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Alterations in the Pituitary- Thyroid Axis in Camel *Camelus dromedarius* Infected by Larvae of Nasal Bot Fly *Cephalopina titillator*

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Abstract: The present study used the Chemiluminescent Microparticle Immunoassay (CMIA) to examine the alterations in pituitary-thyroid function, in camels infected with third instar larvae of *Cephalopina titillator*, by measuring the levels of triiodothyronine (T3) and thyroxine (T4) of the thyroid gland and level of thyroid stimulating hormone (TSH) of the pituitary gland. The results indicated that the infection of camels by larvae of the nasal bot fly caused a case of hypothyroidism. This was evidenced from the declines recorded in blood levels of T3 and T4. Also the data obtained point to the occurrence of a parallel decrease in the level of blood TSH. It appears that the depressed release of TSH during infection with *C. titillator* together with the subsequent decline in T3 and T4 levels from thyroid gland, might reflect the direct effect of infection on pituitary gland, and suggest decreased synthesis of T3 and T4 in response to larval infection of the nasal bot fly.

Key words: *Cephalopina titillator- Camelus dromedarius-* T3- T4- TSH

Introduction

The camel nasal bot fly, *Cephalopina titillator* (subfamily: *Oestrinae*) is the only species in its genus (Sharma, 1992). It develops in the nasal cavities of camels and shows a high degree of host specificity. High level of infestation causes congestion of nasal cavity with mucous, severe inflammatory and degenerative changes, leading to extensive damage of nasopharyngeal tissues and the formation of lymphoid nodules at the site of larval attachment in the pharynx. The affected camels may snort, show abnormal behaviour and nervous symptoms including restlessness, cramp, excitation, convulsions, difficulties in breathing and may lead to death following complications due to secondary infections (Hussein *et al.*, 1982 and 1983; Higgins, 1985; Derhalli *et al.*, 1989 and Musa *et al.*, 1989).

In the previous studies, no results have linked *C. titillator* -infected camels with serum thyroid hormone concentrations (T3 and T4) or serum thyroid stimulating hormone (TSH) level. On the other hand, it was reported that *Trypanosoma congolense* infection rapidly impaired the function of the thyroid gland in goats as defined by considerable plasma thyroxine (T4) decrease (Mutayoba *et al.*, 1988) and hypothyroidism in cattle (Abebe and Eley, 1992). Experimental infection of rabbits with *Trypanosoma congolense* induced a rapid decline in both T3 and T4 (Lomo *et al.*, 1996). Similarly, studies on human sleeping sickness showed a significant decrease in 3, 5, 3`-triiodothyronine (T3) and (T4) without TSH variation (Boersma *et al.*, 1989). Al-Qarawi *et al.* (2001) indicated that *Trypanosoma evansi* caused a significant case of hypothyroidism evidenced as a decrease in the thyroid triiodothyronine (T3) and thyroxine (T4) blood levels associated with a parallel decrease in the level of blood pituitary thyrotrophic hormone (TSH).

The objective of the present investigation was to measure the levels of T3, T4 and TSH in the camel *Camelus dromedarius* during the infection with larvae of *Cephalopina titillator*.

Materials and Methods

Experimental Animals: For this study, adult male and female camels, *Camelus dromedarius* were used. Animals were obtained from abattoir of El-Basatein, Cairo, Egypt

Groups of Animals Under Investigation: Camels were divided into two main groups. Each group consists of 7 animals

Group 1: This group is the control animals. They were free from any larval instars of the studied insect, *Cephalopina titillator*

Group 2: The animals of this group were infected by the larvae of *C. titillator* with third instar larval burdens of 10 – 15 (mean 13) per each camel

Blood and Tissue Sampling: Animals were sacrificed by cervical dislocation. Blood was collected in separated clean centrifuge tubes, allowed to coagulate and serum was separated by centrifugation at 3000 r.p.m. for 20 min. Serum specimens were quickly kept frozen at – 20°C until needed for analysis of thyroid hormones (triiodothyronine, T3 and thyroxine, T4) and thyroid stimulating hormone (TSH). The levels of T3, T4 and TSH in blood serum were determined using the Chemiluminescent Microparticle Immunoassay (CMIA). CMIA kits were provided by Abbott Laboratories Diagnostics Division. Abbott Park, IL 60064, USA.

Statistical Analysis: The results are reported as the mean ± S.E. Differences between means were determined by using one way analysis of variance (ANOVA) and F-test followed by Tukey's multiple range test using the Statistical Package for the Social Sciences (SPSS) version 10. Non- significant level was taken at $P > 0.05$.

Table 1: Changes in levels of triiodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) in serum of camels infected with third instar larvae of *Cephalopina titillator*.

