

Canine Adult-Onset Hypothyroidism: Prevalence, Clinical and Laboratory Findings with Special Reference to Therapeutic Approach

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1. Abstract

Hypothyroidism is one of the most common endocrinopathies in dogs, it is defined as a decrease in production of thyroid hormones. Hypothyroidism results in vague clinical of signs but metabolic and dermatological signs are the most reported manifestations. This investigation aimed to study canine hypothyroidism in terms of clinical, haemato- biochemical, and thyroid panel alterations and evaluate response to treatment in adult onset hypothyroidism in dogs' cosmopolitan in Cairo and Giza governorates. To crude determination of disease in dog cosmopolitan in Cairo and Giza governorates, multicenter study was conducted. In the period from December-2019 to May-2020, 220 dogs with various dermatologic signs represented to different clinics, after ruling out other causes, 40 with signs consistent with hypothyroidism were subjected to initial screening for hypothyroidism using TT4. Only 15 dogs showed decrease in TT4 and these dogs were further investigated, additional 8 clinically healthy dogs enrolled as control group. Blood sample was taken from both hypothyroid dogs [N=15] and control dogs [N=8] for hematology analysis, TT4, fT4, TSH. Cholesterol, ALT and ALP. Diseased group [15 dogs] were treated with levothyroxine and re-evaluated after 1-month period. Overall prevalence of hypothyroidism in this investigation was 7.5 percent. Significant decrease in RBCs, PCV, TT4 and fT4 along with non-significant increase in TSH and cholesterol were recorded in hypothyroid patients compared to control group. Treatment with levothyroxine caused thyroid hormones to be within normal reference range. The Prevalence of hypothyroidism in studied cases in this investigation was 7.5 % and is similar to the reported prevalence; diagnosis of hypothyroidism should be relying on combination of clinical and laboratory data. Usage of human levothyroxine can successfully manage canine hypothyroidism.

Key words: Hypothyroidism, Dogs, Levothyroxine, Thyroid panel.

2. Introduction

Endocrinology and Dermatology are specialties in veterinary medicine on the rise nowadays. In veterinary clinics and hospitals, about 20-75% of cases are related to skin problems, 8.6% of these problems are caused by endocrine disorders [1]. Hypothyroidism is the most common endocrine disorder in dogs, it may be congenital or acquired and the later can be primary or secondary [2]. Thyroid hormones responsible for most of metabolism in the body, so any alteration in thyroid hormone affects most of body metabolism particularly lipids and protein [3].

Hypothyroidism accounts for variety of clinical manifestations among them dermatological and metabolic signs are the most encountered in clinics [4]. Although hypothyroidism is considered the most common endocrine disorder in dogs, its exact prevalence is largely unknown, sometimes it is overestimated others, it is underestimated [5]. Diagnosis of canine hypothyroidism is mainly based on historical and clinical findings in addition to laboratory findings and the response to hormonal therapy [6]. The major dermatological changes are non-inflammatory, non-pruritic, bilaterally symmetrical alopecia, dry or oily seborrhea, rat's tail, and hyperpigmentation [7], with

anemia and hyperlipidemia as major biochemical alterations [6,8,9]. In some cases, there are a moderate increase in ALT and AST liver enzymes [6].

Diagnosis of hypothyroidism is not always straightforward with reduction in TT4 and fT4 and elevation in TSH, sometimes response to hormonal replacement therapy is confirmatory of diagnosis [1]. Usually, TT4 is used as screening test for hypothyroidism as normal level of TT4 rule out diagnosis but not confirm it, and additional fT4 and TSH tests are warranted for suspected cases [10,11].

Treatment of hypothyroidism depends on replacement of depleted hormone via oral administration of levothyroxine and clinical improvement can be achieved quickly [11]. Therefore, this investigation aimed to study canine hypothyroidism in terms of clinical, haemato-biochemical, and thyroid panel alteration and evaluate response to treatment in adult onset hypothyroidism in dogs.

