

In Vivo Anabolic Androgenic Steroid Alters Thyroid Gland Functions in Female Rats

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Abstract

Introduction: Because androgen receptors are expressed in this tissue, sex hormones may affect thyroid function by, in addition to TSH, promoting thyrocyte proliferation in culture. **Aim:** The study's goal is to see how androgenic steroid hormone influences the thyroid. **Materials and methods:** Adult female wistar rat (no. 12) and weight (180-200 g) were housed and divided into two groups (no.6 with each group). Control group was injected with propylene glycol which used as a vehicle, while the treated group injected with testosterone propionate subcutaneous with 100mg/kg dose dissolve in propylene glycol for 30 days. **Results:** there is no significant differences in T3, T4 and TSH between control and treated groups. Possible toxic goiter seen and there was scalloping of the follicular epithelial cells, also thyroid tissue showed in colloid goiter with cold follicular in which follicles lined by cuboidal follicular epithelial cells and thus may decrease secretion of thyroid hormone. **Conclusion:** it is suggested that hyperthyroidism occurred in the young man because administration of androgenic steroid does not only affect T3, T4 and TSH levels as animal studies showed that androgenic steroid in rats exert a proliferative effect on thyroid cells and affect peripheral metabolism.

Keywords: Thyroid Gland, Androgenic Steroid, Rats.

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INTRODUCTION

Since its creation in 1935, many testosterone derivatives have been synthesised in an effort to lengthen its biological activity in vivo, create orally active androgens, and elaborate products commonly known as anabolic-androgenic steroids (AAS) that are more anabolic and less androgenic than the parent molecule. Synthetic derivatives of testosterone [2] with increased anabolic potency and reduced androgenic effects are known as anabolic-androgenic steroids (AAS). The activity of androgens is mediated by their interaction with the androgen receptor (AR) [4]. The human body contains a plethora of androgen receptors dispersed across many organs and tissues. Specifically, androgens can exert their effects in three ways: I by binding directly to androgen receptors; (ii) by acting on oestrogen receptors via estradiol generated by CYP19 aromatase; and (iii) by acting on dihydrotestosterone (DHT) generated by the activity of 5-alpha-reductase. Mainly, free testosterone is transported into the cytoplasm of target tissue cells, where it binds to the AR either directly or after being converted to 5--dihydrotestosterone (DHT) by the cytoplasmic enzyme 5-alpha reductase. Both free and bound testosterone binds to predetermined chromosomal DNA nucleotide sequences in the nucleus of a cell. The newly produced DNA stimulates the transcription of specific

responsive genes, which in turn has a major impact on protein synthesis. The complex dimerizes, then binds to androgen response elements (AREs) in the promoter regions of target genes, where it regulates transcription. The G-protein coupled receptor is an intracellular transmembrane receptor that may be activated quickly by non-genomic processes that interact with it. In this regard, thyrocyte proliferation in culture independent of TSH may be caused by sex hormones due to the presence of androgen receptors in this tissue. Similar mechanisms have been seen in other types of tissues [6]. In order to achieve a low-fat, high-muscle mass body composition and to enhance athletic performance, the use of anabolic-androgenic steroids (AAS) has skyrocketed during the past three decades. Although anabolic androgenic steroids (AAS) were once exclusive to professional and Olympic weightlifters, recreational sportsmen and bodybuilders are now common consumers of these substances [3]. There are various medical applications for AAS treatment beyond just replacing lost testosterone. In addition to treating breast cancer and hereditary angioedema, they are also used to treat low stature (as shown in Turner's syndrome) and hereditary angioedema (as an anti-estrogen). This review does not focus on these kinds of software. Instead, the anabolic effects of these medicines on persons with chronic diseases are the primary focus of

