The Effect of Anabolic Steroids on Lean Body Mass: The Dose Response Curve

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Data from human subjects given various amounts of anabolic steroids show that the resultant increment in lean body mass (LBM) has the features of a typical dose response curve. Low doses produce a very modest effect, while large doses result in a progressive augmentation of the LBM. Endogenous testosterone production during male adolescence is accompanied by a sex differential in LBM that is comparable to the LBM increment generated by exogenous steroids given to adults.

IT HAS BEEN known for many years that certain steroid compounds have anabolic activity when administered to animals, manifested by an increase in the weight of at least two muscles, the levator ani and the temporalis, an enhancement of amino acid uptake in muscle, and an increase in nitrogen retention.[1] Early studies in humans[2-5] showed positive nitrogen balances of 15 to 92 g with the administration of a total of 140 to 375 mg of anabolic steroids for a week or two.

Now that the taking of anabolic steroids has become popular with athletes,[6] a number of studies have been done using modern body composition techniques. However, the results have not been consistent; some observers reported a modest increase in lean body mass (LBM) and a decrease in body fat, while others failed to find a significant change.[7-9] It should be noted that the steroid doses used in most of these studies, as well as in those referred to above, were not very large; indeed most were only two to five times the endogenous testosterone production rate for males (estimated at 6 mg/d[10,11]), and they were not given for very long periods.

However, a few investigators have studied the effect of larger doses. Harris[12] gave androstalone 100 mg/d to a group of chronically ill women and recorded positive nitrogen balances of 20 to 54 g over an 18 day period. Hervey et al[13,14] gave dianabol 100 mg/d to normal males and recorded a significant increase in LBM at the end of six weeks. Kilshaw et al[15] studied a man who took up to 100 mg/d methandrostenolone and trained vigorously for 2 years. This individual gained 12.7 kg in weight and exhibited "spectacular muscular development"; however, no studies of body composition were done. Recently I had the opportunity of making assays of LBM in four adult males who took large doses of anabolic steroids for several months.

In order to explore the possibility of a dose response phenomenon, data were collected from reports in which body composition assays were done on human subjects both prior to and following a course of anabolic steroids. These data together with those on nitrogen retention and on the four subjects studied by myself form the basis of this report.

MATERIALS AND METHODS

Two of my subjects have been reported in the literature.[16] The first, a professional body builder, took an average of oxandrolone 55 mg/d for 76 days and then an average of 87 mg/d for an additional 64 days. The second, a weight lifter, took dianabol 25 mg/d plus 200 mg testosterone cyclopentyl-propionate intramuscularly (IM) each week for a total of 125 days. The steroids were self prescribed. Both trained very hard in preparation for a contest and took a high protein-high energy diet. Potassium-40 assays were made prior to and at the end of the period of training and steroid administration; LBM was calculated on the basis that this body component contains 68.1 meEq K/kg.[17]

The other two subjects were given testosterone for several months as controls for patients with myotonic dystrophy who were undergoing a trial of anabolic steroid therapy.* Following four initial daily doses of 50 to 60 mg testosterone propionate po they received IM injections of 300 to 350 mg testosterone enanthate weekly for 11 to 12 weeks. During this time they received a constant diet, with all meals taken at the Clinical Research Center. The 20 year old subject weighed 71 kg (LBM 60 kg), was 176 cm in height, and consumed 3100 kcal and 91 g protein daily. The 28 year old weighed 89 kg (LBM 72 kg), was 185 cm tall, and consumed 3700 kcal and 122 g protein daily. Both continued their customary program of very modest physical exercise. Potassium-40 assays were made before and after the course of testosterone, LBM being calculated as noted above.

RESULTS

Each of the four subjects sustained a significant increment of LBM, and decrease in body fat, during the period of anabolic steroid administration, and it

*This study was conducted by Dr Robert Griggs with the approval of our Institutional Committee on Human Investigation. I am indebted to him for the opportunity of making ^{40}K assays on these two subjects.

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Table 1. Effect of Anabolic Steroids on Weight and LBM

Subjects (no./sex)	Dose Rate	Total Dose (mg)	Δ Weight (kg)	Δ LBM (kg)	Method	Remarks	Reference
4 M	25 mg/d IM[1]	225-350	+2	+1.3	N balance	eunuchs	Keynon '38 (2)
2 F, 2 M	25 mg/d IM[1]	225-375		+0.8	N balance	normals	Kenyon '40 (3)
1 M	25 mg/d IM[1]	200	+1	+1.4	N balance	eunuch	Knowlton '42 (4)
3 F, 6 M	10-30 mg/d po[2]	140-420		+1.0	N balance	hemiplegics	Albanese '62 (5)
8 M	10 mg/d po[3]	350	+0.3	+2.0	density	normals, exercise	Ward '73 (18)
14 M	75 mg/wk IM[4]	225	+1.6	+1.1	density	normals, exercise	Fahey '73 (19)
9 M	100 mg/wk IM[1,4]	300	+0.6 (±.4)*	+1.0 (± .4)*	density	normals, exercise	Crist '83 (9)†
15 F	100 mg/d po[5]	1800	+0.7	+1.2	N balance	pulmonary tuberculosis	Harris '61 (12)
11 M	100 mg/d po[3]	4200	+3.5	+5.1	density, ^{40}K	normals, exercise	Hervey '76 (13)
7 M	100 mg/d po[3]	4200	+3.5	+5.2	density, ^{40}K, body N	normals, exercise	Hervey '81 (14)
1 M	300 mg/wk IM[1]	3500	+3.0	+6.2	^{40}K counting	constant diet, no exercise	Author
1 M	350 mg/wk IM[1]	4500	+1.1	+8.5	^{40}K counting	constant diet, no exercise	Author
1 M	variable, 125 d po IM[1,3]	6720	+5.1	+9.1	^{40}K counting	vigorous exercise	Forbes (16)
1 M	variable, 140 d po[2]	9760	+9.7	+19.2	^{40}K counting	vigorous exercise	Forbes (16)

