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SERUM SYMMETRIC DIMETHYLARGININE (SDMA) IN DOGS WITH HYPOTHYROIDISM

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BACKGROUND

Canine hypothyroidism is associated with decreased glomerular filtration rate (GFR), while serum creatinine (SCr) concentrations are rarely increased above the reference interval (RI) in hypothyroid dogs.

Symmetric dimethylarginine (SDMA) is considered a biomarker for early detection of renal dysfunction and resulted strongly correlated with GFR in dogs. In humans, SDMA is significantly higher in hypothyroid compared to healthy people.

OBJECTIVES

The aim of this study was to evaluate the SDMA concentrations in a population of hypothyroid dogs (HD) at the time of diagnosis (T0) and after treatment (T1).

MATERIAL AND METHODS

14 DOGS WITH SPONTANEOUS HYPOTHYROIDISM:

- Consistent clinical signs and laboratory findings
 - Serum total T4 and cTSH concentrations below and above the RI, respectively.
 - In dogs with normal cTSH, rhTSH stimulation test was performed to confirm the diagnosis
- 20 HEALTHY DOGS (CONTROL GROUP)
- Normal physical examination
 - Normal complete blood cell count, serum biochemistry profile and urinalysis

- SCr was measured for diagnostic or check-up purposes
- SDMA was measured afterwards from surplus of serum stored at -20°C using a validated immunoassay (IDEXX SDMA test)
- In HD SCr and SDMA were measured at T0 and after 15 to 112 days (median 64.5 days) of treatment (T1) with levothyroxine (10-15µg/kg q12h PO).

RESULTS

HD had a median age of 9.1 years (4.0-15.7), median body weight (BW) of 29 Kg (7.9-53), 7/14 were male (1 castrated) and 7/14 female (3 spayed). There were no significant differences regarding signalment and BW between HD and control group. Median SDMA concentrations (RI <14 µg/dL) were 10 µg/dL (6-17), 13.5 µg/dL (7-20) and 10.5 µg/dL (5-17) in healthy dogs, HD at T0 and HD at T1, respectively. SDMA concentrations were significantly higher in HD at T0 in comparison with healthy dogs ($p = 0.029$) and HD at T1 ($p = 0.031$) (Fig 1). Among HD, 7/14 (50%) had SDMA above the RI at T0 and only 1/14 (7.1%) at T1. At T0, 4/14 (28.6%) HD had SCr above the RI (>1.35 mg/dL) and only 1/14 (7.1%) dogs had SCr above the RI at T1. SCr concentration was significantly higher in HD at T0 compared to HD at T1 ($p < 0.0082$). No significant correlation was observed between SDMA and T4, and SDMA and SCr in the HD at T0 and T1.

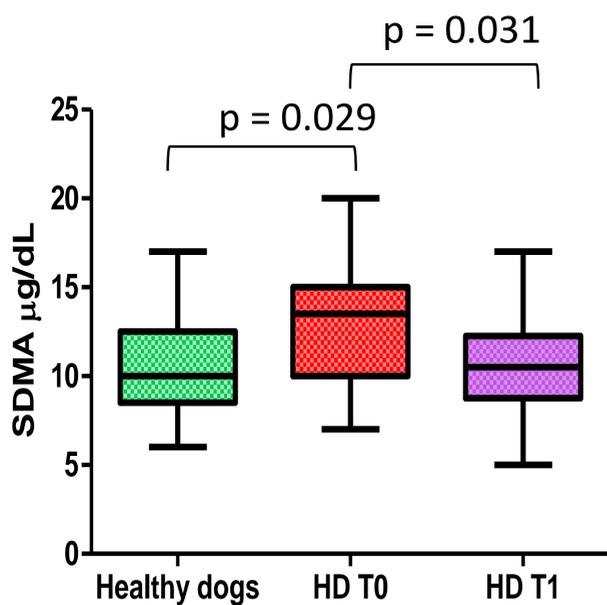


Figure 1: Box plots comparing the medians of SDMA concentration in healthy dogs, HD at T0, and HD at T1.

The horizontal lines of the box represent the 25th, 50th (median) and the 75th percentiles. Outlying horizontal lines of the box represent minimum and maximum values.

CONCLUSION

This study shows that in HD SDMA concentrations are frequently above the RI at diagnosis and normalize after treatment. The GFR modifications that are present in canine hypothyroidism may be better detected with SDMA compared to SCr.

USE OF TANDEM MASS SPECTROMETRY (LC-MS-MS) FOR THE MEASUREMENT OF THYROID HORMONES IN DOGS WITH SPONTANEOUS HYPOTHYROIDISM

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BACKGROUND

In human medicine liquid chromatography tandem mass spectrometry (LC-MS/MS) is actually considered the "gold standard" for measurement of many hormones concentration and it is widely used in clinical practice; its diagnostic performance has never been investigated in dogs with hypothyroidism (DWH).