Parameter	Groups	Mean ± S.E	% of Change
Triiodothyronine (T3)	Non-infected (Control)	120.0 ± 20.80	- 78.52 ***
	Infected	25.78 ± 7.08	
Thyroxine(T4)	Non-infected (Control)	11.62 ± 1.33	- 23.58 *
	Infected	8.88 ± 1.89	
Thyroidstimulatinghormone(TSH)	Non-infected(Control)	0.014 ± 0.003	- 14.29
	Infected	0.012 ± 0.002	

Numbers of camels in each group = 7
Non-significant at P>0.05.
*** Very highly significant at P<0.0001.
* Significant at P<0.01

Absolute value is measured by ng/ml for T3; mg/dl for T4 and μIU/ml for TSH.
* Significant at P<0.01.
Each bar represents a percentage of change value.
*** Very highly significant at P<0.0001

Results and Discussions

Results of thyroid hormones (T3 and T4) and thyroid stimulating hormone (TSH) in blood serum of non-infected (control) and infected camels are shown in Table (1) and graphically illustrated in Fig. 1.

Triiodothyronine (T3): The response of thyroid hormones for the action of third larval instar of *C. titillator* infection shows a very highly significant decrease (F=146.35, P<0.0001) in the level of T3 in serum. The value (expressed as percentage of change) was -78.52%.

Thyroxine (T4): The analysis of T4 level in serum of infected camels showed a value of -23.58%. (expressed as percentage of change). This value indicates the occurrence of a significant decrease (F=6.07, P<0.01).

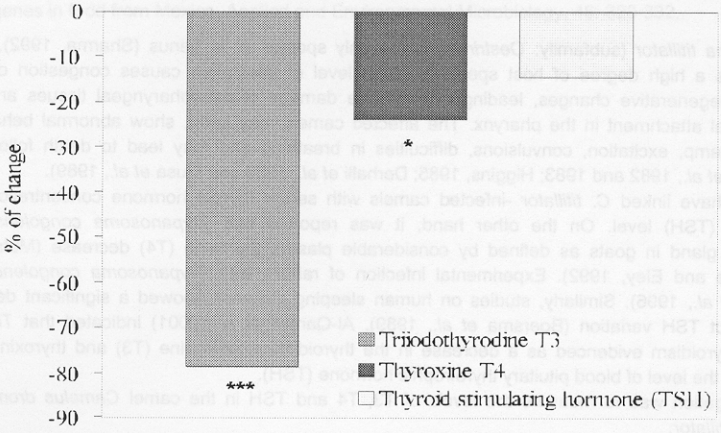

Fig. 1: Effect of infection with 3rd instar larvae of Cephalopina titillator on triiodothyrodine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) in serum of camels□

Thyroid stimulating hormone (TSH): Studies were undertaken to examine the TSH level of serum in response to third larval instar of *C. titillator* infection. The results revealed the occurrence of a non-significant decrease (F=0.40, P>0.05) of -14.92%.

Although the literature contains many references to the effect of different parasites on the pituitary- thyroid axis in mammals (Ikede and Losos, 1975; Mutayoba *et al.*, 1988; Boersma *et al.*, 1989; Abebe and Eley, 1992; Abebe *et al.*, 1993; Lomo *et al.*, 1996; Haroun *et al.*, 2000 and Al-Qarawi *et al.,* 2001), no direct estimates of the effect of nasal bot fly *C. titillator* on serum T3, T4 and TSH in camels have been made before.

The present results indicated that larvae of *C. titillator* caused a significant case of hypothyroidism evidenced as decrease in the thyroid triiodothyronine (T3) and thyroxine (T4) blood levels associated with a parallel decrease in the level of blood pituitary thyrotropic hormone (TSH). These data suggest that the depressed release of TSH during infection together with the subsequent decline in T3 and T4 levels from thyroid gland, might reflect the direct effect of infection on pituitary and thyroid gland. In support of these observations, Al-Qarawi *et al.* (2001) indicated that decreases in the levels of T3, T4 and TSH of blood in camels infected with *Trypanosoma evansi* were recorded.

In hypothyroid animals the synthesis of long chain fatty acids from glucose and other carbohydrate precursors, as well as their oxidation, were reduced (Bray and Goodman, 1968). Since both of these processes require movements of metabolites across the mitochondrial membrane, it has been postulated that the metabolic defect in hypothyroidism may reside in the mitochondrial membrane (Bray and Goodman, 1968). Lipogenesis as well as lipolysis were reported to be largely affected by thyroid hormones (Fisher and Bull, 1967)

Roncari and Murthy, 1975): T3 and T4 have pronounced physiological effects in the control of respiration and energy metabolism as well as in the biogenesis of the mitochondria. Their production is important in conditions such as disease that leads to alter metabolic

status. The thyroid gland is one of the endocrine glands, which is affected during parasite infection.

