EXPERIMENTAL INDUCTION OF HYPERTHYROIDISM IN FEMALE BALADI GOATS WITH SPECIAL REFERENCE TO SOME BIOCHEMICAL AND PATHOLOGICAL PARAMETERS

A.M. Bakeer*, Iman B. Shaheed*, Sherein, S.A El Gayed*, Reda M.S. Korany* and Naela M. Ragaa**

*Pathology Department, Faculty of Veterinary Medicine, Cairo University, Egypt.
**Nutrition and Clinical Nutrition Department, Faculty of Veterinary Medicine, Cairo University, Egypt.

ABSTRACT

This study was conducted to investigate the effect of experimental induction of hyperthyroidism on ten female Baladi goats, five months old. Levothyroxine sodium at the rate 1300 µg/animal/day as oral drench was used for four weeks to induce hyperthyroidism. Hormonal assay showed significant increase in both T3 and T4 levels, whereas total lipid showed significant decrease in its level. Clinically the animals showed round areas of alopecia at the face and ear with emaciation. Gross examination of the sacrificed goats revealed enlargement of kidneys and liver with distention in the gall bladder. Histopathologicaly, the kidneys revealed vacuolar degeneration in the epithelium of renal tubule and endothelium of glomelular tuft. Liver of goats with induced hyperthyroidism showed vacuolar degeneration and necrosis of hepatocytes. Microscopic examination of the thyroid glands of affected cases revealed large dilated follicles with abundant colloid, the lining epithelium of the follicles were low cuboidal to squamous (colloid goiter).

Keywords: hyperthyroidism, goat, kidneys, liver, thyroid, goiter

1st International Scientific conference of Pathology Department, Faculty of Veterinary Medicine (179-190)
INTRODUCTION

The thyroid hormones, tetraiodothyronine or thyroxine (T4) and triiodothyronine (T3) act on many different target tissues, stimulating oxygen utilization and heat production in every cell of the body. The overall effects are increasing the basal metabolic rate (Todini et al., 2006).

Breed, age, sex and season are the most frequent factors that affect the concentration of thyroid hormones (Tuckova et al., 2001). The changes of blood thyroid hormone concentrations are an indirect measure of the changes in thyroid gland activity and circulating thyroid hormones and can be considered as indicators of the metabolic and nutritional status of the animals (Todini, 2007).

Aim of work: This study was planned to study the thyrotoxic effect of levothyroxine sodium on the thyroid glands and some other organs of goats as an experimental animal model, and also its effect on thyroid hormonal assay {triiodothyronine (T3) and thyroxin (T4)}.

MATERIALS AND METHODS

I-Animals:–

Ten Baladi female goats, five months of age, 10-12 Kg body weight were used. They were purchased from El-Fayoum governorate Markets. Goats were acclimatized for seven days before the onset of the study, they were fed balanced ration and hey. The drinking water was offered ad libitum.

II-Experimental design:

The goats were randomly divided into two groups. The 1st group (contain four goats) served as a control. The 2nd group (contain six goats) was given levothyroxine sodium (Euthyrox® tablet) which were obtained from Amoun Company at the rate of 1300 µg/animal/day as oral drench for four weeks.
The clinical signs and the changes in behavior were recorded. Two goats from the 1st group and three goats from the 2nd groups were slaughtered at the end of each two weeks of the experiment.

III-Postmortem and histopathological examination:

At the time of slaughter the goats were subjected to postmortem examination after slaughtering to detect any abnormal gross changes. Tissue specimens form kidneys, liver, thyroid glands, skin of goats were collected, fixed in 10 % neutral buffered formalin, processed and embedded in Paraffin wax, sectioned at 4 µm and stained with Hematoxylin and Eosin and Prussian blue (Bancroft and Gamble, 2008)

IV-Clinicopatlological examination:

The whole blood was collected from goats at the time of slaughter in plan centrifuge tubes. The blood was centrifuged at 3000 rpm/ 5 minute for serum separation and then kept in sterile test tubes at –20oC till used for determination of total T3 and total T4 using RADIOIMMUNOASSAY (RIA) kits (Beckman Coulter, Immunotech a.s., Czech Republic) according to the method described by Nixon et al., 1988. The bound radioactivity was determined in a gamma counter set for 125 iodine. A standard curve was constructed and unknown values were obtained from the curve by interpolation. Assay sensitivity was 0.3 and 13 nmol/l for T3 and T4 respectively. Intra and inter-assay coefficients of variation (CV) were respectively 6.3% and 7.7% for T3 and 6.2% and 8.6% for T4 assay.

Total lipid was by enzymatic colorimetric method (kits obtained from Bio Analytics, Palm City, FL) according to method of Stein, 1986.

