INTRODUCTION

SDMA is the acronym for Symmetric DimethylArginine. SDMA is a methylated form of the amino acid arginine that is produced when protein breakdown occurs in all cells in the body and is excreted through the kidneys. SDMA correlates with the gold standard for assessing kidney function, a test called Glomerular Filtration Rate, or GFR, in dogs and cats. GFR is expensive and not an easy test to perform from a practical perspective. Hence, being able to use SDMA as a surrogate for GFR is helpful to assess kidney function, using a simple blood test.

SDMA is different from creatinine because it is an earlier assessment of loss of kidney function or decrease in GFR compared with creatinine. SDMA increases when there is on average 40% loss of kidney function whereas creatinine increases when there is 75% or more loss of kidney function. SDMA levels can be increased in instances of acute kidney injury (AKI) and with chronic kidney disease (CKD) in both dogs and cats. SDMA is a more reliable and sensitive indicator of loss of kidney function. SDMA is not affected by loss of lean muscle mass unlike creatinine. In thin patients with loss of lean muscle, creatinine does not accurately estimate loss of kidney function.

SDMA is important as it has been included in the International Renal Interest Society (IRIS) guidelines for diagnosing, staging and monitoring chronic kidney disease (CKD) in dogs and cats. The IRIS guidelines can be found on the website: http://www.iris-kidney.com. It is important to always evaluate kidney function biomarkers, like creatinine and SDMA, with a complete urinalysis to determine if there is a pre-renal, renal or post-renal cause of the patient’s azotemia and increased SDMA. Examples of pre-renal causes of azotemia and increased SDMA include dehydration; and, post-renal causes include urethral obstruction.

SDMA can be measured using different methodologies. Antech SDMA is measured using an Enzyme Linked ImmunoSorbent Assay or ELISA; it is fast, sensitive, and provides reproducible results. IDEXX SDMA is a high-throughput, homogenous immunoassay. The ELISA used to measure Antech SDMA is a competitive enzyme immunoassay.

STUDY DESIGN

Correlation study with IDEXX SDMA

Antech SDMA was correlated with IDEXX SDMA reference laboratory testing using 70 dogs and 65 cats.

Correlation between Antech SDMA and Liquid Chromatography Mass Spectrometry (LCMS) was performed by an external medical laboratory in Germany, Medizinisches Labor Bremen (https://www.mlhb.de/english/).

Reference Interval Study

The reference interval study for dogs and cats was performed using 95 dogs and 95 cats. All dogs and cats were between the ages of three to six years. The creatinine range for the dogs used was < 1.8 mg/dL and the creatinine range for the cats used was < 2.4 mg/dL.

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**RESULTS**

Correlation study with IDEXX SDMA
Correlation coefficient in cats is 0.92 and the correlation coefficient is 0.93 in dogs.

Figure 1 (right) shows the regression line with 95% confidence interval (shaded blue line) comparing Antech SDMA (ug/dL) on the x-axis with IDEXX SDMA (ug/dL) on the y-axis for cats.

Canine Data: n = 70, $R^2 = 0.93$
IDEXX SDMA vs. Antech SDMA

Figure 2 (right) shows the regression line with 95% confidence interval (blue shaded line) comparing Antech SDMA (ug/dL) on the x-axis with IDEXX SDMA (ug/dL) on the y-axis for dogs.

Canine Data: n = 65, $R^2 = 0.92$
IDEXX SDMA vs. Antech SDMA

Correlation between Antech SDMA and Liquid Chromatography Mass Spectrometry
Correlations studies performed with the Antech SDMA and Liquid Chromatography Mass Spectrometry (LCMS) show excellent correlation of > 95% ($R^2 = 0.952$).

Figure 3 (right) shows the regression line with 95% confidence interval (blue solid and shaded area) comparing Antech SDMA (ug/dL) on the x-axis with LC-MS (ug/dL) on the y-axis.

N = 65 (dogs and cats). Correlation = 0.975. Slope = 0.968
LC-MS/MS ug/dl vs. Antech ELISA
Reference interval study

The reference intervals for dogs and cats with the Antech SDMA are similar to that reported for the IDEXX SDMA (< 14 ug/dL in dogs and cats). The normal reference ranges for Antech SDMA in dogs is < 14 ug/dL, and in cats < 15 ug/dL.

<table>
<thead>
<tr>
<th>Reference Range for Antech SDMA in Dogs</th>
<th>Reference Range for Antech SDMA in Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>&lt;14.0 µg/dL</td>
<td>&lt;15.0 µg/dL</td>
</tr>
<tr>
<td>Mild Increase</td>
<td>Mild Increase</td>
</tr>
<tr>
<td>14.0 -16.0 µg/dL</td>
<td>15.0 -20 µg/dL</td>
</tr>
<tr>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>&gt;16.0 µg/dL</td>
<td>&gt;20.0 µg/dL</td>
</tr>
</tbody>
</table>

DISCUSSION

The processes that lead to formation of SDMA are highly conserved across species and SDMA values between 14-16 ug/dL in dogs and 15-20 ug/dL in cats should warrant further investigation for an underlying cause of an increased SDMA. Additionally, repeat testing of SDMA in two to four weeks is recommended to evaluate trends and persistence of SDMA results.

Correlation studies performed internally have shown that the IDEXX SDMA and Antech SDMA tests have a very high degree of correlation in both dogs and cats, at greater than 90%. Correlation coefficients were interpreted as follows: r = 0.90–1.0, defined as high correlation; 0.70–0.89, high correlation; 0.50–0.69, moderate correlation; 0.30–0.49, low correlation; and 0–0.29, little, if any, correlation.

Liquid Chromatography Mass Spectrometry (LCMS), which has shown good correlation with glomerular filtration rate, is considered the gold standard methodology for measuring SDMA. LCMS is an advanced analytical technique that is used to accurately identify and quantify molecules within a sample. It is not used routinely by commercial laboratories because it cannot process large volumes of samples.

Precision refers to the repeatability of a measurement of an analyte. This is different from accuracy, which refers to the how close the value reported for an analyte is to the true value. The Antech SDMA measured by ELISA shows a total coefficient of variation (CV) of 9.6% (range of 6.6% to 10.6%). This is acceptable and is consistent with the high throughput immunoassay for IDEXX SDMA which is reported at < 10%.

CONCLUSIONS

SDMA is an earlier, more reliable biomarker of kidney function in dogs and cats compared with creatinine. The Antech SDMA ELISA test compares extremely well with IDEXX SDMA immunoassay in dogs and cats with a correlation of greater than 90%. Antech SDMA correlates highly at greater than 95% with LCMS, the gold standard for assessing kidney function. The reference ranges for dogs and cats with Antech SDMA is comparable to IDEXX SDMA, with reference ranges of < 14 ug/dL in dogs and < 15 ug/dL in cats.

REFERENCES