THE EFFECTS OF TESTOSTERONE AND OF TESTOSTERONE PROPIONATE ON RENAL FUNCTIONS IN MAN

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The renotropic effects of testosterone and testosterone propionate have been demonstrated repeatedly in mice and rats (1, 2, 3). Whether or not the induced increase in size and weight of the organ is associated with any enhanced functional capacity thus far has not been determined. It has been found, however, that the administration of testosterone propionate to female castrated dogs will augment the maximum tubular secretory capacity but does not influence the creatinine clearance (4). That testosterone propionate is particularly effective as a renotropic agent in rats and dogs which develop compensatory hypertrophy of the remaining kidney after unilateral nephrectomy has been indicated (5). In these animals, the increase in mass of the kidneys was paralleled by an increase in both glomerular filtration rate (inulin clearance) and tubular excretory mass (Tm_D). The parenteral administration of 25 mgm. of the hormone, daily for 2 weeks, to normal individuals and patients with renal disease failed to increase the renal functions measured.

Despite this last observation, it appeared possible that the administration of testosterone or testosterone propionate might increase the functional capacity of the human kidney if given in amounts comparable (on a weight basis) with those used in animal experiments. A clinical study was undertaken, therefore, to ascertain the effects of large amounts of these steroids on human renal function. The results of that study form the basis of the present report.

METHODS

1. Effective renal flow was ascertained from the plasma clearance (C_{PAH}) of sodium-p-aminohippurate (PAH [1]), a compound which has been recommended by Smith and his associates as a substitute for diodrast. During the determination of renal blood flow, the plasma concentration of PAH was maintained at levels of from 1.0 to 3.1 mgm. per cent.

2. The rate of glomerular filtration was measured by the clearance of mannitol (C_M) (7). Plasma levels of mannitol during these observations ranged from 125 to 168 mgm. per cent.

3. The tubular excretory mass was indicated by the clearance of PAH when the plasma concentration of that compound was greater than 66.5 mgm. per cent (Tm_{PAH}).

4. The maximal rate of tubular resorption of glucose (Tm_G) was measured at plasma glucose concentrations above 350 mgm. per cent (8). All determinations were checked both before and immediately after the administration of the hormones.

In a previous communication (9) it was demonstrated that simultaneous measurements of Tm_G, Tm_{PAH} could not be made satisfactorily since the values obtained were effected by the plasma concentration of the test substance. Hence, in the present study, separate periods were used to determine first C_{PAH}, then Tm_{PAH}, and finally Tm_G.

CLINICAL MATERIAL

A total of 9 subjects was studied. Four of these were normal adult males. The first (E. C.) received intramuscularly 90 mgm. of testosterone [2] in sesame oil daily for 23 days. The second (V. F.) received 100 mgm. per day of testosterone propionate [2] for a total of 8 days. The third (E. M.) and fourth (D. H.) were injected with 300 mgm. daily of testosterone propionate for 8 and 14 days, respectively.

The fifth subject was a eunuchoid male (M. H.) whose daily excretion of 17-ketosteroids was consistently less than 3 mgm. This subject was included to ascertain whether or not the hypogonadic state affected the renal functions measured. This subject was given 100 mgm. of testosterone propionate per day for 29 days.

The remaining 4 patients investigated each had disorders commonly associated with renal insufficiency. Two had essential hypertension (M. F. P. and J. McG.) and 2 had chronic bilateral pyelonephritis (E. O. and B. H.), The patients with hypertension received daily 100 mgm. of testosterone propionate intramuscularly for 12 and 33 days and those with pyelonephritis each were given 300 mgm. per day for 14 and 16 days.

[1] The authors gratefully acknowledge the gift of this material from Sharp & Dohme, Inc., Philadelphia, Pennsylvania.

[2] The testosterone and testosterone propionate were donated by the Schering Corporation, Bloomfield, New Jersey.