V-Statistical analysis:-

The obtained data from experimental animals were statistically analyzed by SPSS 14 version for Windows. The differences between groups were determined with variance analysis (one-way
analysis of variance [ANOVA]). When the differences were significant, Student-Newman-Kuels test was performed. All data were recorded on an individual basis. Data were expressed as means ± standard error (SE).

RESULTS

Concerning to group 1 (Control group), there was no any abnormal clinical signs or pathological changes were detected in this group.

Group 2 (goats treated with levothyroxin sodium), showed round areas of alopecia especially at the face and ear in 2nd week of the experiment. The same lesion was observed at the 4th week of the experiment (Fig. 1). The goats of this group showed poor body condition and emaciation.

After two weeks from the onset of the experiment, gross examination of the animals treated with levothyroxine sodium revealed; large pale kidneys, while microscopical finding showed slight hydropic degeneration of lining epithelium of renal tubule associated with vacuolation of lining endothelium of glomelular tuft (Fig. 2).

Concerning to liver, gross finding revealed distended gall bladder. Microscopical findings were irregular vacuoles inside the cytoplasm of hepatocytes with irregular outline cells contour associated with periductal mononuclear (lymphocytes, macrophages and plasma cells) inflammatory cells infiltration with fibroplasia (Fig. 3). Individual cell necrobiosis in hepatocytes was detected (Fig. 4).

There was no any macroscopic alteration detected in thyroid glands of this group, while microscopical examination revealed large dilated follicles with abundant colloid, while the lining epithelium of the follicles showed low cuboidal to squamous epithelium (Fig. 5). The previous mentioned description was categorized under (colloid goiter).
Gross finding of skin showed round areas of alopecia especially at the face and ear of the experimental animals. The histopathological examination of skin of treated goats revealed signs of alopecia represented by complete absence of hair follicles. Some areas showed atrophied hair follicles.

Animals treated with levothyroxine sodium at the fourth week from the start of the experiment revealed mild paleness of the kidneys. Microscopic examination showed degeneration of lining epithelium of renal tubule and vacuolization in the lining endothelium of glomerular tuft (Figs. 6&7).

Concerning the liver, gross examination revealed distended gall bladder, while microscopical findings were degenerative changes of hepatocytes with multiple irregular vacuoles in the cytoplasm, while the nuclei were centrally located. There were portal as well as periductal fibrosis with hyperplasia of bile duct epithelium (Figs. 8). There were congestion of hepatic blood vessels and activation of Kupffer cells in all examined cases (Fig.9).

There was no observable gross abnormality in thyroid gland, while microscopic examination revealed cystically dilated follicles with large amount of colloid. The lining epithelium of the follicles showed low cuboidal to squamous lining epithelium (Fig. 10).

There was round areas of alopecia especially at face and ear. The previous lesions which were recorded in the skin at 2nd week of the experiment were detected also at the 4th week. (Figs. 11&12).

Hormonal assay of this group showed significant increase in both T3 and T4 levels, whereas total lipid showed significant decrease in its level (Table 1 &2).
Table (1): Thyroid hormonal assay and total lipid of goats after two weeks from the experiment

<table>
<thead>
<tr>
<th>Group</th>
<th>T3(nmol/L)</th>
<th>T4(nmol/L)</th>
<th>Total lipid(mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>3.05±0.577b</td>
<td>97.18±0.577b</td>
<td>502.38±0.577b</td>
</tr>
<tr>
<td>hyperthyroidism</td>
<td>6.37±0.94a</td>
<td>190.56±55.61a</td>
<td>431.73±0.408c</td>
</tr>
<tr>
<td>P value</td>
<td>0.001</td>
<td>0.05</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Table (2): Thyroid hormonal assay and total lipid of goats after four weeks from the experiment

<table>
<thead>
<tr>
<th>Group</th>
<th>T3(nmol/L)</th>
<th>T4(nmol/L)</th>
<th>Total lipid(mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5.66±0.577b</td>
<td>95.08±1.154b</td>
<td>502.38±0.577b</td>
</tr>
<tr>
<td>hyperthyroidism</td>
<td>6.11±0.408a</td>
<td>316.50±47.458a</td>
<td>453.57±7.56c</td>
</tr>
<tr>
<td>P value</td>
<td>0.0001</td>
<td>0.001</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

The values are the mean ± standard error of mean (SEM)

Values with different super script are significantly different at p ≤0.05
Fig. 1: Goat treated with levothyroxine sodium after four weeks from the experiment showing round area of alopecia at face and ear.

