine (3,6 mg/dl) and SDMA (19 µg/dl) levels were high but not so high like in patient 7. And the other values like BUN (29 mg/dl), Phosphorus (5,1 mg/dl), Total Protein (8,8 g/dl) and Calcium (10,7 mg/dl) were in normal ranges. When there was no improvement in the general condition 2 months after treatment, a blood sample was taken again to compare the values. This time the values were higher than the previous sample. SDMA: too high to measure, Creatinine: 4,4 mg/dl (H), BUN: 42 mg/dl (H), Total Protein: 8,4 g/dl (N), Phosphorus: 5,1 mg/dl (N) and Calcium: 10,5 mg/dl (N). This cat passed away.

SDMA is an early diagnosis biomarker which is important for CKD. İn this case we can see the importance of early diagnosis. İncrease in SDMA will occur much earlier than creatinine, so by checking SDMA during blood analysis is vital for early diagnosis of kidney dysfunction. To be sure we have to check out SDMA. Early diagnosis saves lives.

REFERENCES

Adalati R, Soyogul Gurer Ü, Cevikbas A, Johansson C. (2003). Investigation of the In Vitro Effect of Cefodizime on Polymorphonuclear Leucocyte Functions in Chronic Renal Failure Patients. Türk Mikrobiyol Cem Derg, 33:85-91.

Braun JP, Lefebvre HP, Watson ADJ. (2008). Creatinine in the Dog: A Review. Vet Clin Pathology, 32(4):162-179.

Glorieux G, Neirynck N, Pletnick A, et al. (2016). Uraemic toxins: overview. In: Turner N, Lamiere N, Goldsmith DJ, et al, editors. Oxford textbook of clinical nephrology. 4th edition. Oxford (United Kingdom): Oxford University Press, p. 2161–73.

Grauer G. (2016). Early diagnosis of chronic kidney disease in dogs & cats: use of serum creatinine & symmetric dimethylarginine. Today's Vet Pract, 6:68–72.

Kielstein JT, Salpeter SR, Bode-Boeger SM, Cooke JP, Fliser D. (2006). Symmetric dimethylarginine (SDMA) as endogenous marker of renal function—a meta-analysis. Nephrol Dial Transplant; 21: 2446–2451.

Nabity MB, Lees GE, Boggess MM, Yerramilli M, Obare E, Rakitin A, Aguiar J, Relford R. (2015). Symmetric dimethylarginine assay validation, stability, and evaluation as a marker for the detection of chronic kidney disease in dogs. J Vet Intern Med, 29:1036–44.

Relford R, Robertson J, Clements C. (2016). Symmetric Dimethylarginine: Improving the Diagnosis and Staging of Chronic Kidney Disease in Small Animals. Vet Clin Small Anim, 46 941–960.

Smeltzer SC, Bare B. (2000). Medical-Surgical Nursing. 9. Baskı, Lippincott, pp.1952-1972.

Tanriverdi MH, Karadag A, Hatipoglu ES. (2010). Chronic Kidney Failure. Konuralp Tip Dergisi, 2(2):27-32.