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Hormonal and Biochemical Alterations in Naturally Occurring and Induced Goitre in Camels (*Camelus dromedarius*)

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ABSTRACT

The present study constituted a detailed account of hypothyroidism (goitre) in camels. It comprised of a survey in three areas of Darfur State (Nyala, Idd Elfursan and Zalingei) and an experimental work which was conducted to induce hypothyroidism in camels using intramuscular injection of sodium thiocyanate (NaSCN). The results showed that camels from Nyala area had significantly ($P<0.05$) low means of serum total thyroxine and serum inorganic phosphorus levels, serum total triiodothyronine, total protein, albumin, globulin and unexpectedly a significantly ($P<0.05$) high creatinine concentrations compared with those of animals from the other two areas. The means of serum total T_4 values of camels from Idd Elfursan and Zalingei were found to be not significantly different from each other. Administration of sodium thiocyanate resulted in a significant increase in serum thiocyanate ion concentration, which was accompanied by a significant decrease in serum total thyroxine and total triiodothyronine levels. The significant reduction in serum total thyroxine, total triiodothyronine, total protein, albumin, globulins and inorganic phosphorus concentration observed in experimentally-induced hypothyroid camels were comparable with the results obtained from camels surveyed in iodine deficient area (Nyala).

Keywords: Goitre, Camels, T3, T4, Sodium Thiocyanate

INTRODUCTION

The thyroid hormones thyroxine (T_4) and triiodothyronine (T_3) increase the metabolic activities of almost all the tissues of the body. About 90% of the hormones secreted by the thyroid gland are T_4 and 10% is T_3. However, most of the T_4 is eventually converted to T_3 in the tissues, so that both are important functionally (Guyton, 1991). Thyroxine stimulates oxygen utilization and heat production by every cell of the body. It causes increased utilization of carbohydrates, increased protein catabolism and greater oxidation of fats (Abebe and Eley, 1992).

Ruminant's hypothyroidism mainly occurs in areas naturally low in available iodine referred to as endemic goitre areas. Formerly, endemic goitre was thought to have been confined to hilly regions only. It is now documented that soils that are poor in

iodine are not only common in mountainous regions, but also in plains and river basins where iodine is periodically washed away heavy rainfalls or floods (Mahadeva and Shanmuganathan, 1967). The natural incidence of colloid goiter in camels has been previously described in iodine deficient areas (Decker *et al.,* 1979; Tageldin *et al.,* 1985; Abu Damir *et al.,* 1990). Iodine deficiency is not the sole cause of goitre in man and animals. Goitrogenic substances in certain foods can cause goitre in man and animals if given in large amounts (Bourdoux, *et al.,* 1978). *T. evansi* trypanosomosis in goats caused thyroid dysfunction (Sarra *et al.,* 2012). Feeding thiourea induces hypothyroidism in sheep (Gupta, *et al.,* 2013).

In Darfur State, Western Sudan, a severe juvenile hypothyroidism was described and related to goitrogenic factors (Moreno *et al.,* 1993). Among the many goitrogenic xenobiotics that increase the incidence of thyroid tumors and exert a direct effect on the thyroid gland to disrupt one of the several steps in the biosynthesis and secretion of thyroid hormones are thiocyanate and perchlorate through inhibition of the iodine-trapping mechanism (Capen, 1994). Thiocyanate has a profound effect on iodide uptake by the thyroid. It prevents accumulation and uptake of iodine by thyroid gland (Abdel Rahman, 1987) by acting either as a potent competitor of iodine at entry into the thyroid cells or as an inhibitor of thyroid hormones synthesis through increased urinary losses of iodine (Bourdoux *et al.,* 1978). It is capable of inducing iodide deficiency within the gland, in presence or absence of adequate iodide intake, sensitizing it to goitrogens and inhibiting iodide organification (Lindsay *et al.,* 1992). It also binds serum albumin and displaces thyroxine and so helps its degradation and excretion (Ermans, *et al.,* 1973). The aim of this study is to compare the hormonal and biochemical changes in natural incidence of colloid goitre in dromedary camels with those of thiocyanate-induced hypothyroid ones.

MATERIALS AND METHODS

***Survey*:** Seventy two male and female adult camels (*Camelus dromedarius*) 5-7 years old were surveyed in Nyala, Idd Elfursan and Zalingei areas (24 in each) of Darfur State to evaluate the impact of iodine deficiency as manifested by goitre on camel thyroid functions and the biochemical changes associated with this deficiency. The survey was carried out in dry season (April-June). Blood samples were collected from animals by jugular vein puncture into plain vacutainers, from Nyala and Zalingei abattoirs before being slaughtered and from Idd Elfursan local market. The samples were allowed to clot and the sera were separated by centrifugation at 3000 rpm for 5 minutes and stored at -20^{o}C until analyzed.