this paper [7]. However, AASs have several negative consequences, including on the liver, serum lipids, reproductive system, and the mind/behavior. Androstenedione is an anabolic androgenic steroid used to increase strength, sexual performance, and lean body mass by boosting testosterone levels in the blood. On the other hand, there is no evidence that androstenedione or similar substances significantly improve strength and/or lean body mass in people via increasing testosterone levels. Long-term androstenedione supplementation hasn't been studied, so we don't know how it will affect your health. Dehydroepiandrosterone (DHEA) is advertised as an anti-obesity and anti-aging medicine that can boost libido, immunity levels, and energy [5]; it is a weak androgen also used to raise testosterone levels. Sex steroids may have an immediate effect on thyroid function because thyroid cells are equipped with androgen receptors. Demonstrated that testosterone alone can stimulate thyrocyte proliferation in culture, independent of the impact of thyroid stimulating hormone. Testosterone may increase TSH production, secretion, and reaction to TRI-I in rats since castrated male rats have lower pituitary and blood TSH levels. Androgens are known to have a beneficial effect on the expression of type 1 iodothyronine deiodinase (DI). Castration of male rats reduces DI activity, but androgen replacement treatment restores normal levels. Thyroid hormone-binding globulin (TBG) in humans is regulated by androgens. TBG binds thyroxine (T4) and 3', 3, 5 - triiodothyronine (T3) in the blood. Weissel and Deyssig found a significant difference in the responses of the pituitary gland to TRH stimulation in the five AAS-using bodybuilders and the eight control patients in their clinical study. Accordingly, there may be a little decrease in thyroid function due to AAS misuse in humans. Similar studies indicated that AAS users had lower levels of total T3, total T4, and TBG compared to the general population. *The raised TSH and free T4 may be related to either an enhanced sensitivity of the pituitary to TRH or a decreased sensitivity of the thyrotroph to hormonal feedback, as suggested by these researchers [3].

MATERIAL AND METHOD

Animals

Adult female wistar rat (no. 12) and weight (180-200 g) were housed in stain steel cages under control condition (14 h light and 10 h dark cycle) and temperature (24°). Animals had a free access to water and was fed daily. In accordance with the guidelines set forth by the university of Baghdad's college of pharmacy's animal care committee, all experiments involving animals were carried out.

Testosterone propionate administration

Rat divided into two groups (no.6 with each group). Control group was injected with propylene glycol which used as a vehicle, while the treated group injected with testosterone propionate (Sustanon 250 mg, organon) subcutaneous with 100mg/kg dose dissolve in propylene glycol for 30 days.

T3, T4 and TSH measurement

After 30 days of testosterone propionate administration to treated group, blood samples drawn by heart puncture technique under anesthetic effect of diethyl ether. T3, T4 and TSH for both control and treated group measured by using COBAS E411 device (ROCHE Company).

IBM's Statistical Software for the Social Sciences was used for the analysis (IBM SPSS Statistics version -25). Charts produced using Microsoft excel 2016.

Statistics are reported as mean SEM, and a P value less than 0.05 is regarded to indicate statistical significance.

RESULTS

Serum T3, T4 and TSH

Table 3.1 below lists the serum values of T3, T4, and TSH in the treated and control groups. Between the control and treated groups, there were no significant variations in T3, T4, or TSH levels ($p>0.05$).

Table 3.1: Shows levels of T3, T4 and TSH of the control group (C1-6) and treated group (T 1-6)

No.	T3	T4	TSH
C1	1.18	106.4	0.14
C2	2.34	143.5	0.13
C3	1.86	96.22	0.43
C4	2.38	148.4	<0.005
C5	1.96	127.2	0.25
C6	2.85	156.7	<0.005
T1	2.77	150.5	<0.005
T2	2.79	153.7	<0.005
T3	1.46	138.4	0.005
T4	1.78	118.7	0.142
T5	2.5	149.1	<0.005
T6	1.85	109.5	0.18

