

Annexure II: Synopsis

Thyroid hormones and (human) male reproduction Prof. Anand Kumar, A.I.I.M.S.

Thyroid hormones have been shown to exert a modulatory influence on the hypothalamic-pituitary-testicular axis. In hypo and hyperthyroidism sperm number and functions are reported to be altered in a few studies. Thyroid hormone receptors are identified in Sertoli cells, Leydig cells as well as in different stages of maturing germ cells. Thyroid hormones are essential for differentiation of mesenchymal stem cells into Leydig cells in adult rats as well as they also stimulate steroid production from primary Leydig cells and their derived cell lines.

Thyroid hormones suppresses the expression of immature Sertoli cells markers, including anti mullerian hormone (AMH) and aromatase and increases the levels of cell cycle inhibitory proteins. Thyroid hormones also help in maintaining Sertoli cell – Sertoli cell tight junctions by upregulating levels of connexin 43 (Gilleron et al, 2006).

In our study we have found that in hypothyroid human males there was a significant decrease in gonadal steroids – progesterone, total testosterone and bioavailable testosterone (BioT). The fall in testosterone levels could be due to 1) low cholesterol uptake by Leydig cells as evident from high serum cholesterol levels 2) lower conversion of progesterone to testosterone as suggested by low testosterone/ progesterone ratio 3) higher conversion of testosterone to estradiol as suggested by high estradiol to testosterone ratio and 4) hyperprolactanemia. Though serum testosterone and BioT levels were low in hypothyroid men we reported a normal levels of gonadotropins and estradiol suggesting the primary role of estradiol in the feedback regulation of pituitary gonadotropin secretion. Hypothyroid men had high TSH levels and low thyroid hormone levels confounding the exact mechanism of inhibition of testicular steroidogenesis - whether it is low levels of T_3 or raised TSH. To address this issue we studied subclinically hypothyroid men with TSH levels lower than 10mIU/L. These patients also showed an endocrine profile similar to frankly hypothyroid males suggesting a role of TSH independent of T_3/T_4 on testicular function.

In hypothyroid men we reported that the serum levels of testosterone and estradiol were doubled along with high levels of LH and FSH suggesting an operation of the positive feedback effect of estradiol on gonadotrophin secretion. This also suggests that sexual dimorphism in humans is not absolute like the one found in rodents.