

قسم الغدد الصماء

مستشفى وزارة الصحة الامريكية - جامعة واشنطن - سياتل
رئيس القسم : د.أ.د / ش.أ.أ بولسن

التغيرات في مستوى هرمون التستوستيرون والدايهيدروتستوستيرون في مصل
الفئران البالغة عقب حقن الهرمون المشيمي الادمي الحاث
للمناسل أوبروبيونات التستوستيرون

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تم حقن الهرمون المشيمي الادمي الحاث المناسل (١٠٠ ، ٢٠٠ وحدة دولية في اليوم)
وبروبيونات التستوستيرون (١ ، ٢ مجم في اليوم) منفردين لذكور الفئران البالغة تحت
الجلد ولمدة سبعة أيام متوالية .

ونج عن هذا العلاج زيادة معنوية في مستوى كل هرموني التستوستيرون والدايهيدروتستوستيرون
دون تغير في نسبة أحد هذين الهرمونين للآخر . ولم تبد الخصية أي تغيير ملحوظ في الوزن
في حين نتج ازدياد ملحوظ في أوزان الغدد الجنسية المساعدة .

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VARIATIONS IN TESTOSTERONE AND DIHYDROTESTOSTERONE SERUM LEVELS IN ADULT RATS FOLLOWING THE ADMINISTRATION OF HUMAN CHORIONIC GONADOTROPHIN OR TESTEOSTERONE PROPIONATE

(With One Table)

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(Received at 19/2/1987)

SUMMARY

Two doses of Human Chorionic Gonadotrophin (100 and 200 i.u./day) and Testosterone Propionate (1 and 2 mg/day) were administered singly to adult male rats for seven successive days subcutaneously. The applied treatment resulted in significant increase in both testosterone and dihydrotestosterone serum levels without change in T / DHT ratio. The testis did not undergo appreciable change in weight. The accessory reproductive glands underwent significant ponderal increment.

INTRODUCTION

The effect of acute administration of Human Chorionic Gonadotrophin (HCG) on serum testosterone (T) level was previously studied in adult male rats (HASHIMOTO and SUZUKI, 1966; BARDIN and PETERSON, 1967; PARLOW, COYOTUPA and KOVACIC, 1973 and HARRIS and BARTKE, 1974). The level of dihydrotestosterone (DHT) was not assayed in these studies. In the present investigation the effect of seven days administration of two doses of HCG on serum T and DHT levels and weights of reproductive organs was studied in adult male rats. For comparison, testosterone propionate (TP) was administered in two doses to similar number of animals.

MATERIAL and METHODS

Twenty-five adult male Sprague-Dawley rats (70 days-old, 300 gm body weight) were randomly divided into five equal groups. The animals were kept under routine standard laboratory conditions and were fed purina rat chow and tap water ad libitum. The first group (CON) were kept as control and received 0.2 ml sesame oil. Human Chorionic Gonadotrophin (HCG) (Serono, USA) was administered in a low dose (100 i.u./day/animal in 0.2 ml distilled sterile water) to the second group (CGL) and in a higher dose (200 i.u.) to the third group (CGH). Testosterone propionate (TP) (Lilly, USA) was administered in a low dose (1 mg/day/animal in 0.2 ml sesame oil) to the fourth group (TPL) and in a higher dose (2 mg) to the fifth group (TPH). The drug or the vehicle were administered subcutaneously in the back for seven successive days at /0800 hr. The animals were decapitated about 24 hours following the last injection, during the morning to avoid circadian variations in T level. The blood was collected from the trunk, the serum separated by centrifugation and stored at -20°C. The reproductive organs were immediately removed, separated from adhering tissues, secretion emptied and the paired organs weighed to the nearest mg. Androgens in the serum were

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extracted by ether, T & DHT were separated chromatographically on celite microcolumns as described by COYOTUPA, PARLOW and ABRAHAM (1972) and the purified hormone determined by radioimmunoassay.

Recoveries of T averaged $83.0 \pm 0.77\%$ (SEM) and between duplicates coefficient of variation averaged 1.85%. Respective figures for DHT were $75.6 \pm 1.58\%$ and 5.66%. The level of T and DHT in normal adult human male serum, run as a quality control, was respectively 6.7 and 0.16 ng/ml.

RESULTS

The treatment did not affect the body weight or percent gain during the experimental period.

The serum T and DHT levels as well as the weights of the paired reproductive organs are presented in Table 1. The results are expressed as mean \pm s.e.m., and student's test used to determine the levels of significance.

Table (1)
Changes in serum testosterone and dihydrotestosterone levels and weights of the reproductive organs

Group	Testosterone ng/ml	Dihydro- testosterone ng/ml	T/DHT Ratio	Weights of paired reproductive organs, mg				
				Testis	Seminal vesicles	Coagulat- ing gl.	Dorsal Prostate	Ventral Prostate
CON	4.786 [§] ± 1.577	0.195 ± 0.040	24.88 ± 4.49	3,572 ± 109	469 ± 39	172 ± 15	377 ± 24	203 ± 26
CGL	21.908 ^{***} ± 2.389	0.760 ^{**} ± 0.128	30.45 ± 3.96	3,445 ± 26	725 ^{**} ± 51	245 [*] ± 19	605 ^{***} ± 16	287 [*] ± 26
CGH	27.478 ^{***} ± 1.951	0.797 ^{***} ± 0.086	35.36 ± 3.19	3,390 ± 108	829 ^{**} ± 95	259 ^{**} ± 19	594 ^{**} ± 55	304 [*] ± 29
TPL	10.326 [*] ± 0.750	0.429 [*] ± 0.074	25.77 ± 3.15	3,439 ± 83	758 ^{**} ± 48	168 ± 11	662 ^{***} ± 34	296 [*] ± 22
TPH	19.752 ^{***} ± 1.908	0.790 [*] ± 0.202	29.69 ± 4.91	3,294 ± 207	826 ^{***} ± 37	300 ^{**} ± 28	766 ^{***} ± 46	322 ^{**} ± 10