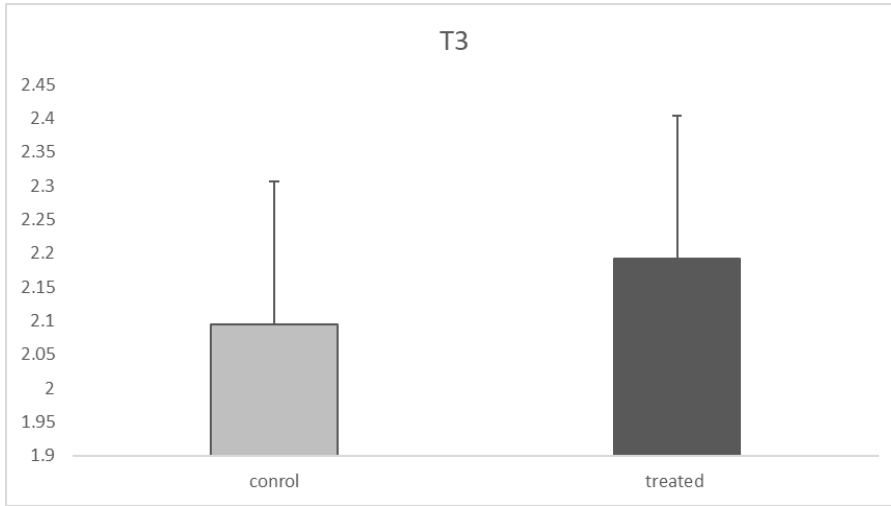


Figure 3.1: Shows serum T3 level of control and treated group, no significant difference was found in T3 between the two groups (2.095 ± 0.2123) vs (2.1917 ± 0.2114) respectively $P > 0.05$

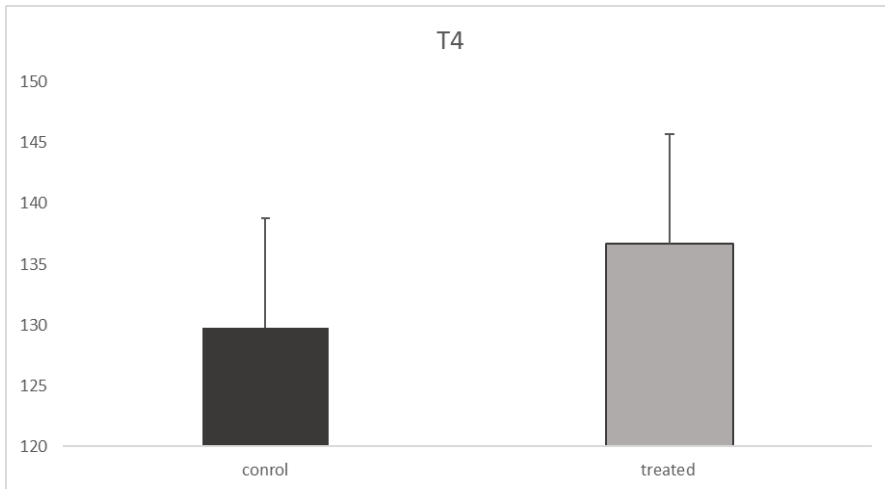


Figure 3.2: Shows serum T4 level of control and treated group, no significant difference was found in T3 between the two groups (129.7 ± 9.036) vs (136.7 ± 6.872) respectively $P > 0.05$

