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# Effect of Exogenous Testosterone, Finasteride, and Castration on Serum Level of Thyroxine

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## ABSTRACT

**Background:** The secretion of thyroxine (T4) as the main hormone of thyroid gland is regulated by androgens. The present study aimed to evaluate the effect of testosterone and finasteride administration and castration on serum levels of T4 and to show the effect of this regulation on total body weight, weight of testis, and the weight of prostate. **Methods:** Male adult rats (n = 32) were divided into 4 groups (n = 8): Group 1 (control), Group 2 (castration), Group 3 (finasteride: 20 mg/kg/day) and Group 4 (testosterone: 5 mg/kg/day). At the end of the study (35 days), serum level of thyroxine, body weight, weight of testis, and prostate were determined. **Results:** The data showed that the body weight increased in castrated ($P = 0.04$) and decreased in testosterone ($P = 0.00$) groups but did not differ in finasteride ($P>0.05$) group. There were not any differences in the weight of testis among control, finasteride, and testosterone groups but the weight of prostate increased in testosterone group ($P = 0.00$) and decreased in castrated ($P = 0.03$) and finasteride groups ($P = 0.04$). In addition, the serum level of T4 (nmo/ml) decreased in the three groups: finasteride ($P = 0.03$), testosterone ($P = 0.04$), and castrated ($P = 0.00$). **Conclusion:** Testosterone in both high and low levels decreased the amount of T4 with a time-dependent manner. *Iran. Biomed. J. 17 (4): 221-224, 2013*

*Keywords*: Finasteride, Rats, Testosterone, Thyroxine

## INTRODUCTION

Testosterone is a key androgen for establishment, maturity, and also functions of male reproductive system. This steroid could be converted to a more potent hormone, dihydrotestosterone (DHT), by 5-α rectudase enzyme [1]. DHT is responsible for male pattern of hair loss, and the men with high level of testosterone but with deficiency in 5-α rectudase enzyme do not have experience of this pattern of hair loss [2]. Finasteride is a lipophilic drug that blocks type II 5-α rectudase and is used for treatment of benign prostate hyperplasia and male pattern of hair loss [3].

Thyroid gland is another target of testosterone. It has been shown that physiological amounts of testosterone stimulate thyrotropin secretion [4] and induce growth of thyroid gland of rats [5]. However, despite the gonadal steroids-induced changes on serum thyroxine-binding globulin concentrations, subjects with normal thyroid glands maintain clinical and biochemical euthyroidism without changes in their serum free thyroxin (T4) or thyroid-stimulating hormone levels. In contrast, the administration of gonadal steroids to patients with thyroid diseases causes significant biochemical and clinical alterations requiring changes in the doses of thyroid medications [6].

Considering the effect of androgens and anti-androgens on development and maintaining of male reproductive system and also on secretion of thyroidal hormones, the present study was conducted to evaluate serum level of T4 following administration to testosterone, finasteride, and castration on adult rats.

## MATERIALS AND METHODS

Male Wistar rats (n = 32), weighing approximately 255 ± 5 g, were purchased from Pasteur Institute of Iran (Tehran) and maintained in the Animal Resource Center, Animal House at Razi University of Kermanshah (Kermanshah, Iran) under controlled conditions of lighting (12-h light, 12-h dark cycle) and temperature (22 ± 2°C). The animals were given free

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access to standard chow and water. All animals received care based on the Research Committee of the Razi University (Kermanshah, Iran). The rats were allocated to 4 groups and each group consisted of 8 animals. Group 1 (control): the animals that received sesame oil (0.2 ml/day, i.p. as vehicle), group 2 (castration): castration carried out at the first day of experiment, group 3 (finasteride): the animals that received finasteride (20 mg/kg/day, dissolved in the drinking water), and group 4 (testosterone): the animals received testosterone (5 mg/kg/day i.p.) dissolved in 0.2 ml sesame oil. The experiment was performed for 35 days. Castration was performed under general anesthesia induced by ether and ketamine (20 mg/kg) in combination [7, 8]. The scrotum was opened, and spermatic cord was legated to remove the testes, then the scrotum was sutured.