[§] Each value represent the mean \pm s.e.m. of 5 animals

* = $P < 0.05$ compared with the control

** = $P < 0.01$ compared with the control

*** = $P < 0.001$ compared with the control

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DISCUSSION

The T level in the control group is in accord with the levels previously reported in Sprague-Dawley rats by RIVAROLA, SNIPES and MIGEON (1968) and KNORR, VANHA-PERTTULA and LIPSETT (1970). The DHT level is lower than that reported by COYOTUPA, PARLOW and KOVACIC (1973) and almost similar to that reported by PUJOL, BAYARD, LOUVET and BOULARD (1976). HCG in both doses resulted in significant increase in both serum T and DHT levels without dose response relationship. The increase in T level is in general agreement with previous reports and which is due to the stimulatory effect of HCG on the interstitial cells. T level increase with time following intraperitoneal injection of LH (MOGER and ARMSTRONG, 1974) or administration of HCG intravenously (HASHIMOTO and SUZUKI, 1966) or subcutaneously (HARRIS and BARTKE, 1974) and the elevation lasted for few hours. The absence of significance in the T/DHT ratio may be due to the general parallel effect of HCG on the secretion of T as well as the transformation to its main metabolite, DHT; since castration usually results in similar decrease in both serum T & DHT levels (COYOTUPA *et al.*, 1973). This is contrary to the condition in immature rats where androstendione (A) dominant pattern was observed, while in adult T/A ratio was significantly increased following HCG administration (HASHIMOTO and SUZUKI, 1966). A dose response relationship in T serum level was found to exist following intravenous injection of LH (PARLOW *et al.*, 1973) or HCG (BARDIN and PETERSON, 1967). That this differs from the present study may be due to the difference in the route of drug administration, the time of sampling following the injection or the frequency of gonadotrophin administration. Nevertheless, the present results are in accord with that of MOGER (1977) who found that increasing the dose of LH up to 30 or 100 $\mu\text{g}/100$ g body weight did not produce any additional increase in the concentration of testosterone (plus dihydrotestosterone). Thus it seems that 100 i.u. (ca 30 i.u./100 g body weight) as used in this study is the highest responsive dose; and increasing the dose to 200 i.u. did not result in higher increase in T or DHT levels.

The administration of TP resulted in significant increase in both T and DHT with significant dose response relationship for T level only. This is in accord with the findings of HARRIS and BARTKE (1974) for T serum level in adult rats. The available literature lacks information on DHT level following the injection of HCG or TP. The T level was significantly higher in the CGL ($P < 0.01$) and CGH ($P < 0.001$) groups than in the TPL group. The difference in the levels was less pronounced in the TPH group which was significantly less ($P < 0.05$) than in the CGH group only. DHT was significantly higher in both HCG treated groups ($P < 0.05$) than in the TPL group only.

None of the applied HCG doses resulted in ponderal changes in the testis. This finding is not in accord with that reported by SAMUELS and HELMREICH (1956) who stated an increase in the weight of the testis of adult rats within 48 hours of a single injection of HCG. Variations in the effect of HCG due to age had been reported previously. SANDLER and KNOBIL (unpublished, cited by HALL, 1970) found that age is an important factor in the response of the testis to ICSH, and that the increase in testicular weight following the administration of ICSH was greater in rats aged 19 days than in younger or older rats. Thus in immature rats (GAARENSTROOM, 1941) and juvenile monkeys (ARSLAN and QAZI, 1976) the testis increase in weight following HCG administration, while in adult male rabbits ponderal changes were not observed even after 15 weeks of daily HCG injection (ABDEL-RAOUF, in progress). Similarly TP did not result in any change in the weight of the testis. This may be due to the relatively short duration of the treatment. Chronic administration of TP result in significant decline in testicular weight in rats (c. f. ALBERT, 1961 and MANN, 1964) and rabbits (ABDEL-RAOUF, in progress).

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Low and high doses of HCG and TP resulted in increase in weight of the studied accessory reproductive glands with different degrees of significance (Table 1), except for the coagulating gland which did not show significant weight increase in response to the low TP dose. For TP dose response relationship was observed for the coagulating gland only, mainly due to absence of response to the low dose, while no response related to the dose was observed for HCG or TP on the other glands. The effect of TP on the weights of the accessory glands is expected and is due to a direct effect on the accessory gland which respond by increase in weight (c.f. MANN, 1964) or height of the epithelium (c.f. PRICE and WILLIAMS-ASHMAN, 1961). Both T and DHT have a high potency in curbing the decrease in weight of ventral prostate and seminal glands following orchietomy in rats (VERJANS and EIK-NES, 1977). The increase in weight following the administration of HCG, as observed in this study, is due to the increased circulating T and DHT levels. Non significant differences were found between the effect of HCG in both doses and TP in both doses (singly or combined) on the weight of the seminal vesicles or dorsal postate. On the other hand, both HCG doses resulted in significant increment in the weight of the coagulating gland than in the TPL group, most probably due to absence of effect of the applied low TP dose on this gland. TP in the high dose resulted in significant higher weight of the ventral prostate than any of the HCG applied doses.

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