The Effects of Estradiol Administration on Testosterone Metabolism in Male Rats

Hosseyni B*, Ahmadi R, and Yari M

***Abstract*—** Studies show that the estradiol and testosterone metabolism are related together on various aspects. The aim of this study was to determine the effects of estradiol administration on testosterone metabolism in male rats. In our study, male Wistar rats were randomly divided into control, olive oil receiving, orchidectomised, sham, testosterone and estradiol receiving orchidectomised groups of 5 rats in each. Estradiol valerate (2µg/kg/body weight) and testosterone enanthate (10mg/kg/ body weight) were administered intraperitoneally. After 7 weeks blood samples were collected using cardiac puncture method and serum testosterone level was measured using radioimmunoassay method and data were statistically analyzed and compared between groups (ANOVA). The results indicated that serum testosterone level was significantly decreased in estradiol receiving and orchidectomised rats compared with control animals ($p<0.001$, $P<0.05$, respectively); however, serum testosterone level was not different between control and estradiol receiving orchidectomised rats. Our finding indicates that estradiol administration reduces testosterone metabolism in non-orchidectomised rats but enhances testosterone metabolism in orchidectomised rats.

***Keywords*—** Testosterone, Estradiol, Orchidectomy, Rat.

I. Introduction

ESTRADIOL(E2) as a sex hormone has two hydroxyl groups in its molecular structure. Estradiol like other steroids is derived from cholesterol. After side chain cleavage and using the delta-5 or the delta-4 pathway, androstenedione is the key intermediary. A fraction of the androstenedione is converted to testosterone, which in turn undergoes conversion to estradiol by an enzyme called aromatase. In both sexes, testosterone is converted by aromatization to estradiol [1]-[2] (figure I).

Testosterone is a steroid hormone from the androgen group and it is selected primarily in the testicle of males and ovaries of females, although small amount are also secreted by the adrenal glands. It is the principle male sex hormone and an anabolic steroid. During the reproductive years, most estradiol in women is produced by the granulosa cells of the ovaries by the aromatization of androstenedione to estrone , followed by conversion of estrone to estradiol by 17 beta_hydroxy steroid dehydrogenase. Testosterone is a hormone which plays a key role in carbohydrate, fat and protein metabolism. It has been known for some time that testosterone has a major influence on body fat composition and muscle mass in the male. As noted, the enzyme aromatase catalyzes the last step of estrogen biosynthesis, the aromatization of ring A of androstenedione and testosterone leading to estrone and estradiol [3]-[5].

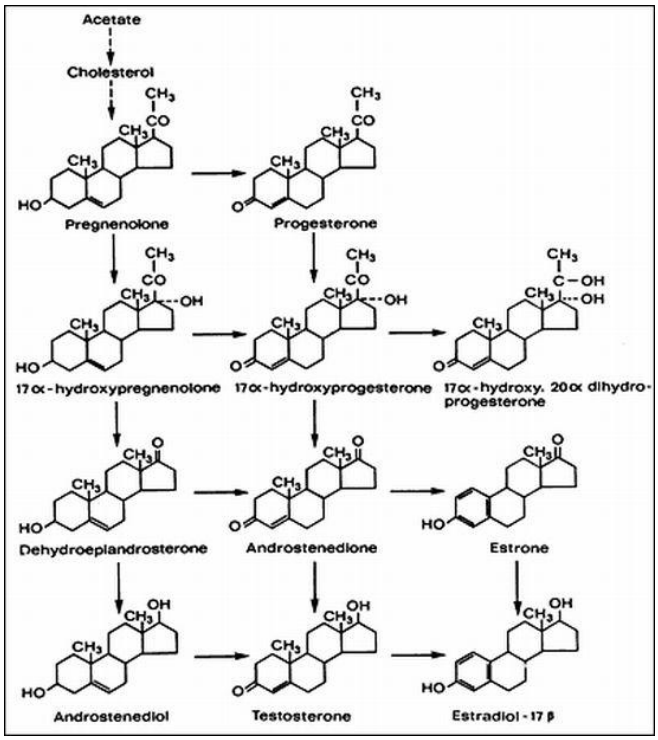

Fig 1 Metabolic pathway of testosterone and estradiol

II. Material and Methods

A. Animlas

Adult male Wistar rats weighting 200±30g were purchased and raised in our colony from an original stock of Pasteur institute (Tehran, Iran).The temperature was at 23±2 ^{0}C and animals kept under a schedule of 12h light: 12h darkness with free access to water and standard laboratory chow.

