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THE EFFECT OF ORCHIDECTOMY AND ADMINISTRATION OF TESTOSTERONE PROPIONATE OR NANDROLONE PHENYLPROPIONATE TO ORCHIDECTOMISED RATS ON THEIR GROWTH AND CARCASS COMPOSITION

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OPSOMMING: DIE INVLOED VAN DIE VERWYDERING VAN DIE TESTES EN DIE TOEDIENING VAN TESTOSTEROON PROPIONAAT OF NADROLOON FENIELPROPIONAAT AAN ROTTE OP HUL GROEI EN KARKASSAMESTELLING

Twee en dertig rotte is gebruik om die invloed van die toediening van 0,7 mg testosteroon of nandroloon fenielpropionaat per dag te vergelyk met die invloed van die teenwoordigheid van funksionele testes op groei en liggaamsamestelling van rotte wat 20 g kommersiële rantsoen of 'n hoë kaloriewaarde rantsoen per dag ontvang het. Die resultate het aangedui dat die merkbare invloed wat die teenwoordigheid van die testes op groei, voerverbruik en proteïeninhoud van die karkas het, nie met die inspuiting van testosteroon of nadroloon fenielpropionaat by rotte waarvan die testes verwyder is, nageboots kan word nie. Dit blyk dus dat een of ander faktor, behalwe testosteroon, afkomstig van die teenwoordigheid van die testes die vernaamste testikulêre anaboliese stof by die rot met testes is.

SUMMARY

Thirty-two rats were used to compare the effects of administration of 0,7 mg/d testosterone or nandrolone phenylpropionate with the effects of presence of functional testes on growth and body composition of rats fed 20 g/rat/d of a commercial ration or of a ration of higher caloric value. Results showed that the marked effect of the presence of the testes on growth, food consumption and protein content of the carcass could not be reproduced by injection of either testosterone or nandrolone phenylpropionate into orchidectomised rats. The results indicated that some factor arising from the presence of the testes other than testosterone was the main testicular anabolic agent in the intact rat.

Hale (1972a) showed that administration of testosterone propionate in doses of between 0,05 and 0,80 mg/rat/day influenced protein anabolism only slightly in castrated male rats. However, it was not clear from this trial whether testosterone propionate had little anabolic effect or whether an almost maximal anabolic response was obtained with the lowest dose of androgen used and thus little further stimulation was obtained with higher doses. Consequently, a further trial was conducted to elucidate this question and to examine whether male rats responded to castration under conditions where an androgenic but not an anabolic response to testosterone was detectable. The effect of another steroid, nandrolone phenylpropionate, was also examined. This steroid has been shown to have a high anabolic : androgenic ratio by Overbeek & de Visser (1957), who compared the response of the levator ani muscle (anabolic response) with the response of the seminal vesicles (androgenic response). On the basis of these criteria, these workers found that for a given androgenic effect nandrolone phenylpropionate was some twelve times more active anabolically than was testosterone propionate.

Many workers have examined the effect of exogenous androgens on the levator ani muscle of rats (e.g. Dorfman & Kincl, 1963; Wainman & Shipounoff, 1941) and have used the response of this muscle as an index of the anabolic activity of administered steroids. The present trial provides information about the effects of administration of androgens on changes in bodymass and carcass mass and protein content. These parameters can be measured directly only by laborious, rather imprecise and time-consuming methods, but are likely to provide useful information to guide future experimentation with farm animals.

Procedure

Thirty-two male albino rats of Sprague-Dawley descent were used. Twenty-four rats were castrated three weeks before the start of the trial. Animals were 8-9 weeks old and weighed between 107 and 164 g when the trial began.

Animals were allocated at random to four groups, each of which contained eight rats. Animals in the first group were castrated controls. In the second group, animals received testosterone propionate (5 mg/rat/week s/c). Animals in the third group were injected with nandrolone phenylpropionate (Durabolin, Organon) (5 mg/rat/week s/c). Animals in the fourth group were intact controls. All control animals were injected subcutaneously each week with 0,2 ml arachis oil.