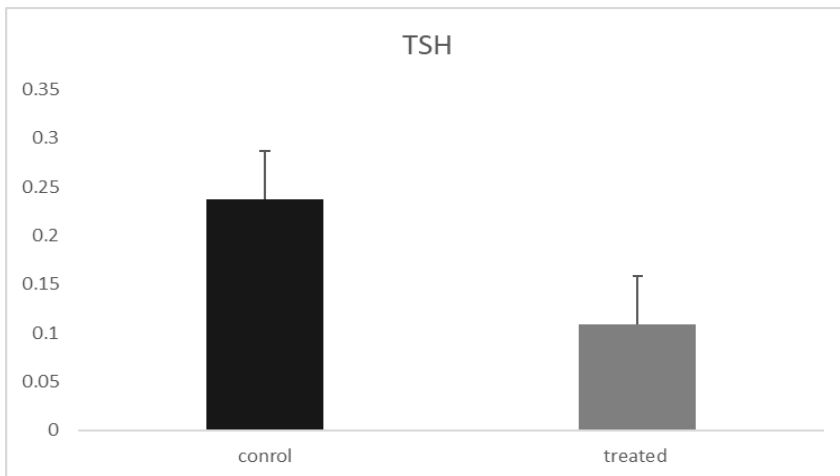
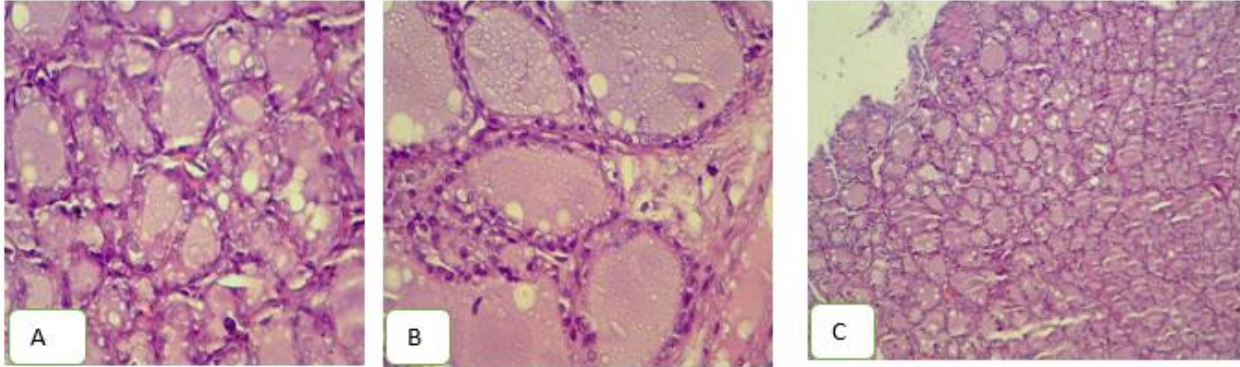


Figure 3.3: Shows serum TSH level of control and treated group, now significant difference was found in T3 between the two groups (0.238 ± 0.049) vs (0.109 ± 0.031) respectively $P > 0.05$

Histopathology

Pictures 3.1 below show different sections of the histology of thyroid gland for the control group.

