J. steroid Biochem. Vol. 23, No. 3, pp. 373–374, 1985
Printed in Great Britain.

0022-4731/85 $3.00 + 0.00

SHORT COMMUNICATION

THE EFFECT OF INFUSIONS OF 5α-DIHYDROTESTOSTERONE OR ESTRADIOL-17β ON THE CONCENTRATION OF SOME STEROIDS IN THE HUMAN TESTICULAR VEIN AND ARTERY

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(*Received* 17 *December* 1984)

Summary—The concentrations of testosterone, 5α-dihydrotestosterone, 5α-androstan-3α, 17β-diol, 5α-androstane-3β, 17β-diol, estradiol-17β and testosterone-glucosiduronate were measured in the plasma of the testicular vein and artery simultaneously with the estimation in peripheral venous and arterial plasma 60 min after an infusion of 3000 μg dihydrotestosterone (DHT) or estradiol (E_2), respectively, in patients undergoing orchiectomy for prostatic cancer. The results were as follows; following infusion of DHT or E_2, both steroids were completely metabolized by the testes. After DHT the testicular secretion of E_2 was significantly reduced. In peripheral plasma 3α-diol concentration was increased. Following E_2 a transient elevation of testosterone in the spermatic vein was observed, whereas a slight decrease of DHT and an increase especially of 3β-diol levels occurred. It is assumed that DHT as well as E_2 plays a role as intratesticular regulator of steroid synthesis and metabolism.

INTRODUCTION

Previous studies on the blood of the human testicular vein [1] and on human sperm plasma [2] have shown that 5α-androstane-3β, 17β-diol (3β-diol) is present at a higher concentration than its 3α-isomer (3α-diol). Thus the 3β-diol appears to be an important metabolite of 5α-dihydrotestosterone (DHT) in the human testicle. In order to obtain more information on this, DHT was infused in patients before they were orchiectomized. Estradiol-17β (E_2) was also infused in order to investigate possible influences of this estrogen, which is synthesized in the male testicle, on androgens in the testicular as well as in the peripheral blood vessels.

Patients and methods

Six male patients who had no pretreatment with drugs received an infusion of 3000 μg DHT in 300 ml physiological saline solution over 3 h prior to orchiectomy for a prostatic neoplasm having no clinically detectable metastases. Anaesthesia was started 30 min after termination of the infusion. Blood samples were taken from the spermatic vein and artery (s.v., s.a.) and from the cubital vein (c.v.) and femoral artery (f.a.) after the anaesthesia was begun. The heparinized blood was immediately centrifuged and treated as described previously [1]. The following steroids were measured: testosterone (T), 5α-dihydrotestosterone (DHT), testosterone-glucosiduronate (TG), 5α-androstan-3α, 17β-diol (3α-diol), 5α-androstane-3β, 17β-diol (3β-diol) and estradiol-17β (E_2). Five other male patients with prostate neoplasms were given infusions of 3000 μg estradiol-17β under the same conditions and the plasma investigated as described above. Written informed consent was obtained from all patients. Student's *t*-test was used for the statistical analysis of the results.

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RESULTS

Previously published mean values of 10 untreated patients having prostate neoplasms served as the control [1]. Table 1 contains the values measured after DHT infusion. A comparison of the values of the untreated group shows the following: Although 60 min had elapsed between the collection of blood samples and the termination of the infusion, the DHT concentrations in peripheral blood and in the afferent s.a. were still significantly higher than in the control group ($P < 0.001$ and < 0.01, respectively). In the s.v. a difference to the control group could no longer be determined. On the other hand, there was a significant drop in the E_2 concentration in this blood vessel ($P < 0.01$) as well as a significant rise in the TG concentration ($P < 0.05$). Likewise, the TG level in the peripheral venous blood was significantly higher than in the control group ($P < 0.05$). At the same time the peripheral plasma E_2 level remained unchanged.

A significant effect on the T concentration in testicular and peripheral blood could not be ascertained. The major metabolites of DHT, 3α-diol and 3β-diol, exhibited a different behaviour when compared to the control group. The concentration of the 3α-diol did not change in the s.v. but increased significantly in the c.v. and f.a. ($P < 0.01$ and $P < 0.05$, respectively) as well as in the s.a. ($P < 0.005$). No significant change in the 3β-diol concentration could be discerned in the testicular and peripheral blood vessels.

Table 2 gives the values measured after an E_2 infusion. As for the DHT infusion, here, too, there was a significantly higher level of the estrogen 60 min, after the E_2 infusion ($P < 0.001$), while the E_2 concentration in the s.v. was not different from that of the control group. On the other hand, a significant increase of T and TG ($P < 0.05$) was observed in the s.v., which, however, did not appear in peripheral blood. In the s.v. the concentration of DHT tended to decrease, whereas the 3β-diol concentration showed an increase. However, both values were not statistically significant because of large fluctuations. The 3α-diol level in the c.v. was significantly lower than that of the control group ($P < 0.02$).