B. Protocol of Study

Male Wistar rats were randomly divided into control, olive oil receiving, orchidectomised, sham, testosterone and estradiol receiving orchidectomised groups of 5 rats in each. Estradiol valerate (2µg/kg/body weight) and testosterone enanthate (10mg/kg/ body weight) were administered intraperitoneally. For orchidectomy, the scrotal sac was cleaned with alcohol and a small incision of approximately 2cm was made midsagitally at the scrotal septum. The spermatic cord was dissected, tied and cut. The testes were carefully removed from the scrotal sac. The incision was

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sutured. In sham operations, the incisions were immediately sutured and the gonadal system was not manipulated.

After 7 weeks blood samples were collected using cardiac puncture method. Blood samples were collected in appropriate tubes by cardiac puncture technique. After collection, the blood samples left to clot at room temperature for 15 minutes and then centrifuged at 2500 r.p.m. for 15 minutes. The serum layer was then separated and aliquoted into small test tubes and stored at -20^{0}C until hormone determination. Serum testosterone level was measured using radioimmunoassay method was measured using radioimmunoassay method.

C. *Statistical Analysis*

All values are presented as mean±SD. Statistical significance was evaluated by one-way analysis of variance (ANOVA) using SPSS 19. Significance was measured using Game-s Howell significant for the exact P values and significant differences are noted in the results. Differences with P<0.05 were considered significant.

III. Results

The results indicated that serum testosterone level was significantly decreased in estradiol receiving and orchidectomised rats compared with control animals (p<0.001, P<0.05, respectively); however, serum testosterone level was not different between control and estradiol receiving orchidectomised rats.

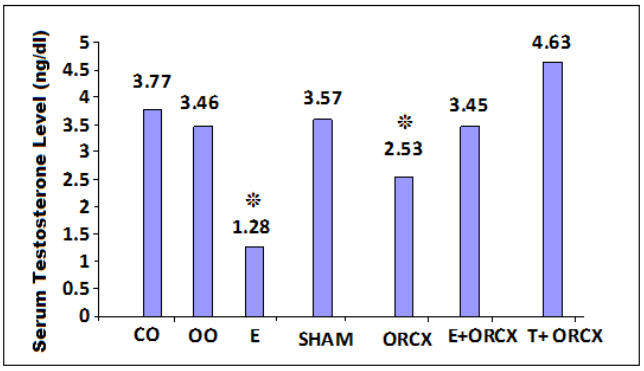

Fig. 1 Serum testosterone levels in CO (control), OO (olive oil receiving), E (etradiol receiving), sham, ORCX (orchidectomised), E+ORCX (estradiol receiving orchidectomised) and T+ORCX (testosterone receiving orchidectomised) rats. * indicates significant difference compared to control group.

IV. Discussion

The results of current research show that serum testosterone level was significantly decreased in estradiol receiving rats (figure II). In line with this findings there are other reports indicating the inhibitory effects of estrogens on male reproductive system. It has been suggested that treatment with estradiol in vivo decreases testosterone production by a direct inhibitory effect on testicular steroidogenesis [6]. The studies also show that neonatal exposure to potent and environmental oestrogens results in abnormalities of the male reproductive system in the rat [7], [8]. On the other hand, in contrast to our finding there are studies showing that estrogens may not influence testosterone or male reproductive system. There is a study showing that diethylstilboestrol exposure does not reduce testosterone production in human fetal testis xenografts [9]. However, other findings also suggest that phytoestrogens can stimulate testosterone synthesis during puberty in male goats by increasing the secretion of T3; a hormone known to stimulate Leydig cell steroidogenesis [10].

In this study we showed that esradiol administration in orchidectomised rats resulted in increased testosterone to control level (figure II). In this case, since there is not testicular system, estradiol administration might acted on adrenal gland to increase adrenal androgens, including testosterone. The investigations on the effects of estrogens on adrenal gland revealed the stimulatory effects of estrogens on adrenal cortex [10]. The studies also show that estrogens replacement can improve some functions of testosterone in patients with low testosterone level [11], [12]. However, increased testosterone in orchidectomised estradiol receiving rats is an intriguing finding required to be further investigated in molecular and cellular level.

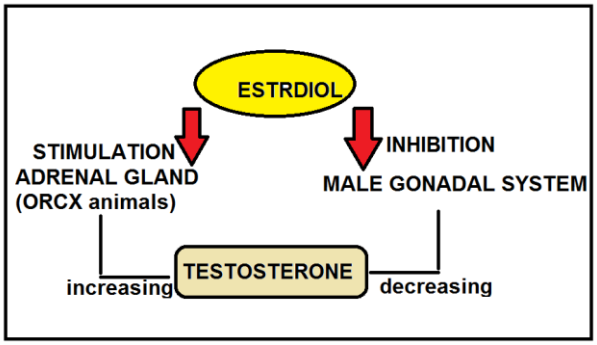

Fig. 2 Serum testosterone level in estradiol receiving rats

V. Conclusion

We have shown that estradiol administration reduces testosterone metabolism in non-orchidectomised rats but enhances testosterone metabolism in orchidectomised rats.

Acknowledgment

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