Experimental design: Four adult female camels (*Camelus dromedarius*) 4-6 years old were brought from Almewelih area, West of Omdurman. The weights of the animals ranged between 350 and 398 kg. They were housed in one large pen at the Radioisotope Department, Soba. They were fed on sorghum (Abu Sabeen) hey and provided with water *ad. libitum*. Before the start of the experiment all animals were clinically examined for their freedom from external and internal parasites.

The camels were then given daily injection of sodium thiocyanate solution (sodium sulphocyanide; NaSCN = 81.07, supplied by Hopkin & Williams, Chadwell Heath, Essex, England), at a dose rate of 3 mg kg-1 Body weight, intramuscularly for three

consecutive months. About 10 ml of blood was collected every three days at 8-10 o'clock am by jugular veinpuncture into plain vacutainers. The samples were allowed to clot and the sera were separated by centrifugation at 3000 rpm for 5 minutes and stored at -20°C until analyzed.

Hormonal Assay: Thyroxine (T_4) and triiodothyronine (T_3) were measured by radioimmunoassay (RIA) technique (Larsen, 1978) with kits (Amersham International, Amersham, Bucks, UK) in a gamma counter (Nuclear Enterprises, NE, 1612 Turbo) at the RIA laboratory of Sudan Atomic Energy Commission (SAEC), Khartoum.

Biochemical Methods: The concentrations of serum constituents were determined by chemical methods using commercial kits (Randox Laboratories Ltd., UK) in a spectrophotometer (Jenway 6105 U. V.Vis, Jenway Ltd, Felsted, Dunmow, Essex CM63LB UK).

Serum total protein expressed in g/dl was measured by biuret reaction according to King and Wooton (1967). Serum albumin expressed in g/dl was determined according to Bartholomew and Delany (1966).

Serum globulins were obtained by subtracting the concentration of albumin from that of total protein. Serum creatinine expressed in mg/dl was determined as described by Henry (1974). Serum inorganic phosphorus expressed in mg/dl was measured by the method used by Varley (1967). Serum thiocyanate concentration was determined by colormetric method according to Varley (1967).

Statistical Methods: The results of serum biochemical and hormonal investigation were statistically analyzed according to Gomez and Gomez, (1984) using ANOVA, where P values higher than 0.05 were considered insignificant.

RESULTS AND DISCUSSION

The results are shown in Tables (1 and 2). The T_4 levels of camels from the three locations in the present work were lower than the values reported by Wasfi, *et al.,* (1987) who reported values as 17.92±1.19 µg/dl (230.63±15.32 nmol/l) in normal Saudi Arabian camels. And also lower than the values of normal, subclinically and clinically goitrous camels of Kordofan reported by Abu Damir, *et al.,* (1990).

Table 1: Hormonal and biochemical values of camels in three iodine deficient localities (*means±SD, ±SE, and range in parenthesis*)

Parameters	Locations			±SE.
	Nyala n=24	Idd Elfursan n=24	Zalingei n=24	
Thyroxine (T_4) *(nmol/l)*	57.37^{b}*±18.30 (33.6-99.6)	80.48^{a}±25.1 (31.82-123)	83.09^{a}±25.55 (49-139.5)	±4.60
Triiodothyronine (T_3) *(nmol/l)*	1.68^{b}±0.61 (0.6-3.5)	1.62^{b}±0.65 (0.7-3.4)	1.88^{a}±1.12 (0.48-4.8)	±0.04
Total protein *(g/dl)*	6.99^{a}±0.80 (5.5-8.5)	6.63^{a}±0.94 (4.0-8.2)	7.25^{a}±0.78 (4.8-8.5)	±0.16
Albumin *(gldl)*	2.93^{b}±0.40 (2.1-3.8)	3.32^{a}±0.48 (2.4-3.9)	2.77^{b}±0.56 (1.3-3.8)	±0.08
Globulin *(g/dl)*	4.05^{a}±0.72 (2.5-5.4)	3.32^{b}±0.98 (2.2-5.1)	4.48^{a}±0.67 (3.6-6)	±0.20
Creatinine *(mg/dl)*	1.93^{a}±0.38 (1.2-2.6)	1.53^{b}±0.28 (1.1-2.3)	1.51^{b}±0.23 (1.04-1.97)	±0.08
Inorganic phosphorus *(mg/dl)*	5.01^{b}±1.58 (2.6-9.8)	6.49^{a}±1.35 (4.1-10.2)	5.23^{b}±2.02 (2.6-10.8)	±0.21

n: Number of animals

* Means in the same row having similar superscripts are not significantly different at P ≤ 0.05.