3. Materials and Methods

Ethical approval

This study was given approval number [vetcu16072020183] from the institution Animal Care and Use Committee, faculty of veterinary Medicine Cairo University, Egypt.

Study population

To crude determination of disease in dog cosmopolitan in Cairo and Giza governorate, multicenter study was conducted. In period of December-2019 to May-2020, 220 dogs with various dermatologic signs represented to different clinics in October city,

EL-Rehab city, Giza, Nasr city and Maddi district, these clinics located in Cairo and Giza governorates. Age range from 2-8 years of both sexes. Dermatologic signs were recorded. Fecal examination, skin scrapping, bacteriological culture and microscopic examination were conducted on suspected animals and diagnosis list is presented in table 1.

After ruling out other causes, 40 with signs consistent with hypothyroidism were

subjected to initial screening for hypothyroidism using TT4. Only 15 dogs showed decrease in TT4. Hypothyroid dogs were from different breeds: Golden retriever [n=6], Rottweiler [n=3], Akita [n=1], Pit bull [n=1], and German shepherd [n=4], and they were 8 females and 7 males. These dogs were further investigated for fT4 and TSH. Additional 8 apparently healthy dogs were enrolled as control group and underwent same clinical and laboratory testing as hypothyroid group.

Blood samples

Blood sample was taken from hypothyroid and control dogs from cephalic vein; samples were divided into two parts, first one collected on EDTA- containing tube for hematology analysis using automated veterinary hematology analyzer. Second part collected on plain tube for estimation of TT4 [IDEXX Catalyst One], FT4 and TSH [Enzyme linked fluorescent assay, VIDAS, Biomerieux], cholesterol, ALT and ALP [Spectrum Diagnostics, Egypt].

Therapeutic trial

Hypothyroidism-confirmed dogs were treated with Levothyroxine [Euthyrox 100mcg®] at a dose of 0.01mg/kg PO BID. Follow-up was conducted after one-month period with clinical improvement recorded and blood samples withdrawn 5-hours post-pill to evaluate response to hormonal therapy.

Statistical analysis

Data are represented as mean \pm standard error, p value ≤ 0.05 considered significant. Student T test was used to compare hemato-biochemical data in both control and diseased patients while one-way ANOVA test were used to compare thyroid hormones profile in control, diseased and treated groups. P value ≤ 0.05 considered significant. Statistical analysis conducted using SPSS program version 16.00.

4. Results

Out of 220 dogs with dermatologic signs, 40 dogs [20%] were presented with signs

compatible with hypothyroidism only 15 dogs showed thyroid profile result confirm the diagnosis [7.5%] Then overall prevalence was 7.5 percent. List of dermatologic diseases recognized in this study is shown in table 1.

Most consistent clinical signs recorded was non-inflammatory non-pruritic bilaterally symmetrical alopecia on the neck and fore-leg, and tail, dry brittle hair coat [Figure 1].

After one month of treatment, clinical signs begun to improve and areas devoid of hair showed regrowth of the hair and better skin coat quality.

Haemato-biochemical alterations in hypothyroid patients

Significant decrease in RBCs and PCV with non-significant decrease in HB and non-significant increase in cholesterol with no statistical changes detected in ALT, ALP in hypothyroid patient were recorded compared to control group [Table 2].

Thyroid hormone status

In hypothyroid patients, significant decrease in TT4 and fT4 along with non-significant elevation in TSH compared to control data recorded. After administration of levothyroxine, TT4, fT4 and TSH were brought to normal levels [Table 3].