***Sample collection.*** At the end of the study, blood samples from all experimental rats were collected directly from the heart [9]. Separation of serum was achieved by centrifugation. The samples were stored at -70°C until use.

***Biochemical analysis.*** The levels of T4 were measured by inductive coupled plasma-optical emission spectroscopy (Perkin Elmer, model 7300, USA). Results were expressed as µg/L. Serum level of T4 was assayed by radioimmunoassay and human diagnostic test kit (Immunotech, USA) using a Gamma counter (Kontron, USA) and results were expressed as nmol/ml [10].

***Statistical analysis.*** Data were presented as mean ± SE, and multiple comparisons were calculated by one-way ANOVA. For comparing the data of three experimental groups with control one, statistical student's *t*-test was used. The significance level chosen was $P<0.05$.

## RESULTS

The weights of animals were measured before and after the experiment. The data showed that the weight change was 31.25 ± 1.56 in control group, 41.63 ± 1.36 in castrated ($P = 0.04$), 23.88 ± 4.98 in finasteride ($P>0.05$), and 3.51 ± 1.47 g in testosterone ($P = 0.00$) groups. Furthermore, there was a significant difference in total body weight between castrated and testosterone groups ($P = 0.000$) (Fig. 1A). The weights of testes and prostates were measured, and the data are presented in Figures 1B and 1C. The weight of testes in control group of rats was 2.791 ± 0.13 g. There were not significant differences in the weight of testes between control group and testosterone (2.84 ± 0.10 g) and finasteride (2.59 ± 0.07 g) administrated ones (Fig. 1B). The weight of prostate was 0.59 ± 0.037 g in control group; however, it increased in testosterone group (1.546 ± 0.08 g, $P = 0.00$) and decreased in castrated (0.30 ± 0.03 g, $P = 0.03$) and finasteride group (0.46 ± 0.06 g, $P = 0.04$) (Fig. 1C).

The serum level of T4 (nmo/ml) was decreased in three experimental groups (finasteride, testosterone, and castrated). Hence, the serum level of T4 was 59.06 ± 0.77 in control group, 43.32 ± 2.6 in testosterone ($P = 0.00$), 52.18 ± 2.40 in finasteride ($P = 0.04$), and 48.87 ± 1.1 in castrated ($P = 0.03$) ones (Fig. 1D).

## DISCUSSION

In the present study, total body weight was reduced in testosterone and increased in castrated groups but did not change in finasteride one. These data are in consistent with the other studies [11, 12] and also indicate that castration increases the lipid component of the animals [12].

The present study showed that although the weight of testis was not affected by both testosterone and finasteride, the prostate weight increased in testosterone and decreased in castrated and finasteride groups. Previously, it has been indicated that castration reduces collagen component of accessory gonadal tissues such as prostate [13]. The data also are in consistent with other research that have been shown that testosterone propionate increases the weight of accessory gonadal organs and do not affect the weight of testis [14]. The data could be described by different regulation manners of androgen receptors in testis and prostate. Although both testis and prostate have androgen receptors, low levels of 5-α reductase enzyme in testis cause different response to exogenous concentration of androgens in this tissue besides prostate [15]. Furthermore, although finasteride reduces DHT, the level of testosterone increases, and the weight of prostate reduces in the rats [7], and also the other study showed that finasteride did not affect the weight of testis of rats [9]. According to our data and of the literature, it seems that endogenous DHT is responsible for controlling the weight of prostate; however, further studies are needed for testis.

Biochemical analysis of the present study demonstrated that the serum level of T4 decreased in castrated animals and also in testosterone and finasteride administrated groups. A study showed that testosterone [16] decreased T4, but another one indicated that testosterone did not affect T4 [17]. Finally, another study showed that following administration with testosterone in rats, firstly, the serum concentration level of T4 decreased and secondly, it increased up to normal level [18].