OBJECTIVES

The aim of this study was to determine whether serum concentrations of ft_4 , ft_3 , rT_3 , $3.3-T_2$, $3.5-T_2$, measured with LC-MS/MS, were able to differentiate DWH (n=13) from dogs with non-thyroidal illness (DNTI) (n=12), septic dogs (SD) (n=12) and healthy dogs (HD) (n=12).

MATERIAL AND METHODS

Hypothyroidism was diagnosed based on consistent clinical signs, laboratory findings, total T₄ (TT₄) and cTSH concentrations below and above the reference interval (RI), respectively; in dogs with normal cTSH, a rhTSH stimulation test was performed to confirm the diagnosis. In DNTI, hypothyroidism was excluded upon a negative result of a rhTSH stimulation test. SD were diagnosed based on alteration of temperature, cardiac and respiratory frequency, differential leukocyte count and C-reactive protein concentration above RI. HD were considered healthy upon history and physical examination. Hormones evaluation were performed with LC-MS/MS on surplus serum stored at -80°C. TT₄ and cTSH were measured using a validated immunoassay (Immulite®).

RESULTS

Non-significant differences considering signalment, age and body weight were found between groups.

Median TT₄ and ft_4 serum concentrations were significantly higher ($p < 0.001$) in HD compared to DNTI, DWH and SD. Median ft_3 serum concentration was significantly lower in DWH and DNTI compared to SD ($p < 0.001$ and $p = 0.0091$, respectively) and HD ($p < 0.001$ and $p = 0.0024$, respectively). Median rT_3 serum concentration was significantly lower in DWH compared to SD ($p = 0.0141$) and HD ($p = 0.0128$). Median $3.3-T_2$ serum concentration was significantly higher in DWH compared to DNTI ($p = 0.0038$) and HD ($p = 0.0447$). There were non-significant differences regarding median $3.5-T_2$ serum concentrations among the dogs of the four groups.

Using the ROC curve analysis to differentiate DWH from DNTI+SD an AUC of 0.86 ($p = 0.003$), 0.76 ($p = 0.009$) and 0.75 ($p = 0.012$) was obtained for ft_3 , ft_4 and TT₄, respectively. Values of ft_3 <0.61 pmol/L better discriminated hypothyroidism with 69% sensitivity (95%CI: 39-91%), 83% specificity (95%CI: 63-95%) and accuracy of 0.86 (95%CI: 0.74-0.98).

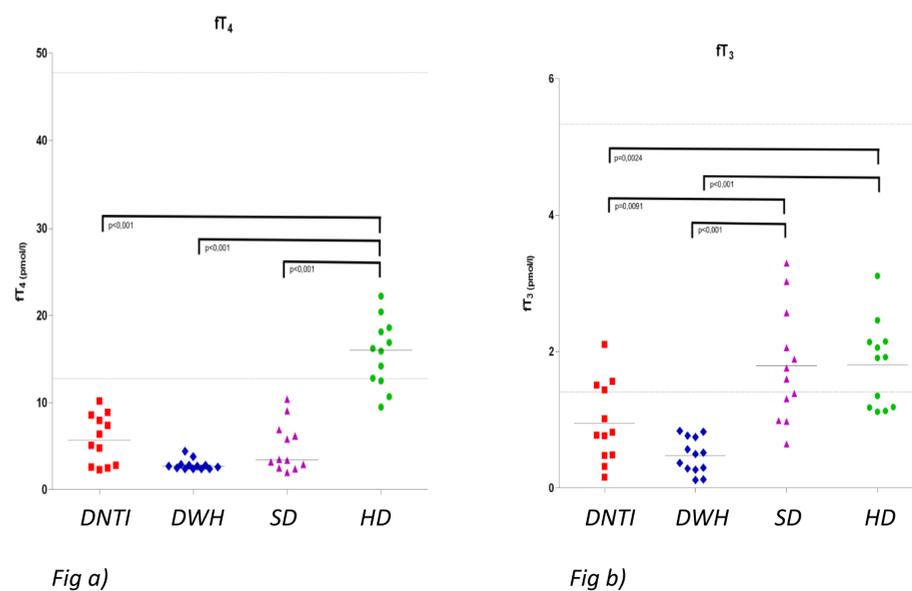


Fig a) Dot plot representing serum concentration of ft_4 in DNTI, DWH, SD and HD. Short horizontal lines represent the median value of each group, while the long continuous lines shows the parameter's reference range.

Fig b) Dot plot representing serum concentration of ft_3 in DNTI, DWH, SD and HD. Short horizontal lines represent the median value of each group, while the long continuous lines shows the parameter's reference range.

CONCLUSION

Although serum ft_3 and ft_4 (LC-MS/MS) have shown better performances than the serum TT₄ (Immulite®) in identifying DWH, the overlap between DWH and DNTI+SD was unfortunately relevant also for the thyroid hormones measurements with LC-MS/MS. Despite the introduction of new analytical methods, the use of dynamic tests (e.g. rhTSH stimulation test) remains the better method to discriminate DWH from DNTI.

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