Four rats in each treatment group were offered 20 g/day of Mouse Comproid meal (Rhomil, Ltd., Salisbury) (Ration B) and the remaining four rats were offered 20 g/day of a ration of higher caloric value (Ration A). Standard procedures of chemical analysis showed that the protein content of Ration A was 17,2% and the energy content 17,79 Kj/g. Ration B contained 21,2% protein and 12,54 Kj/g energy. Water was freely available at all times and contained tetracycline (Hostacycline, Hoechst) in a prophylactic dosage.

All rats were weighed twice weekly and food consumption was measured daily as described previously (Hale 1972a). The trial lasted twenty-eight days.

At the end of the trial, animals were killed with chloroform and the following masses noted:

- Final live mass
- Carcass
- Skin
- Seminal vesicles
- Ventral prostate
- Adrenals

Testes of intact rats were weighed. Fat and protein content of the carcass were measured as described previously (Hale 1972a).

Data were subjected to statistical analysis as described previously (Hale 1972a).

Results

Castrated immature male rats exhibited lower rate of increase in bodymass (P< 0,001, Table 1), final bodymass (P < 0,05, Table 1), food consumption (P < 0,001, Table 2) and efficiency of conversion of food into increase in bodymass than did intact controls (P < 0,05, Table 2). These differences were greater for rats fed Ration A than those fed Ration B, but the interactions were not significant. Administration of testosterone propionate or nandrolone phenylpropionate did not affect any of these parameters. Type of ration fed to the rats affected growth rate of the intact animals only. Thus, intact rats fed Ration A grew more rapidly than those fed Ration B (P < 0,05) (Table 1). Efficiency of food conversion (g food consumed/g gain in bodymass) was better (P < 0,001) for all groups of animals which were fed Ration A, than for animals fed Ration B (Table 2).

Carcass, expressed as a proportion (%) of final bodymass was greater for animals fed Ration A than for those fed Ration B (P < 0,001, Table 3). Both androgens increased this parameter relative to castrate and intact controls (P < 0,05), but castration itself had no significant effect. Conversely, castrated rats had lighter carcasses than intact rats (P < 0,01), particularly where animals were fed Ration A, but administration of androgens did not affect mass of carcass (Table 3). Interaction between effects of castration and plane of nutrition was significant statistically

Table 1

The effect of castration, administration of androgen and type of ration on rate of increase in bodymass (g/day) and final bodymass (g) of male rats[1]

Treatment		Ration B			Ration A		
Castrate	Rate of increase (g/d)	2,29	±	0,20	2,19	±	0,13
	Final (g)	203,8	±	7,21	200,0	±	8,54
Castrate + testosterone[2]	Rate of increase (g/d)	2,42	±	0,31	1,79	±	0,29
	Final (g)	208,6	±	6,97	190,1	±	24,57
Castrate + nandrolone[3]	Rate of increase (g/d)	1,74	±	0,21	1,82	±	0,18
	Final (g)	188,4	±	10,65	191,1	±	9,63
Intact	Rate of increase (g/d)	2,87	±	0,19	3,79	±	0,44
	Final (g)	214,7	±	10,12	240,3	±	7,35

Note:

1. Each figure represents the mean (± Standard Error) of 4 animals.
2. The equivalent of 0,7 mg/rat/d testosterone propionate was injected subcutaneously once each week.
3. The equivalent of 0,7 mg/rat/d nandrolone phenylpropionate was injected subcutaneously once each week.