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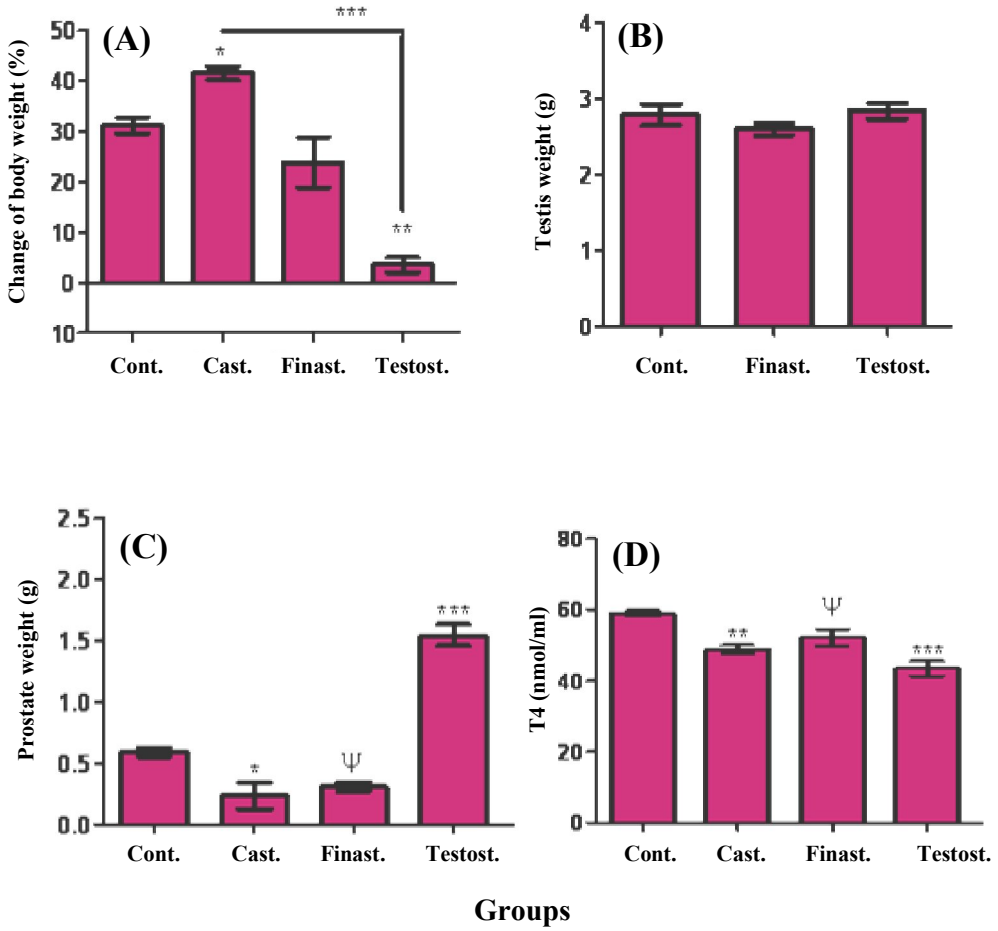


**Fig. 1.** Effect of testosterone (Testost.), finasteride (Finast.) administration and also castration (Cast.) during 35 days of the study (n = 8) on the total weight, weight of testis, weight of prostate, and the scrum level of T4 (nmol/ml). **(A)** The change in the weight level significantly increased in castrated animals, whereas it increased in testosterone group. **(B)** Testis weight did not change in testosterone and finasteride administrated groups. **(C)** Prostate weight increased in testosterone administrated group, whereas it decreased in castrated and finasteride administrated animals. **(D)** The serum level of T4 significantly decreased in castrated animals and also in testosterone finasteride administrated groups. **P*<0.05, ***P*<0.01, ****P*<0.001 and *t*-test (Ψ) = *P*<0.001

Physiological amount of testosterone regulates both the secretion of thyroid-stimulating hormone and the amount of its receptor; however, in higher amounts of testosterone, this function would be reversed [5]. This effect of testosterone is seemed to be unique for thyroid regulation, and as we showed previously only high level of testosterone could trigger the secretion of hormones like insulin [8]. This pivotal role of testosterone that is derived by the concentration could be the cause of lowering the serum level of T4. The present study also adds this data that decreased amount of testosterone in castrated animals causes T4 down regulation. Therefore, in this study, testosterone in both high and low levels decreased the amount of T4 with a time-dependent manner.

In conclusion, the secretion of T4 is regulated by both high level and low level of testosterone and the weight of testis but not prostate is under influence of serum level of testosterone.

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