Thyroid dysfunction status with special reference to polymorphism of thyroid peroxidase (TPO) gene

CHAPTER-II

The effect of thyroid deregulation on rat liver
INTRODUCTION

Thyroid hormones are known as important factors in gene regulation in tissues such as brain, liver, muscles and adipose tissue (Viguerie and Langin 2003). The present experiment is aimed to understand the relationship of the level of thyroid hormones with liver function and histology.

MATERIALS AND METHODS

The laboratory experiment carried out in the common rat (Rattus rattus) as a mammalian model. Methimazole (Sigma, USA) was used for the induction of hypothyroidism and Eltroxin (Glaxo, India), thyroxine sodium tablets for hyperthyroidism. Normal young adult rat aged 8-10 weeks and weight 70-80g were housed in polypropylene cages and were acclimatized in laboratory condition for a week with natural light and dark schedules prior to experimentation. The animals were fed standard rodent diet and water. For hypothyroid animals treated with Methimazole 20 mg/kg body weight/day and for hyperthyroid Eltroxin 600 μg/kg body weight/day for 14 days respectively. After experimentation blood was drawn directly from heart for serum T3, T4 hormones, SGPT and SGOT. Liver was dissected out and fixed
Thyroid dysfunction status with special reference to polymorphism of thyroid peroxidase (TPO) gene in Bouin’s fixative (Parakal, 1961). Then tissues were processed and stained as described earlier.

**Serum Glutamic oxaloacetate transaminase (SGOT)** & **Serum Glutamic pyruvate transaminase (SGPT) assay:**

SGPT and SGOT are present in cardiac and liver tissues of the body and come out in the blood upon deregulation of these organs. Both SGOT and SGPT measurements are useful in the diagnosis of liver dysfunction (Nabili, [www.medicine.net.com](http://www.medicine.net.com)).

**Principle of the method:**

Transamination is the process in which an amino group is transferred from amino acid to keto acid. The substrates in the reaction are a -ketoglutaric acid (a KG) plus L-aspartate for SGOT, and a KG plus L-alanine for SGPT. The products formed by enzyme action are glutamate and oxaloacetate for SGOT and glutamate and pyruvate for SGPT. A red colour is produced on the addition of sodium hydroxide. The intensity of colour is related to enzymic activity (Reitman and Frankel, 1957).
RESULTS

$T_3$ and $T_4$

The serum $T_3$ and $T_4$ level was significantly reduced in hypothyroid rat whereas in contrast the level significantly increased in hyperthyroid rat as expected and confirming that they were indeed in a hypo and hyperthyroid state (Data not shown as the results followed the same trend as in Fig. 4 A&B).

Body weight:

In case of hypothyroid rat the body weight was increased in compare with the normal rat and in the hyperthyroid rat group the body weight was decreased (Fig. 8).
Liver histology:

Hyperthyroid rats exhibited marked changes in the general histology of hepatocytes as evidenced by the enlargement of central terminal hepatic venules and disorientation of the nuclei and the loss of the individual boundary. Small numbers of hepatocytes were found to be picnotic. Few uniform sized cell bodies stained in eosin were found in the periphery of central terminal hepatic venules (Fig. 9). No discernible change in liver histology was detected in hypothyroid rats.
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Fig. 9: Histology of Normal and Hyperthyroid rat liver. Arrow indicates changes in liver sinusoids.
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Serum SGPT and SGOT:

Hyperthyroid rats showed dramatic increments in SGPT and SGOT level (by ~9.8-fold) as compared to a modest (by ~0.5 fold) increase in hypothyroid rats (Fig. 10 & 11).

Table 4: Serum glutamic pyruvic transaminase (SGPT) level (U/L) in normal, hypothyroid and hyperthyroid rats. Values are expressed as mean ± SE from 6 rats. P values: *<0.001

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<thead>
<tr>
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<th>Normal</th>
<th>Hypothyroid</th>
<th>Hyperthyroid</th>
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<tr>
<td>Serum SGPT (U/L)</td>
<td>53.58±1.62</td>
<td>79.60±0.48 *</td>
<td>525.66±0.60*</td>
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Fig. 10: Serum glutamic pyruvic transaminase (SGPT) level (U/L) in normal, hypothyroid and hyperthyroid rats. Values are expressed as mean ± SE from 6 rats. P values: *<0.001
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**Table 5** Serum glutamic oxaloacetate transaminase (SGOT) level (U/L) in normal, hypothyroid and hyperthyroid rats. Values are expressed as mean ± SE from 6 rats. *P* values: **< 0.001

<table>
<thead>
<tr>
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<th>Control</th>
<th>Hyperthyroid</th>
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<td><strong>428.80 ± 0.4</strong></td>
<td>2529.60 ± 0.42**</td>
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**Fig. 11:** Serum glutamic oxaloacetate transaminase (SGOT) level (U/L) in control and hyperthyroid rats. Values are expressed as mean ± SE from 6 rats. *P* values: **< 0.001
DISCUSSION

In the present investigation, we used methimazole treatment to induce hypothyroidism and thyroxine to induce hyperthyroidism, as reflected in the serum T₃, T₄ levels (Pantos et al., 2005; Grofte et al., 1997). A complex relationship exists between thyroid disease, body weight and metabolism. It is well known that hyperthyroidism causes extensive weight loss despite normal or increased calorie intake (Lonn et al., 1998; Mackowiak et al., 1999). The weight loss is related to the severity of the overactive thyroid. In congruence with these findings 18% loss of body weight was observed in hyperthyroid rats. Weight loss reflects not only a depletion of body adipose tissue stores but also a loss of muscle mass caused by accelerated catabolism and heat elimination. Because of low BMR hypothyroidism is generally associated with some weight gain (Mackowiak et al., 1999). There was an 18% increase in body weight in the present experimental hypothyroid which is in line with reported observation. SGPT and SGOT are the markers of the liver toxicity. The activities of SGPT and SGOT were significantly higher in the hyperthyroid rats than in the control and hypothyroid group (Patil et al., 2008). In both hypo and hyperthyroid rats we found dramatic changes in SGPT enzyme levels in these rats. It is believed that abnormal liver enzyme
Thyroid dysfunction states with special reference to polymorphism of thyroid peroxidase (TPO) gene levels may cause liver damage. SGOT is normally present in liver and heart cells. SGOT is released into blood when the liver or heart is damaged. The blood SGOT levels are thus elevated with liver damage or with an insult to the heart (Nabili, www.medicine.net.com). Profound alteration in liver histology in hyperthyroid rats is a reflection of changes in SGPT and SGOT level in the liver an observation that is unique to this study.