Table 2

The effect of castration, administration of androgens and type of ration on food consumption (g/d) and efficiency of food conversion (g/ feed consumed/g increase in bodymass) of male rats[1]

Treatment		Ration B			Ration A		
Castrate	Consumption (g)	17,03	±	0,73	13,90	±	0,27
	Efficiency	7,58	±	0,61	6,40	±	0,27
Castrate + testosterone[2]	Consumption (g)	17,97	±	0,54	13,12	±	0,63
	Efficiency	7,86	±	1,19	7,85	±	1,09
Castrate + nandrolone[3]	Consumption (g)	14,97	±	0,73	12,59	±	0,60
	Efficiency	8,87	±	0,90	7,11	±	0,71
Intact	Consumption (g)	18,58	±	0,60	17,24	±	0,47
	Efficiency	6,52	±	0,29	4,78	±	0,71

Notes 1, 2 and 3 as for Table 1

Table 3

The effect of castration, administration of androgens and type of ration on the mass of the carcass (g) and the mass of the carcass expressed as a proportion (%) of final bodymass of male rats[1]

Treatment		Ration B			Ration A		
Castrate	Mass of carcass (g)	100,8	±	2,14	100,7	±	5,07
	Carcass (%)	49,55	±	1,05	50,30	±	0,43
Castrate + testosterone	Mass of carcass (g)	108,8	±	4,39	99,8	±	7,85
	Carcass %	52,11	±	0,61	52,44	±	0,36
Castrate + nandrolone[3]	Mass of carcass (g)	96,7	±	6,96	99,8	±	5,75
	Carcass (%)	51,17	±	0,81	52,17	±	0,79
Intact	Mass carcass (g)	105,7	±	5,75	124,7	±	4,38
	Carcass (%)	49,19	±	0,59	51,90	±	0,70

Notes 1, 2 and 3 as for Table 1

Table 4

The effect of castration, administration of androgens and type of ration on the mass of skin (g) and adrenals (mg) of male rats[1]

Treatment		Ration B			Ration A		
Castrate	Skin (g)	28,7	±	2,4	27,3	±	1,7
	Adrenals (mg)	34,3	±	0,5	26,5	±	3,4
Castrate + testosterone[2]	Skin (g)	28,1	±	0,5	21,8	±	1,1
	Adrenals (mg)	32,3	±	1,8	24,8	±	3,2
Castrate + nandrolone[3]	Skin (g)	23,9	±	1,9	24,0	±	1,9
	Adrenals (mg)	28,5	±	1,6	26,3	±	4,9
Intact	Skin (g)	30,0	±	1,9	36,3	±	0,6
	Adrenals (mg)	28,3	±	2,5	26,0	±	5,6

Notes 1, 2 and 3 as for Table 1

Table 5

The effect of castration, administration of androgens and type of ration on the mass (mg) of seminal vesicles (S.V.) and ventral prostate (V.P.) of male rats[1]

Treatment		Ration B			Ration A		
Castrate	S.V. (mg)	25,3	±	4,0	40,3	±	4,8
	V.P. (mg)	15,5	±	1,0	17,8	±	4,4
Castrates + testosterone[2]	S.V. (mg)	574,5	±	95,6	524,0	±	79,0
	V.P. (mg)	394,8	±	47,6	318,0	±	57,7
Castrate + nandrolone[3]	S.V. (mg)	591,3	±	68,2	690,0	±	37,9
	V.P. (mg)	284,5	±	51,5	424,8	±	62,8
Intact	S.V. (mg)	155,3	±	53,4	169,5	±	24,5
	V.P. (mg)	86,8	±	45,0	72,0	±	10,8

Notes 1, 2 and 3 as for Table 1

(P< 0,05).

Administration of androgens to castrated rats apparently reduced mass of skin (Table 4). However, skins of castrated rats were lighter than those of intact rats (P < 0,05). Neither castration, administration of androgens nor type of ration affected mass of adrenals (Table 4).