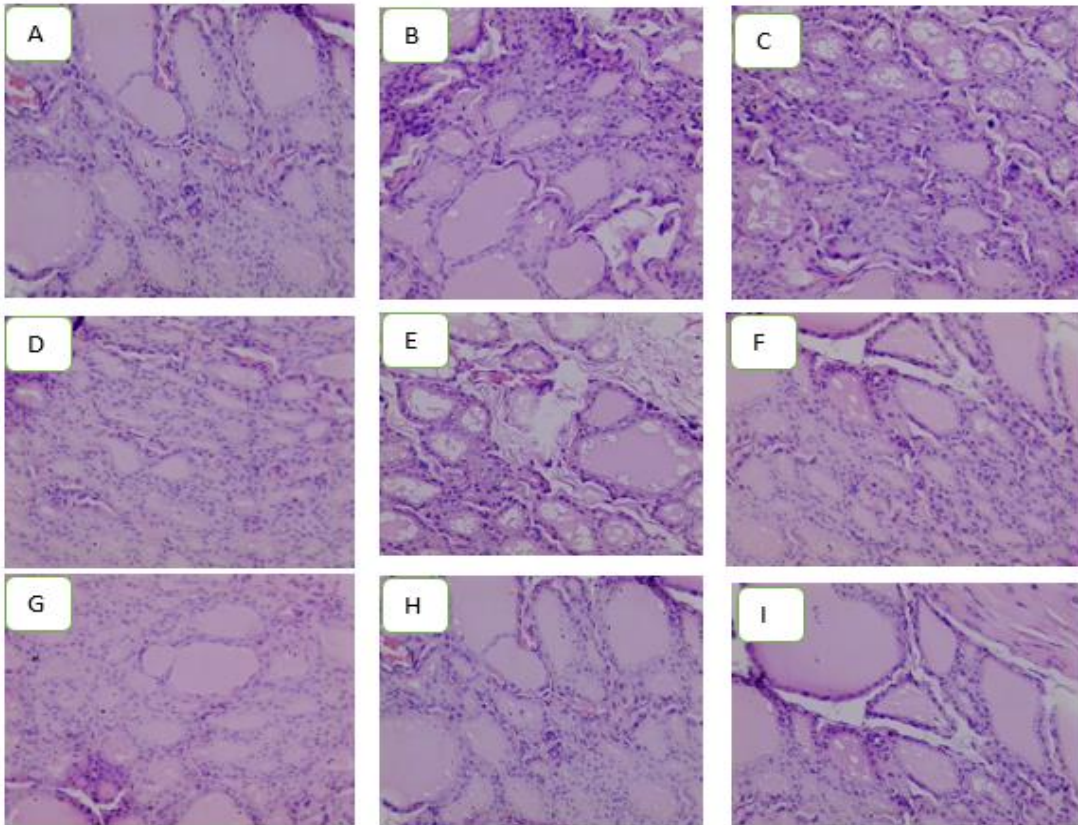


Pictures 3.1 show different sections (A-C) of the thyroid gland of control group

Histology of thyroid gland for the treated group

Pictures below show different sections of thyroid gland for

the treated group.



Picture 3.2 show different sections (A-J) of thyroid gland of the treated group

Possible toxic goiter seen in section (E) there was scalloping of the follicular epithelial cells, section (F) showing thyroid

colloid goiter with cold follicular in which follicles lined by cuboidal follicular epithelial cells and thus may decrease secretion of thyroid hormone.

DISCUSSION

Thyroid hormone deficiency causes several endocrine alterations that influence glucocorticoids, corticotrophin, growth hormone, and gonadal function, among other organs and systems. Hypogonadotropic hypogonadism is common in people with primary hypothyroidism, however it is treatable with thyroid hormone replacement treatment. (8)

It is well known that metabolism of testosterone and other androgens is affected by TSH, in which TSH can alter the level sex hormone binding globulin and thus affect the level of bound and free testosterone (9).

The results shown that 30 days of treatment with testosterone propionate (Sustanon 250 mg) does not significantly altered levels of T3, T4 and TSH as compared with control group. Interestingly, additional studies have shown the following changes in thyroid function in athletes who used high-potency anabolic steroids (for a period of 12 weeks): TSH, TBG, triiodothyronine, thyroxine, and free thyroxine serum concentrations all dropped significantly, as did free thyroxine (10). Exogenous androgen therapy altered the endocrine function of the testicles, as evidenced by the fact that all measured values reverted to normal with the exception of testosterone once treatment was discontinued (10). Therefore, the treatment time should be longer than 30 days to see a significant effect as compared to control group. Aljaberi *et al.* in 2019 reported a case of 25 years old male using AAS for the previous 2 years and presented to the hospital with signs and symptoms of thyrotoxicosis even upon discontinuation of AAS and concomitant therapy the patient remained suffering from hyperthyroidism for a year later (11). Aljaberi *et al* suggested that hyperthyroidism occurred in the young man because administration of AAS does not only affect T3, T4 and TSH levels as animal studies showed that AAS in rats exert a proliferative effect on thyroid cells and affect peripheral metabolism (3, 11).

The histopathological studies showed signs of goiter in some sections. Possible toxic goiter seen in section there was scalloping of the follicular epithelial cells, other section showed thyroid in colloid goiter with cold follicular in which follicles lined by cuboidal follicular epithelial cells and thus may decrease secretion of thyroid hormone. Additionally, the impact of AAS on the proliferation of thyrocytes may be responsible for this outcome (3, 11).

CONFLICT OF INTEREST

Non.

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