PROLACTIN AND THYROID HORMONES IN DOGS

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Abstract: *There is very scarce information concerning prolactin (PRL) serum concentrations under pathologic conditions in dogs. To describe the relationship between PRL and thyroid hormones serum concentrations forty-five cross- and pure-bred male and female dogs with clinical suspicious of hypothyroidism were blood sampled for PRL and thyrotropin (TSH), thyroxin (T4) and/or free T4 (FT4) serum determinations. Prolactin concentrations in hypothyroid and euthyroid dogs were compared by the Mann-Whitney test. For further description of data correlation analyses between PRL and TSH, FT4 or T4 were also tested. Percentage PRL change was calculated in the patient in which the TRH stimulation test was carried out. Overall serum PRL concentrations in hypothyroid (n= 34) and euthyroid (n= 11) dogs were 25.9±4.8 and 14.6±6.5 ng/ml, respectively (p >0.05). No significant correlation could be found between PRL and the different thyroid hormones in any group. The stimulated dog was classified as subclinical a hypothyroid (grade I). Prolactin increased 5 times (from 0.4 to 2.1 ng/ml) after TRH injection in this animal. Further work should be done to describe prolactinemia in canine hypothyroidism.*

Key words: prolactin, canine, thyroid gland, hypothyroidism

PROLACTINA Y HORMONAS TIROIDEAS EN CANINOS

Resumen: *Muy poco se conoce sobre la concentración sérica de prolactina (PRL) bajo condiciones patológicas en perros. Para describir la relación entre las concentraciones séricas de PRL y las hormonas tiroideas se usaron cuarenta y cinco perros machos y hembras de raza pura y mestizos con sospecha clínica de hipotiroidismo, de los cuales se tomaron muestras de sangre para determinaciones séricas de PRL y tirotrofina (TSH), tiroxina (T4) y/o T4 libre (T4L). Las concentraciones de PRL en perros hipotiroideos y eutiroideos se compararon con el test de Mann-Whitney. Para la descripción adicional de los datos se correlacionó la PRL y la TSH, T4L o T4. El porcentaje cambio de la PRL se calculó en los pacientes en los que se realizó la prueba de estimulación con TRH. La concentracion sérica de PRL de la totalidad de los perros hipotiroideos (n= 34) y eutiroideos (n= 11) fue de 25.9±4.8 y 14.6±6.5 ng/ml, respectivamente (p >0.05). No se encontraron diferencias significativas entre la PRL y las diferentes hormonas tiroideas en ninguno de los grupos. El perro estimulado se clasificó como hipotiroideo subclínico (grado I). En ese animal la prolactina aumentó 5 veces (de 0.4 a 2.1 ng/ml) después de la inyección de TRH. Deben realizarse trabajos adicionales para describir la prolactinemia en caninos con hipotiroidismo.*

Palabras clave: prolactina, canino, glándula tiroidea, hipotiroidismo

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INTRODUCTION

Prolactin (PRL) is a peptide hormone produced and secreted by the lactotropic cells of the anterior pituitary. In mammals, PRL is essentially involved in the control of reproduction (1). Particularly, in the domestic dog this hormone regulates gonadal function, mammary development and reproductive behavior (2, 3). Prolactin secretion is regulated by a constant inhibitory tone of hypothalamic origin, whose main mediator is dopamine. Dopamine acts on D2 type dopamine receptors on the lactotropic cells. Prolactin secretion is further regulated by numerous neurotransmitters and peptide factors. They may have either an inhibitory or stimulatory effect. The latter are histamine, oxytocin, vasopressin, thyrotropin releasing hormone (TRH), estrogens, GnRH and opiods (1).

In human beings, pathologic hyperprolactinemia is a common condition that can result from a number of causes including use of medications (dopamine antagonists, estrogens), compression of the pituitary stalk by other pathology, hypothyroidism, renal failure, cirrhosis, or pituitary prolactinomas. Hyperprolatinemic patients can present with hypogonadism, infertility, galactorrhea (4).

There is very scarce information concerning PRL serum concentrations under pathologic conditions in dogs. This may be due to the lack of pituitary imaging techniques in most veterinary hospitals as well as to the fact that prolactinemia is not a routine determination in clinical practice. In this species, hyperprolactinemia has only been described in clinically overtly pseudopregnant bitches (5, 6, 7) and in one case of hypothyroidism (8). Knowing that primary hypothyroidism is the most prevalent endocrine disease in dogs it was of interest to describe the relationship between PRL and thyroid hormones serum concentrations in primary hypothyroid and euthyroid dogs.