Castration caused a marked reduction in mass of seminal vesicles (P < 0,001, Table 5) and ventral prostate (P < 0,001, Table 5). Administration of steroids to castrated rats resulted in an androgenic response which was greatly in excess (P < 0,001) of the level noted in control intact rats as regards mass of secondary sex organs. No difference in androgenic potency was detectable between the two steroids used. Type of ration fed to the rats did not influence these responses. Testes of intact rats fed Ration A tended to be slightly, but not significantly, heavier than those of intact rats which were fed Ration B. Mean masses were 2,7 ± 0,09 g and 2,2 ± 0,29 g respectively.

Castration did not affect the proportion (%) of protein in the carcass (Table 6). However, because carcasses of intact rats weighed more than those of castrates (Table 3), total yield of protein was greater in the carcasses of intact rats (P < 0,05), particularly for rats fed Ration A. This interaction between effects of castration and ration was significant (P < 0,05). Both androgens led to an increase in percentage of protein in the carcasses of rats fed Ration (P < 0,05) but not in rats fed Ration B. Overall, testosterone propionate had a slight stimulatory effect on total yield of protein in the carcass (P < 0,05) whereas nandrolone phenylpropionate had no effect.

Table 6

The effect of castration, administration of androgens and type of ration on the total mass (g) and percentage of protein in the carcass of male rats[1]

Treatment		Ration					
		B			A		
Castrate	Mass of protein (g)	19,97	±	0,59	19,11	±	0,58
	% Protein	19,81	±	0,33	19,05	±	0,44
Castrate + testosterone[2]	Mass of protein (g)	21,39	±	0,24	19,72	±	1,38
	% Protein	19,74	±	0,62	19,80	±	0,34
Castrate + nandrolone[3]	Mass of protein (g)	19,27	±	1,41	20,59	±	1,03
	% Protein	19,95	±	0,29	20,61	±	0,24
Intact	Mass of protein (g)	20,69	±	0,87	23,30	±	1,09
	% Protein	19,62	±	0,37	18,67	±	0,28

Notes 1, 2 and 3 as for Table 1

Table 7

The effect of castration, administration of androgens and type of ration on total mass (g) and percentage of fat in the carcass of male rats[1]

Treatment		Ration					
		B			A		
Castrate	Mass of fat (g)	8,77	±	0,15	12,07	±	1,98
	% Fat	8,72	±	0,20	11,40	±	0,92
Castrate + testosterone[2]	Mass of fat (g)	7,66	±	0,81	11,17	±	2,73
	% Fat	6,99	±	0,28	10,82	±	2,03
Castrate + nandrolone[3]	Mass of fat (g)	6,75	±	0,50	7,73	±	0,54
	% Fat	7,08	±	0,75	7,82	±	0,69
Intact	Mass of fat (g)	9,52	±	1,14	15,67	±	1,91
	% Fat	8,91	±	0,61	12,65	±	1,78

Notes 1, 2 and 3 as for Table 1

Percentage of fat in the carcass (Table 7) was not affected by castration. Consequently, because they were heavier, carcasses of intact rats tended to yield more fat on an absolute basis than those of castrates. However, this effect was not significant statistically. Both steroids markedly depressed percentage ($P < 0,001$) and yield ($P < 0,001$) of fat in the carcass, particularly in those rats which had been fed Ration A. Injection of nandrolone phenylpropionate led to a lower yield of fat in the carcass than did injection of testosterone propionate ($P < 0,05$). When data for all groups were combined, both fat content and concentration in the carcass were greater in rats which had been fed Ration A than in those which had eaten Ration B ($P < 0,001$).

Discussion

Results of the present trial show that castration reduces growth rate (Table 1), the efficiency of conversion of food into increase in bodymass (Table 2) and the amount of protein in the carcass of male rats (Table 6). These findings are in accord with the results of Hale (1972b). Furthermore, administration of either testosterone propionate or nandrolone phenylpropionate replaced only partially the anabolic action of the rat testes, despite the ability of either substance to replace more than completely testicular androgenic function, as measured by mass of secondary sexual organs (Table 5). This result confirmed the findings of Hale (1972b) and eliminated the possibility that a maximal anabolic response was achieved with the lowest dose of androgens administered in that trial. Present findings indicate that the anabolic effect of the testes in intact rats can be ascribed only partially to testicular testosterone production.