This finding might indicate that Nyala area is more affected by iodine deficiency followed by Idd Elfursan, while Zalingei is the least affected compared to the other two groups. Regarding the thiocyanate-induced goitrous camels the mean values of T_4 in the second and third months of the experiment (60.70±12.06 and 56.49±7.48 nmol/l respectively) although non-significantly different but both were significantly lower than that of the first month (72.91±7.18 nmol/l) the three values were lower than that of normal camels reported by Abu Damir *et al.,* (1990). The values were also were lower than the values reported by Wasfi *et al.,* (1987). Ahmed (2008) reported value of 121.70±5.0 and 117.60±5.5 ng/ml in North Kordofan and South Kordofan, respectively.

The mean of T_3 value of camels from Zalingei, though lower, was comparable to that of normal camels reported by Abu Damir *et al.,* (1990). However, the values of camels from all three locations were higher than the values of the 1st, 2nd and 3rd months and the findings of Wasfi *et al.,* (1987) who reported values of 9.33±1.15 ng/ml (1.43±0.18 nmol/l) for T_3 concentration in normal Saudi Arabian camels, while the values of camels from Nyala and Idd Elfursan were lower than the values reported by Abu Damir *et al.,* (1990). It was also noticed that the mean values of T_3 of the three months (0.43±0.19, 0.26±0.19 and 0.17±0.14 nmol/l, respectively) were significantly different and were lower than the values reported by Wasfi *et al.,* (1987). Ahmed (2008) reported value of 3.14±0.11 and 2.40±0.2 ng/ml in North Kordofan and South Kordofan, respectively. Since 90% of iodine circulating in the animal's blood is in the form of T_4 (Wilson, 1975) and lack of iodine prevent production of both T_4 and T_3 (Guyton, 1991), the present findings imply that Nyala area is deficient in iodine. Differences in thyroid hormones concentration within normal camels can be expected as a result of pregnancy, season, dehydration and rehydration (Yagil *et al.,* 1978), but iodide deficiency is the primary cause of hypothyroidism.

The values of total protein and albumin in the three locations were found to be higher than the mean values of the 1st, 2nd and 3rd months and all values of the two parameters were lower than the findings recorded by Idris and Tartour, (1977); Abdel Gadir, *et al.,* (1984) who reported 7.3±0.51 and 3.8±0.32 g/dl, respectively and Abu Damir, *et al.,* (1990) who recorded 6.30±1.17 and 3.4±0.2 g/dl, respectively in normal camels.

The mean serum globulin concentration of camels from Nyala and Zalingei were higher than the values of the 1st, 2nd and 3rd months and all values were lower than the findings recorded by Idris and Tartour, (1977); Abdel Gadir *et al.,* (1984) who reported 3.5±0.47 g/dl and Abu Damir, *et al.,* (1990) who reported 2.87±1.01 g/dl, and that of Idd Elfursan was lower than the values of the 1st, 2nd and 3rd months but comparable with the normal values reported by Idris and Tartour, (1977) and Abdel Gadir *et al.,* (1984) and higher than the values of normal camels reported by Abu Damir, *et al.,* (1990).

The elevation of serum total proteins together with globulins observed in this study agrees with the findings of Abu Damir *et al.,* (1990) in camels with goitre. The degree of hyperglobulinaemia observed was explained by the fact that bacterial and viral infection, parasitic infestation and liver disease cause increase of gammaglobulins (Kelly, 1984) as goitre may play a role in reducing animals' resistance, thus increasing the chance of infection (Abu Damir, *et al.,*

1990).

The serum total protein, albumin and globulins concentration of the 1st, 2nd and 3rd months for the three parameters were non-significantly different and all values were lower than the findings recorded by Idris and Tartour (1977), Abdel Gadir *et al.*, (1984) and Abu Damir *et al.*, (1990) in normal camels suggesting that this state of reduced serum total hypoproteinaemia, hypoalbuminaemia and hypoglobuinaemia is attributed to low levels of circulating T_4 and T_3 produced by administration of NaSCN. This agrees with Murray *et al.*, (1999) who stated that the major effect of T_3 and T_4 is to enhance general protein synthesis and cause a positive nitrogen balance. This observation suggests a direct relation between the level of T_3 and serum total protein in camels.

Serum creatinine concentration observed in camels from Nyala was not significantly different than the values of the 1st, 2nd and 3rd months.

The values of Idd Elfursan and Zalingei were significantly lower than those of the 1st, 2nd and 3rd months. The values were similar to the findings in normal camels reported by Abdel Gadir, *et al.*, (1984).

