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

CHAPTER-III

The effect of thyroid deregulation on rat testis
INTRODUCTION

Hypothyroidism results in generalized slowing down of metabolic processes associated with abortion, stillbirth, higher infant mortality, congenital anomalies, retarded growth, endemic goitre and endemic cretinism (Lal et al., 1996). In recent times, thyroid diseases are being diagnosed very common and its relation with reproductive failure has been the topic of intense investigation. Ovulation may be impaired in both hypo and hyperthyroidism (Davis, 1999). Studies revealed that neonatal onset of hypothyroidism adversely affect Leydig cell proliferation and regeneration along with impaired steroidogenesis (Ariyaratne et al., 2000). Significant decrease in sperm motility also observed in hypothyroid men (Hudson and Edward, 1992). This study looks at the histological changes of testes in rat under experimentally induced hypo and hyperthyroid condition. This will help us understand how thyroid dysfunction is correlated with the function of reproductive organs.
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) for hyperthyroidism. Normal young adult rat aged 8-10 weeks and weight 80-85 g 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 completion of the experimentation blood was drawn directly from heart for serum T₃ and T₄ hormones. Testis was dissected out and fixed in Bouin’s fixative (Parakal, 1961). Then tissues were processed and stained as described earlier.
RESULTS

Rats were induced experimentally to be hypo and hyperthyroid. The results showed significant changes in histology of testis (Fig. 12). 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. The experiment was to induce hypothyroid and hyperthyroid. As like previous chapter Fig. 4 A&B we found lower $T_3$ and $T_4$ in hypothyroid and higher in hyperthyroid. Significant changes were observed in the cytomoiphology of testis in the hypothyroid group when compared with the control group under light microscopy (Fig. 9). General morphology of the seminiferous tubules was altered in hypothyroid rat. The tubules were shrunken, reduced in size and the normal shape altered with very few mature sperm in the lumen. Spermatogonial cells were immature and highly compressed. Further, the individual boundary of the spermatogonial cells was not maintained. Interestingly no significant changes were observed in the hyperthyroid rats.
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Fig.12: Histology of normal and hypothyroid rat testis

*In the picture I mentioned the total magnification*

Total magnification = magnification of eyepiece x magnification of objective lens

In case of Hyperthyroid rat any change in the histology of testis was not found.
DISCUSSION

In the present investigation, we used methimazole treatment to induce hypothyroidism and thyroxine to induce hyperthyroidism, as reflected in the serum $T_3$, $T_4$ levels (Pantos et al., 2005; Grofte et al., 1997). Methimazole induced hypothyroidism adversely affects the normal process of spermatogenesis (Chakrabarti et al., 2006).

Control rats showed active spermatogenesis whereas in hypothyroid rats, the proliferation and differentiation of germ cells were arrested and their number was decreased. The present study clearly indicates that hypothyroidism adversely affects spermatogenesis. It also indicates that thyroid hormones are essential for normal spermatogenesis. Their effect may be either direct or indirect.

In present observation the size, shape and maturation of spermatogonial cells were significantly changed and hypothyroidism significantly affects the Leydig cells. Previous research had revealed that thyroid hormone exerts its effect on sertoli cell maturation via thyroid hormone receptor (TR) (Holsberger and Cooke, 2005; Maran, 2003). In the present investigation
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significant histological changes in testes might be due insufficiency of thyroid hormones.

However, significant gap in our knowledge remain on the molecular sequence of events that occur how thyroid hormones stimulates germ cell maturation in testes. Our results also indicate that thyroid hormones may have direct regulation on testicular functions. Thyroid hormones modulate the Sperm production and maturation. Therefore, thyroid dysfunction may be an important cause for infertility in males.