The anabolic effect of androgens has usually been assessed by the response of specific muscles to administration of these steroids. For convenience, muscles which are particularly sensitive to androgens have been studied. Thus, the response of the levator ani muscle in the rat has been widely accepted as an index of anabolic activity of exogenous steroids (e.g. Dorfman & Kincl, 1963); Wainman & Shipounoff, 1941; Overbeek & de Visser, 1957), because of the similarity of its histological and anatomical structure with that of the general body musculature. The present studies emphasise the caution which must be exercised in the interpretation of results of studies in which this index of anabolic function has been used. Overbeek & de Visser (1957), using the levator ani muscle as a criterion of anabolic activity, showed that nandrolone phenylpropionate has an anabolic : androgenic ratio some twelve times greater than that of testosterone propionate. Conversely, in the present study, where total carcass protein was measured as an index of anabolic activity, no differences were noted between the two steroids as regards anabolic : androgenic ratio. Further, testosterone propionate has been shown to have a marked effect on the levator ani muscle of rats (Dorfman & Kincl, 1963; Overbeek & de Visser, 1957). However, in the present study, only a very slight effect was noted on more general and representative measurements of anabolism such as total bodymass and carcass mass and protein content. Thus the response of the levator ani muscle to exogenous androgens would appear to reflect poorly the anabolic response of the body in general.

The principal effect of administration of either of the steroids in the present study was apparently a depression of the proportion (%) of fat in the carcass (Table 7). This is in accord with the conclusion of Laron and Kowadlo-Silbergeld (1965) that administration of testosterone propionate causes mobilization of fat reserves in rats. In this respect, the action of these steroids differed from the effect of the presence of the testes in intact rats. Thus castration did not affect the relative amounts of fat and protein in the carcass (Tables 6 and 7), but markedly reduced the absolute amounts of protein because castrated rats had lighter carcasses than those of intact rats (Table 3).

Simpson, Marx, Becks & Evans (1944) concluded that androgens interacted with growth hormone to stimulate an increase in bodymass of rats. Rowe (1968) suggested that the greater diameters of muscle fibres of intact male mice relative to castrates were attributable to the greater work loads imposed on the phasic muscles (muscles responsible for body movement) by the greater bodymass of intact male animals. However, a direct effect of androgens at the cellular level cannot be excluded.

Testosterone may be considered to be anabolically active in rats in terms of responses of: the levator ani muscle (e.g. Uzan, Roubertou, Thevenot & Ledieu, 1967; Kassenaar, Querido & Haak, 1962); the cellular ultrastructure (Failoni & Scarpelli, 1965) and transamidinase activity (van Pilsum & Ungar, 1968) of the kidney; transfer RNA synthesis (Wicks & Kenney, 1965) and uric acid metabolism (Leeling & Lata, 1965) in the liver; blood amylase levels (Kalitzin & Pentschewa, 1968); urinary calcium excretion (Rice, Pontheir & Millar, 1968); and a syngeristic action with oestrogens on the reticulo-endothelial system (Nicol, Vernon-Roberts & Quantock, 1965). In terms of gross body measurements, too, testosterone has been shown to exert an anabolic affect (Kochakian, Tillotson & Endahl, 1956; Simpson *et al.*, 1944; Hale 1972a and the present study) but this gross effect has been too small to account for the total anabolic action of the rat testes. Consequently, the testes must produce some other endocrine secretion/s which is/are primarily responsible for their anabolic activity in rats. The nature of the secretion/s must remain a matter for speculation until further studies are conducted to elucidate this question and the possibility of secondary interactions cannot be excluded.

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