In our study, the infection was indicated by a significant reduction in the level of T3 and T4 blood concentrations. This impairment in thyroid function could be explained on the basis of a direct or/and an indirect (through the pituitary gland) effect of the larvae on the thyroid gland. The direct effect may be mediated by biologically active factors of parasite origin such as phospholipase A (Tizard *et al.*, 1978), protease (Lonsdale-Eccles and Grab, 1986) and peptidase (*Knowles et al., 1989*) thereby causing thyroid dysfunction. On the other hand, indirect pathological changes which occur during parasites infection can lead to pituitary dysfunction (Ikede and Losos, 1975 and Mutayoba, *et al.*, 1988). The presence of larvae of *C. titillator* within the nasopharyngeal cavity and their causes for abnormal movement of the head, bleeding from the nostrils and meningitis in camels (Hussein *et al.*, 1982; AL-Ani *et al.*, 1991 and Bekele, 2001), might alter the pattern of pituitary TSH production and thereby prevent normal thyroid function. Proteases of parasitic origin have been implicated in the gonadotrophic dysfunction in rats infected with *T. brucei brucei* (Humblart *et al.*, 1990). Thus, an indirect antithyroid effect could have been mediated through; activation of epithelial cells, monocytes and macrophages in the immune system during infection releasing cytokines which activate and down regulate the endocrine system. The results of De Souza *et al.* (1989) and Honegger *et al.* (1991) suggested that IL-1 may be involved in the paracrine and/or autocrine regulation of pituitary function. The two molecular forms of IL-1: IL-1á and IL-1β affect the CNS and the endocrine system (Schmidt and Tocci, 1990), in addition, IL-1 and Il-6 (Sapolsky *et al.*, 1987; Battman *et al.*, 1989 and Tsagarakis *et al.*, 1989) are known to be stimulants of the hypothalamic-pituitary axis while TNF (cachectin) is known to inhibit the secretion of pituitary hormones such as growth hormone (Walton and Cronin, 1989) and TSH (Pang *et al.*, 1989). Pang *et al.* (1989) implicated TNF in causing impairment of hypothalamic-pituitary-thyroid function in rats and suggested that TNF is one of the mediators responsible for alterations in the thyroid function. On the other hand, thyroid-stimulating hormone concentrations decline following subcutaneous injection of recombinant human IL-1β in rats (Dubois *et al.*, 1988).

The weakness that has been pointed to in the study implemented by Abebe and Eley (1992) and Al-Qarawi *et al.* (2001) in their failure to study the pituitary TSH output has been our target to strengthen the present study and achieve our conclusion which indicated a dysfunction of the servomechanism in the pituitary-thyroid axis during the state of larvae of *C. titillator* infection in camel.

The alteration in the T3 and T4 dynamics in the study of Al-Qarawi *et al.* (2001), in the camels infected with *Trypanosoma evansi* was not consistent with the results of Lomo *et al.* (1996) in the rabbits infected with *Trypanosoma congolense*. The depression in the T3/T4 ratio in the previous study of Al-Qarawi *et al.* (2001), may be due to the release of T3 by the thyroid gland under the influence of small amounts of pituitary hormones (Nejad *et al.*, 1973).

According to the above developments, it is evident that infection with larvae of *C. titillator* would tend through their multiple functions to cause decrease in thyroid hormones synthesis which might explain the decrease in T3 and T4 during the experiment. Also the concomitant decrease in blood TSH level might as well as stimulate the decline of the T3 and T4 in blood.

التغيرات في محور الغدة النخامية - الدرقية في الجمل

المصابة بيرقات نغف الجمل

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تناولت الدراسة في هذا البحث التغيرات التي تحدث في محور الغدة النخامية - الدرقية أثناء الإصابة بالطور الثالث ليرقات نغف الجمل في الإبل والتي تتمثل في انخفاض مستوى كل من الثيروكسين (T4) والثيرونين (T3) أيضاً في الدم وانخفاض الحالة للغدة الدرقية (TSH).

كشفت النتائج عن أن إصابة الجمال بيرقات نغف الجمل أدت إلى حدوث انخفاض في مستوى كل من الهرمونين الخاصين بالغدة الدرقية في الدم وهرمون T3 و T4.

أيضاً بينت النتائج حدوث نقص في هرمون TSH للغدة النخامية في الدم.

تُظهر النتائج أن النقص في إنطلاق الهرمون الحاث للغدة الدرقية TSH أثناء الإصابة بيرقات الحشرة في الجمال مع النقص المصاحب في مستوى T3 و T4 بدم العينة من الثدييات المصابة على الغدة النخامية و الغدة الدرقية، كما تقترح النتائج أيضاً أن الإصابة بالطور الثالث ليرقات نغف الجمل تسبب نقص في تكوين كل من T3 و T4.

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