5. Discussion:

Hypothyroidism considered one of the most common endocrinopathies in dogs, its origin may be congenital [very rare] or acquired [most common]; hypothyroidism develops as a result of defect in any part of the hypothalamic pituitary thyroid axis, so it classified according to its cause into primary, secondary and tertiary [12,13]. The prevalence of hypothyroidism in the studied cases in the present investigation was 7.5%. In veterinary settings, about 20-75% of cases are related to skin problems, 8.6% of these problems are caused by endocrine disorders [1]. As hair loss usually among first sign appear in hypothyroid dogs and also in countless disorder; determination of TT4 as a screening test is particularly helpful in

ruling out hypothyroidism as approximately 98% of the hypothyroid dogs have low TT4 concentrations [14]. Exact prevalence of hypothyroidism in dogs is largely unknown, as it is subjected to over or under estimation [5].

Non-pruritic alopecia along with dry brittle coat was the most recorded dermatologic signs in this study. Clinical signs are often vague as thyroid hormones has a direct impression on metabolic status and therefore dysfunction in thyroid gland impacts most of body systems [15] and most of signs appear after destruction of 70% of thyroid gland [5]. Dermatological and metabolic signs are frequently occurred together [15]. Thyroid hormones play integral role in skin homeostasis; therefore, it is not surprising that dermatological signs occur in up to 80% of hypothyroid dog and are the most consistent signs. The major alterations are non-inflammatory, non-pruritic, bilaterally symmetrical alopecia, most affected areas are dorsal region of the neck, lateral and ventral of the thorax, abdomen, and tail [2]. Alopecia mainly occurs as thyroid hormones are necessary to initiate the growth phase [anagen phase] of the hair follicle [16]. Other dermatological signs are dry brittle hair coat, "rat's tail" which is alopecia in the tail with hyperpigmentation though its exact mechanism is unknown [1].

Thyroid hormone deficiency may also cause reduction in consumption of oxygen in the skin, synthesis of protein, and mitotic activity, thus leading to abnormal keratinization, epidermal atrophy, and sebaceous gland atrophy and this predispose affected dogs to recurrent bacterial skin infections as pyoderma which may be a common finding [15].

In this study, significant decrease in RBCs and PCV were reported. Hypothyroidism leads to decrease oxygen consumption, which leads to decreased erythropoietin [EPO] production, and consequently reduce tissue response to EPO which leads to reduction in red blood cell production [5].

Serum biochemistry analysis revealed non-significant increase in cholesterol with no statistical changes detected in ALP, and ALT in hypothyroid patient, these findings agreed with other reports [17,18]. Synthesis, mobilization, and degradation of lipids are stimulated by thyroid hormones [19], therefore, decreases the lipid metabolism may leads to hypercholesterolemia [20] in up to 75% of dogs with hypothyroidism [21]. It was reported that biochemical changes are not always present in hypothyroid dogs [15, 22].

Diagnosis of hypothyroidism was done depending on thyroid panel. In this study, TT4 and fT4 were both decreased. Although hypothyroidism is the most frequent endocrine disorder in dogs [23], its definitive diagnosis is not always straightforward and remains a challenge for veterinary clinicians due to its countless clinical signs [24]. Diagnosis depends on results of TT4, fT4 and TSH [14]. As TT4 can be suppressed due to numerous non-thyroidal factors [16], TT4 used primarily as a screening test as TT4 does not, by itself, confirm hypothyroidism but its normal values rule it out, fT4 measurement is ideal to help confirm the diagnosis, low serum fT4 together with TT4 can confirm the diagnosis of hypothyroidism .

TSH might provide additional evidence for or against the diagnosis of hypothyroidism [2]. Non-significant increase in TSH was reported in this study, though theoretically, TSH should increase, it was found that up to 40% of dogs presented with normal TSH levels [21, 25,26, 27]

The difference in estimation methods and scant availability of specific canine TSH test could be implicated [13].

Levothyroxine was given as initial dose 0.01mg/kg BID, and first check-up was done 1-month later as recommended [2]. Clinical response was documented by clinical improvement and normalization of thyroid hormones. The treatment of choice for dogs is synthetic levothyroxine [14,28]. Treatment with levothyroxine sodium

conserves normal regulation of T4 to T3 deiodination, which allows physiologic regulation of individual tissue T3 concentrations [22]. Plasma half-life of Levothyroxine sodium in dogs ranges from 9 to 14 hours and depends on the dosage and frequency of administration [13].