TABLE I

The effects of testosterone and of testosterone propionate on the renal functions of the subjects studied

Subject	Disorder	Period	Daily amount given i.m.	Days	C_M	Tm_{PAH}	Tm_G	C_{PAH}	Blood pressure
			mgm.		*ml. per min.*	*mgm. per min.*		*ml. per min.*	*mm. Hg*
E. C.	Normal male	Control			114		232	637	120/60
					104	98		640	
		Testosterone	90	22	121		205	813	120/70
				23	112	89			115/70
V. F.	Normal male	Control			119	95	288	711	110/70
		Testosterone propionate	100	9	107	104	310	718	120/70
E. M.	Normal male	Control			165		431	580	90/50
		Testosterone propionate	300	8	143		389	730	100/50
D. H.	Normal male	Control			122		323	650	120/70
		Testosterone propionate	300	14	124		294	740	120/80
M. H.	Eunuchoid male	Control			87	66		358	100/70
					76		240	375	
		Testosterone propionate	100	14	79	60	190	383	110/60
				29	86	55			
M. F. P.	Essential hypertension; male	Control			68	47		265	220/120
					77		198		
		Testosterone propionate	100	12	75	50	217	179	180/110
J. McG.	Essential hypertension; male	Control			64	52		196	200/100
					63	46		208	
		Testosterone propionate	100	33	62	53		217	180/90
E. O.	Bilateral pyelonephritis; female	Control			30		107	56	170/80
		Testosterone propionate	300	16	31		81	57	160/80
B. H.	Chronic bilateral pyelonephritis; male	Control			52	48	107	212	150/100
		Testosterone propionate	300	14	56	46	107	216	150/100

RESULTS

The essential data are presented in Table I. Before the administration of the steroids, the values obtained for C_M, C_{PAH}, and Tm_G in the normal subjects, the patients with essential hypertension, and those with chronic pyelonephritis agree well with those found by other investigators in similar clinical material (8, 10, 11). However, it is interesting to note that although the eunuchoid male consistently had normal arterial tension and no history of renal disease, the values of C_M, C_{PAH}, and Tm_{PAH} were all abnormally low.

Neither testosterone nor testosterone propionate in the amounts administered apparently had any effect on C_M nor on the Tm_{PAH}. Neither was there obtained any consistent or significant effect of the hormones administered on the C_{PAH} nor the Tm_G.

COMMENT

Maximal renal hypertrophy in the mouse is effected by the administration of 0.1 mgm. per day of testosterone propionate for only 9 days (4). An increase in tubular function in dogs has been observed (4) after the administration of a

single dose of 100 mgm. in 1 case and after 4 daily doses of 100 mgm. each in 2 other animals. On a comparative weight basis, this would indicate about 300 mgm. per day as an effective renotropic dose in man. Hence, had the same relationship existed between administered steroids and renal function in man, the amounts of the compound employed in the present study should have been effective in at least 4 subjects.

Evidently certain steroids do not influence renal functions in general. This has been found true, for example, for alpha estradiol benzoate (12). The administration of this compound appears to be without effect on the clearance of mannitol. It does, however, markedly depress the tubular reabsorption of ascorbic acid. Likewise, in the dog, testosterone propionate apparently does not change the filtration rate but does increase markedly the tubular secretion of diodrast (4). It is possible, therefore, that although the administration of testosterone or testosterone propionate to human beings did not alter the filtration rate nor renal blood flow or Tm_{PAH} or Tm_G, other renal functions might have been affected. This possibility now is under further investigation.

Whereas the administration of the steroids might not increase renal function in normal subjects above their normal level, the compound might increase depressed function of the diseased kidney. For this reason, patients with impairment of renal function were included, but in these, too, the administered hormones were without measured effect.

CONCLUSION

The administration of testosterone or testosterone propionate in amounts presumed to be adequate for renotropic effects did not alter significantly the rate of glomerular filtration, renal blood flow, the maximum rate of tubular secretion of p-aminohippurate, or the maximum rate of tubular reabsorption of glucose in 4 normal subjects or in 5 patients with impaired renal function.

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