[1]Testosterone; [2]Oxandrolone; [3]Dianabol; [4]Nandrolone; [5]Androstalone.
*SEM.
†Also personal communication.

appeared that the magnitude of the increment in LBM was related to the total amount of steroid given.

Table 1 lists these subjects and those reported in the literature according to the total amounts of anabolic steroids given during the experimental periods, together with the average observed changes in LBM and body weight. Some authors included a control group who did not receive steroids, and in such instances the values listed represent the difference in LBM and weight increments between the control and experimental groups. Nitrogen (N) retention data were converted to LBM increments by dividing grams of N retained by 33, the N content of the LBM.[20]

It is evident that the observed increments in LBM, whether derived from N balance or from body composition techniques, depend on the dose of anabolic steroids employed. This relationship is also shown in Fig 1, where the observed change in LBM is set against the total steroid dose on semilogarithmic coordinates. At low doses the increment in LBM is only 1 to 2 kg, which represents but 1½% to 3% of the initial value, and so falls within the precision of the techniques used for estimating body composition. Although the number of subjects who have been given large doses of steroids are few, there is seen to be a progressive effect on LBM from higher doses. The x-axis intercept of the calculated regression line is 2535 mg total steroid dose, which suggests that doses of this approximate magnitude constitute a threshold for a significant effect on LBM in humans.

DISCUSSION

The human appears to respond to anabolic steroids in a manner similar to animals, in whom a log dose response relationship has been found for both N retention and individual muscle weight.[1] Unfortunately, the reports reviewed in this book show only the linear portion of the dose response curve so one cannot judge the magnitude of the response, if any, produced by low doses.

Included in Fig 1 is a datum that illustrates the

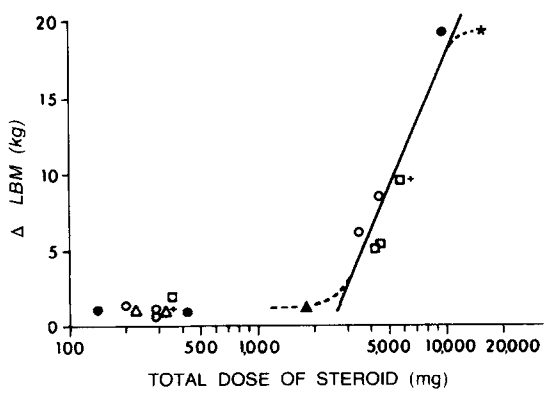

Fig 1. Semilogarithmic plot of increment in LBM against total dose of anabolic steroid (data from Table 1). Symbols: ○ = testosterone, ● = oxandrolone, □ = dianabol, ▲ = androstalone, Δ = nandrolone, + = also testosterone. Equation for the regression line for total dose of 3500 mg and greater is: y = 29.1 log x − 99(r 0.91). Point (*) represents estimate of the effect of endogenous testosterone production by males during the teen years; this point was not used in calculating the regression line.

effect of endogenous testosterone production. The sex difference in production rate is about 6 mg/d in adults,[10,11] and blood testosterone levels rise abruptly by age 13 years in males;[21,22] furthermore, the sex difference in LBM reaches its maximum of 19 kg by age 20 years.[23] Hence one can calculate that from age 13 to 20 years males will have produced about $6 \times 365 \times 7 = 15{,}330$ mg more testosterone than females. Of great interest is the fact that the datum point so defined fits the trend derived from exogenous steroid administration rather well.

This datum suggests that the upper limit to the curve shown in Fig 1 cannot be much greater than 19 kg of LBM increment in males even with very large doses of anabolic steroids. Certainly, the sex difference in LBM does not continue to increase beyond age 20 years despite the continued sex difference in testosterone production rate.

The list in Table 1 includes a variety of steroid compounds and both the oral and IM routes of administration. Although studies of N retention in humans show that the IM route produces a more prolonged, and somewhat greater effect, and although animal studies have shown that various steroid compounds differ somewhat in their ability to promote N retention,[1] the overall picture as depicted in Fig 1 suggests that the dose response relationship is not greatly affected by such variations. Furthermore, the data in Fig 1 suggest that endogenous testosterone produces a response similar to that achieved by exogenous steroids.

The possible influence of concomitant vigorous exercise and/or training is difficult to evaluate. Of those human subjects given large doses of anabolic steroids, only two have not engaged in exercise programs, and these two achieved an increment in LBM comparable to others who did exercise.

This report should not be construed as advocating the use of anabolic steroids by athletes, a practice that is said to be widespread.[6,7,8] While the data do demonstrate an increase in LBM when large doses are given, it is known that toxic effects can occur,[6,7,8] and these would be expected to be greater with large doses.

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