6. Conclusion

Diagnosis of hypothyroidism in dogs is not always straightforward and its one of the most over diagnosed endocrine disorder in dogs. Therefore, depending on T4 alone cannot confirm hypothyroidism but rule it out. A normal or low TSH does not rule out hypothyroidism. FT4 measurement is ideal to help confirm the diagnosis. The Prevalence of hypothyroidism in the studied cases in this investigation was 7.5 % and this is similar to the reported prevalence, diagnosis of hypothyroidism should be relying on combination of clinical and laboratory data. Usage of human levothyroxine can successfully manage canine hypothyroidism.

7. References

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Table 1

Distribution of dermatologic affections in the studied dogs.

Disease	Number	Percentage %
Hypothyroidism	15	7.5
Demodicosis	35	17.5
Flea Allergic Dermatitis	30	15
Pyoderma	80	40
Dermatophytosis	20	10
Malassezia Dermatitis	10	5
Scabies	30	15

Table 2

Hematological and Biochemical alterations in hypothyroid dogs.

Parameter/Unit	Control group [N=8]	Hypothyroidism group[N=15]
RBCs[10⁶/μl]	6.64 ± 0.24	4.52 ± 0.63*
PCV [%]	42.81 ± 1.58	29.61 ± 3.10*
HB[g/dl]	13.49 ± 0.40	11.67 ± 1.18
MCV[fl]	62.65 ± 2.39	65.79 ± 1.77
MCH[pg]	19.62 ± 1.168	21.56 ± 1.83
MCHC[g/dl]	31.60 ± 0.85	31.16 ± 1.68
RDW [%]	16.73 ± 0.40	15.93 ± 1.21
WBCs[10³/μl]	9.50 ± 0.86	15.75 ± 2.95
Lymphocytes [%]	12.13 ± 1.13	11.56 ± 1.20
Neutrophils [%]	66.64 ± 3.51	76.46 ± 2.56
Monocytes [%]	8.81 ± 0.78	8.90 ± 1.56
Eosinophil [%]	3.22 ± 0.48	2.45 ± 0.77
Basophils [%]	0.58 ± 0.08	0.32 ± 0.14
Platelets[10³/μl]	270.47 ± 43.07	290.57 ± 63.81
Cholesterol[mg/dL]	219.67 ± 15.12	241.75 ± 20.43
ALP[U/l]	115.60 ± 7.49	118.00 ± 12.46
ALT[U/l]	57.85 ± 4.87	59.25 ± 10.80

* p value ≤0.05 considered significant, data are represented as mean ± standard error

Table 3

Thyroid hormones in control, hypothyroid and treated dogs.

Parameter/Unit	Control group [N=8]	Diseased group[N=15]	Treated group [N=15]
TT4[$\mu\text{g/dl}$]	1.80 ± 0.14^a	$0.81 \pm 0.02^{*b}$	$1.50 \pm 0.35^{*a}$
FT4[$\mu\text{g/dl}$]	1.12 ± 0.10^a	$0.50 \pm 0.06^{*b}$	$1.02 \pm 0.02^{*a}$
TSH[mIU/L]	7.77 ± 1.47	13.72 ± 5.16	3.85 ± 0.45

The same symbols in the same row are not significant.

The different symbols in the same row are significant.

* p value ≤ 0.05 considered significant, data are represented as mean \pm standard error

Fig .1.

a. A-3-years old male akita with hypothyroidism showing non inflammatory non-pruritic bilaterally symmetrical alopecia on the neck.

b. A-3-years old male akita after one month of treatment with levothyroxine showing improvement in clinical signs whereas areas devoid of hair showed regrowth of the hair and better skin coat quality.