In the present work, the high serum creatinine concentration observed in camels from Nyala suggests that oxygen concentration required for generation of the equivalent amount of ATP was reduced. Therefore, the utilization of the readily available high-energy phosphate of phosphocreatine might have resulted in high production of creatinine in camels of Nyala. However, lower muscle mass was expected in camels from Nyala, as thyroid hormones are essential for skeletal muscle maturation. Although there was a non-significant difference between the means of the values for the 1st, 2nd and 3rd months, the means of the second and third months were slightly higher than that of the first one. The values were similar to the findings in normal camels reported by Abdel Gadir *et al.*, (1984).

Table 2: Hormonal and biochemical changes in sodium thiocyanate-induced hypothyroid camels (*Means±SD, ±SE. and range in parenthesis*)

Parameters	Time			
	1st month	2nd month	3rd month	±SE
Thiocyanate	2.92^{c}*±0.32	3.81^{b}±1.23	5.30^{a}±2.47	±0.27
(mg/dl)	(2.2-3.4)	(1.8-4.6)	(2.4-10.1)	
Thyroxine (T_4)	72.91^{a}±7.18	60.70^{b}±12.06	56.49^{b}±7.48	±2.03
(nmol/l)	(64.1-89.2)	(44.7-85.6)	(48.6-71)	
Triiodothyronine (T_3)	0.43^{a}±0.19	0.26^{b}±0.14	0.17^{c}±0.14	±0.02
(nmol/l)	(0.14-0.79)	(0.11-0.48)	(0.1-0.5)	
Total protein	6.46^{a}±0.42	5.98^{a}±0.57	5.62^{a}±0.48	±0.26
(g/dl)	(5.9-7.1)	(5.1-6.8)	(4.5-6.1)	
Albumin	2.68^{a}±0.21	2.26^{a}±0.30	2.30^{a}±0.11	±0.17
(g/dl)	(2.3-3.1)	(1.9-3)	(2.2-2.5)	
Globulin	3.79^{a}±0.53	3.73^{a}±0.47	3.34^{a}±0.44	±0.16
(g/dl)	(3-4.5)	(3-4.4)	(2.3-3.9)	
Creatinine	1.93^{a}±0.24	1.88^{a}±0.26	1.86^{a}±0.17	±0.20
(g/dl)	(1.6-2.4)	(1.6-2.4)	(1.6-2.1)	
I. phosphorus	6.14^{a}±1.03	5.98^{a}±0.69	4.60^{b}±0.77	±0.08
(mg/dl)	(4.3-7.6)	(4.5-6.8)	(3.2-6)	

* Means in the same row having similar superscripts are not significantly different at $P \leq 0.05$

The relatively low serum inorganic phosphorus level of camels from Nyala may be attributed to the low circulating T_4 and T_3 levels. This supports the findings of McCaffrey and Quamme, (1984) who observed a significantly

higher urinary phosphate in thyroid deficient rats resulting in hypophosphataemia due to increased tubular phosphate leak. Kelly, (1984) reported that blood inorganic phosphorus level fall in periods of high carbohydrate utilization.

Comparison of the mean values of serum inorganic phosphorus level for the three months showed that there was a non-significant difference between the mean of values of the first and second months and they were comparable with the values of both normal and goitrous camels reported by Abu Damir, *et al.,* (1990) but somewhat higher than the values of normal camels recorded by Wahbi, *et al.,* (1984). The mean value from the third month was significantly (P>0.05) lower than those from the first two months, and lower than the previous reports of Wahbi, *et al.,* (1984) and Abu Damir, *et al.,* (1990) in both normal and clinically goitrous camels. The decreased serum inorganic phosphorus level is attributed to the hypothyroid state induced by thiocyanate which supports the findings of McCaffrey and Quamme, (1984) who observed a state of hypophosphataemia in ^{131}I-sodium radioiodide-induced hypothyroid rats. This was explained by increase in urinary excretion of phosphate due to tubular leakage.

This reduction of thyroid hormones might be attributed to thiocyanate overload, as it competes with iodine at entry into the thyroid glands, increasing its urinary losses and producing a relative or absolute iodine deficiency, hence inhibiting thyroid hormones synthesis (Bourdoux, *et al.,* 1978; Thilly, *et al.,* 1990 and Rao and Lakshmy, 1995).

The significant reduction in serum total thyroxine, total triiodothyronine, total protein, albumin, globulins and inorganic phosphorus concentration observed in experimentally-induced hypothyroid camels were comparable with the results obtained from camels surveyed in iodine deficient area (Nyala).

It is concluded that:

(1) Thiocyanate induces a state of hypothyroidism in camels.
(2) Similar alterations in serum constituents might be produced in camels living in iodine deficient areas and thiocyanate overload.
(3) Provision of iodinated salt is recommended to camels raised in areas of endemic goitre.
(4) The presence of high serum creatinine concentrations in camels from the iodine deficient areas needs more investigation.

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