Table 1. Mean concentrations of blood steroids in spermatic and peripheral blood following an intravenous infusion of 3000 μg 5α-dihydrotestosterone (nmol/l) ($N = 6$) (range of age 68 to 81).

		T	DHT	TG	E_2	3α-diol	3β-diol
s.v.	Mean	840.81	22.26	11.62	4.75	5.81	19.13
	SD	668.27	6.75	4.49	3.53	3.11	10.41
c.v.	Mean	10.61	9.52	5.36	0.24	1.93	1.51
	SD	3.83	4.03	1.91	0.05	0.90	0.63
s.a.	Mean	36.03	11.83	5.61	0.56	2.13	2.25
	SD	30.79	3.95	1.92	0.18	1.01	1.40
f.a.	Mean	5.45	7.66	4.65	0.30	1.25	0.98
	SD	2.25	3.86	1.46	0.20	0.64	0.46

(Abbreviations: s.v. = spermatic vein. s.a. = spermatic artery. c.v. = cubital vein. f.a. = femoral artery. T = testosterone. DHT = 5α-dihydrotestosterone. TG = testosterone glucosiduronate. E_2 = estradiol-17β. 3α-diol = 5α-androstan-3α, 17β-diol. 3β-diol = 5α-androstane-3β, 17β-diol).

DISCUSSION

The experimental design described here—i.e. patients with an age dependent reduction of testicular activity—together with the fact that exogenously administered steroids can only partially pass the blood–testicle barrier permit only a limited interpretation of the results. However, the following observations are permissible from our data. Sixty minutes after the DHT and E_2 infusions were concluded considerably increased concentrations of the infused steroid are still found in the afferent testicular artery and in the peripheral blood vessels. In the efferent testicular vein, however, DHT or E_2 levels were normal, indicating that the human testicle must have largely metabolized both steroids.

After the DHT infusion the E_2 level in the s.v. was clearly lowered, suggesting that DHT has a transitory inhibitory effect on the aromatase. As there are no comparable studies in the literature, further experiments are necessary to determine if this is an intratesticular regulatory mechanism. The "secretion" of the major metabolites of DHT did not change significantly in the s.v. Here, the blood–testicle barrier already mentioned could possibly play a role, as it is known that the formation of androstanediols takes place predominantly in the tubules [3]. As the results show, in the periphery DHT is metabolized largely to the 3α-diol [4]. This supports our earlier finding that the 3β-diol is predominantly a DHT metabolite of the human testicle [1]. The increased release of TG from the testicle after the infusion of DHT, which was also significant in the peripheral blood, is a secondary finding, and its biological significance must still be elucidated.

The effect of a long-term estrogen therapy on the T biosynthesis in human testes has long been known [5]. Here, in addition, the inhibitory effect of estradiol on the gonadotropin secretion of the anterior pituitary also plays a role. The short-term effect of an E_2 infusion described produced above all the surprising result of an increased "T secretion". As the T concentration in the peripheral blood remains unchanged, this is most likely only a transitory phenomenon. Since E_2 is not capable of enhancing the biosynthesis in the testicle, it is probably a displacement effect on the T stored in small concentrations in the testicle. Like DHT, there was also an increased testicular "TG secretion" which, however, did not extend to the peripheral blood. Since the above described changes of the concentrations of DHT, 3α- and 3β-diol in the s.v. following E_2 infusion are not significant it can only be assumed that the estrogen stimulated the intratesticular metabolism of DHT. On the other hand, there was a significant inhibition of peripheral 3α-diol formation after E_2 infusion.

Table 2. Mean concentrations of blood steroids in spermatic and peripheral blood following an intravenous infusion of 3000 μg estradiol-17β

		T	DHT	TG	E_2	3α-diol	3β-diol
s.v.	Mean	1389.81	18.74	14.89	10.45	8.71	39.54
	SD	367.99	4.39	7.71	2.86	3.15	17.33
c.v.	Mean	16.92	2.32	2.83	4.80	0.50	1.51
	SD	6.24	0.76	0.75	1.46	0.15	0.65
s.a.	Mean	38.15	3.23	4.05	4.43	0.98	3.00
	SD	36.52	0.92	1.58	0.78	0.64	2.38
f.a.	Mean	8.47	2.33	2.95	3.05	0.62	1.15
	SD	3.85	0.95	0.53	0.74	0.18	0.40

(Legends see Table 1 ($N = 5$) range of age 69–80).

Acknowledgements—The experiments have been supported by the Deutsche Forschungsgemeinschaft (SPP Biologie und Klinik der Reproduktion. Ta 20/10-2).

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