Fig. 2: Micrograph of Kidney, goat treated with levothyroxine sodium after two weeks. Note slight vacuolar degeneration of lining epithelium of tube (V) and vacuolation of endothelium of glomelular tuft. (H&E X 40)

Fig. 3: Micrograph of Liver, goat treated with levothyroxine sodium after two weeks. Note periductal mononuclear inflammatory cells infiltration at portal area with fibroplasia. (H&E X 20)

Fig. 4: Micrograph of Liver, goat treated with levothyroxine sodium after two weeks, showing individual cells necrosis (N). (H&E X 40)
Fig. 5: Micrograph of thyroid, goat treated with levothyroxine sodium after two weeks. Notice inactive thyroid follicles that filled with large amount of colloid material which pressed on the epithelial lining. (H&E X 40)

Fig. 6: Micrograph of Kidney, goat treated with levothyroxine sodium after four weeks, showing vacuolar degeneration and necrosis of tubular epithelium (V). (H&E X 40)

Fig. 7: Micrograph of Kidney, goat treated with levothyroxine sodium after four weeks. Note vacuolation of glomelular lining endothelium. (H&E X 40)

Fig. 8: Micrograph of Liver, goat treated with levothyroxine sodium after four weeks. Notice periductal fibrosis and hyperplasia of the lining epithelium of the duct. (H&E X 20)
Fig. 9: Micrograph of Liver, goat treated with levothyroxine sodium after four weeks. Note vacuolar degeneration (V) and necrosis (N) in hepatocytes with proliferation of Kupffer cells (K). (H&E X 40)

Fig. 10: Micrograph of Thyroid, goat treated with levothyroxine sodium after four weeks, showing cystic dilatation of follicles that filled with colloid and lined by low cuboidal to flattened epithelium. (H&E X 40)

Fig. 11: Micrograph of Skin, goat treated with levothyroxine sodium after four weeks, showing area devoid of hair follicle. (H&E X 20)

Fig. 12: Micrograph of Skin, goat treated with levothyroxine sodium after four weeks, showing atrophied hair follicles. (H&E X 20)
DISCUSSION

The experimental study was designated to investigate the effect of hyperthyroidism on some body organs and hormonal assay especially T3 and T4 and also total lipids in goats.

Hyperthyroidism induced significant increase in T3 and T4 and this result was compatible with that recorded by Panciera et al., 1989. Total lipid decreased significantly and this result was observed by Varas et al., 2001.

Half of circulating T3 is derived from deiodination of T4 in peripheral tissue, so peripheral conversion of T4 is the principal source of T3 in animals administered thyroxin (Panciera et al., 1989) and this could be interpret our result in increasing the level of T3 in case of thyroxin treatment.

Hyperthyroidism affects lipid metabolism in liver and induces hypolipemia (Varas et al., 2001).

The clinical signs appeared on goats of this group were, round areas of alopecia at their face and ear and this sign was not mentioned in the available references, with poor body condition and emaciation and these result was mentioned by Vegad and Katiyar, 2000. These signs may be due to direct thyrotoxicosis which cause dermatosis and inturn skin alopecia, and increased basal metabolic rate and increased body catabolism which inturn cause emaciation and poor body condition.

Few studies discussed the pathological changes in different organs in case of hyperthyroidism.

Liver of hyperthyroid animals showed vacuolar degeneration and necrosis of hepatocytes and this picture was similar to that observed by Lawrence et al., 1991.

Degenerative changes in the liver in animal suffered from hyperthyroidism were believed to be evidence of direct toxic effect of thyroxin on hepatocytes (thyrotoxicosis) (Lawrence et al., 1991).
Microscopic examination of kidneys revealed presence of vacuolar degeneration of lining epithelium of renal tubule and lining endothelium of glomelular tuft. This change may be also as a result of thyrotoxicosis as in liver as mentioned by Lawrence et al., 1991.

Results of microscopic examination of the thyroid glands of experimental animals of this group revealed large dilated follicles with abundant colloid, the lining epithelium of the follicles were low cuboidal to squamous (colloid goiter) and this result was previously recorded by Panciera et al., 1990. Alterations of the pituitary thyroid axis were reflected in the histologic appearance of the thyroid glands. The thyroid glands reflected decreased TSH secretion with decreased epithelial hight and increased colloid volume. It is known that thyroid glands become atrophied when the trophic effects of TSH are lacking. The flattened epithelium and increased colloid were due to TSH deficiency secondary to thyroxine administration (Panciera et al., 1990)

From these results we concluded that,

1- Experimental hyperthyroidism has moderate effects on different body organs (kidneys, liver, thyroid glands and skin) and also some blood parameters (T3,T4 and total lipid).

2- Hyperthyroidism induced colloid goiter.

REFERENCES