MATERIALS AND METHODS

ANIMALS

Forty-five client-owned cross- and purebred male and female dogs, aged 5.9 ± 3.2 years, weighing 10 to 35 kg that were referred to us were included in this study. All the animals had a clinically strong suspicious of hypothyroidism. They were obese or presented either dermatologic or reproductive problems. None of them had galactorrhea. Primary hypothyroidism was defined as serum thyrotropin (TSH) > 0.4 ng/ml with low free thyroxin (FT4 < 0.7 ng/dl) or thyroxin (T4< 1μg/dl; 9).

BLOOD SAMPLING AND HORMONE ASSAYS

Blood samples for PRL and different thyroid hormone determinations were collected by direct peripheral venipuncture (jugular/cephalic/saphenous). In one case, basal and 15 minutes after the iv administration of 10μg/kg TRH (Threlea 200®, Elea, Argentina) samples were also taken. All the samples were centrifuged at 4,000 g for 15 minutes, serum obtained and stored at 20º C until hormone assay.

Serum PRL was measured by a homologous endpoint enzyme immunometric assay (Milenia, DPC®, Bad Nauheim, Germany). The intraassay and interassay coefficients of variation (CV) of the kit were 5.3 and 8.7, respectively. The lowest limit of detection at 95 % binding (sensitivity) was 0.4 ng/ml.

Canine thyrotropin (cTSH) was determined by a solid phase canine immunoradiometric assay (IRMA, DPC®, Los Angeles, CA, USA), sensitivity was 0.03 ng/ml. The intraassay and interassay CV were 3% and 4.3%, respectively. Canine T4 was carried out by solid phase radioimmunoassay (RIA), sensitivity was 0.16 μg/dl (DPC®, Los Angeles, CA, USA). Free T4 was measured by a solid phase human RIA (DPC®, Los Angeles, CA, USA). The intraassay and interassay CV were 2% and 3.5%, respectively while sensitivity was 0.05 ng/dl.

DATA ANALYSIS

Descriptive statistics (mean ± SEM) was carried out for PRL serum concentrations in hypothyroid and euthyroid dogs. Prolactin concentrations in hypothyroid and euthyroid dogs were also compared by the Mann-Whitney test. For further description of data, correlation analyses between PRL and TSH, FT4 or T4 were also tested. The level of significance was set at 0.05. Percentage PRL change was calculated in the patient in which the TRH stimulation test was carried out.

RESULTS

Overall serum PRL concentrations in hypothyroid (n= 34) and euthyroid (n= 11) dogs were 25.9±4.8 and 14.6±6.5 ng/ml, respectively (p >0.05). No significant correlation could be found between PRL and the different thyroid hormones in any group. The stimulated dog was classified as subclinical hypothyroid (grade I; 10). Serum PRL increased 5 times (from 0.4 to 2.1 ng/ml) after TRH injection in this animal.

DISCUSSION

In euthyroid dogs PRL serum concentrations were within the range previously reported for this species using the same homologous assay (6, 11, 12). Although no statistically significant difference could be found for PRL serum concentrations between hypothyroid and euthyroid dogs, a tendency to higher values could be observed

in the hypothyroid animals. It may be the case that in a larger population significant differences appeared. Hyperprolactinemia is believed to develop following thyroid hormone deficiency - induced increase in TRH secretion which, in turn, stimulates PRL production in hypothyroid patients (13).

Although the authors have observed previous cases of galactorrhea associated with hypothyroidism none of the animals of this study presented galactorrhea. Galactorrhea has been associated with primary hypothyroidism in several species including dogs (8,13,14). It seems that the appearance of this clinical sign requires facilitating factors such as an entire state and previous endocrine mammary stimulation (13). In a human study, galactorrhea has been found in only 24% of cases of severe hyperprolactinemia (15).

In the present study neither hypothyroid nor euthyroid dogs showed a significant correlation between PRL and thyroid hormones. Similar results were found in several human studies where no correlation was found between TSH and PRL concentrations (16, 17, 18).

In human medicine, stimulatory TRH test was devised to determine the etiology of hyperprolactinemia. Patients with prolactinomas have a diminished PRL response to exogenous TRH, although this test is not specific as the response may not be consistent (1). In this hypothyroid dog, PRL markedly increased after TRH stimulation demonstrating an exaggerated lactotropic cell response to exogenous TRH. Similarly, in men post stimulation PRL concentrations were significantly higher in primary hypothyroid than in controls (16, 17).

It is concluded that these hypothyroid dogs had a tendency to present higher PRL serum concentrations, although further work should be done to describe prolactinemia in hypothyroidism and other pathological conditions in this species.

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