The Influence of 6 Months of Oral Anabolic Steroids on Body Mass and Respiratory Muscles in Undernourished COPD Patients*

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Study objective: To evaluate the influence of oral anabolic steroids on body mass index (BMI), lean body mass, anthropometric measures, respiratory muscle strength, and functional exercise capacity among subjects with COPD.

Design: Prospective, randomized, controlled, double-blind study.

Setting: Pulmonary rehabilitation program.

Participants: Twenty-three undernourished male COPD patients in whom BMI was below 20 kg/m² and the maximal inspiratory pressure (PImax) was below 60% of the predicted value.

Intervention: The study group received 250 mg of testosterone IM at baseline and 12 mg of oral stanozolol a day for 27 weeks, during which time the control group received placebo. Both groups participated in inspiratory muscle exercises during weeks 9 to 27 and cycle ergometer exercises during weeks 18 to 27.

Measurements and results: Seventeen of 23 subjects completed the study. Weight increased in nine of 10 subjects who received anabolic steroids (mean, 1.18 ± 0.60 kg; p < 0.05), whereas the control group lost weight (−2.0 ± 0.4 kg). The study group’s increase in BMI differed significantly from that of the control group from weeks 3 to 27 (p < 0.05). Lean body mass increased in the study group at weeks 9 and 18 (p < 0.05). Arm muscle circumference and thigh circumference also differed between groups (p < 0.05). Changes in PImax (study group, 41%; control group, 20%) were not statistically significant. No changes in the 6-min walk distance or in maximal exercise capacity were identified in either group.

Conclusion: The administration of oral anabolic steroids for 27 weeks to malnourished male subjects with COPD was free of clinical or biochemical side effects. It was associated with increases in BMI, lean body mass, and anthropometric measures of arm and thigh circumference, with no significant changes in endurance exercise capacity. (CHEST 1998; 114:19-28)

Key words: anabolic steroids; body mass index; chronic obstructive pulmonary disease; nutrition; respiratory muscle function

Abbreviations: BMI = body mass index; DEXA = dual energy x-ray absorptiometry; IMT = inspiratory muscle training; LH = luteinizing hormone; PEmax = maximal expiratory pressure; PImax = maximal inspiratory pressure; V̇O₂max = maximal oxygen consumption

Malnutrition is associated with severe COPD, having been observed in 10 to 26% of outpatients with COPD and in up to 47% of patients hospitalized with acute respiratory failure. Although the underlying mechanisms and pathophysiology remain unclear, at least one report has noted that individuals who lost weight had a higher morbidity and mortality compared with those whose weight was within predicted values for their age, height, and sex. When compared with normal-weight patients with similar airflow limitation, low-weight COPD patients had more hyperinflation, more gas trapping, a lower diffusing capacity, more dyspnea, and reduced exercise capacity.

Malnutrition affects the composition and the function of the respiratory muscles. As in other
skeletal muscles, protein is degraded to produce energy and to assist with the synthesis of visceral protein. In subjects with COPD whose weight was reduced to 70% of predicted values, diaphragmatic mass was reduced to 60%. Reductions in the thickness of the sternocleidomastoid muscles also have been reported. This reduction in respiratory muscle mass reduces the capacity of the ventilatory system to respond to the increases in elastic and resistive loads, such as those present during exercise or with respiratory exacerbations.

Over the past 20 years, a variety of reports have claimed that anabolic steroids improved the performance of high-level athletes consequent to improvements in skeletal muscle mass and strength. Although in some individuals the gains in muscle strength associated with good nutrition and exercise appear to be further enhanced by the addition of anabolic androgenic steroids, errors in design, analysis, and reporting have limited the credibility of many studies. A recent meta-analysis on the effects of anabolic steroids in healthy volunteers concluded that there were slight improvements in strength among previously trained athletes. However, the authors were unable to reach a conclusion regarding the influence of anabolic steroids on overall athletic performance.

In a well-designed, randomized, controlled trial, testosterone combined with strength training was found to increase fat-free mass as well as muscle size and strength among healthy male volunteers. The authors suggested that by extension, androgens may be beneficial when administered for a limited period in those with cachexia associated with chronic conditions. Schols and colleagues reported that subjects with COPD sustained greater improvements in fat-free muscle mass and in maximal inspiratory pressure (PImax) when anabolic steroids were added to nutritional supplementation than when they received only nutritional support. The subjects were given anabolic steroids IM at baseline and at 2, 4, and 6 weeks, and their primary outcomes (body composition and respiratory muscle function) were measured after 8 weeks.

We were interested in learning whether oral anabolic steroids improve respiratory muscle function and exercise capacity if administered over a more protracted period of 6 months. Therefore, we undertook a randomized, controlled trial in which an anabolic steroid (stanozolol) was administered orally for 27 weeks to ambulatory undernourished individuals with COPD. During the period of steroid administration, study participants participated in respiratory rehabilitation, including cycle ergometry and inspiratory muscle training. Our primary outcome measures were body mass index (BMI), muscle mass, respiratory muscle strength, and functional exercise capacity.

Materials and Methods

Population

Twenty-three ambulatory male patients with stable COPD (no respiratory exacerbation for at least 6 weeks) were selected for the study. Inclusion criteria included a BMI below 20 kg/m² and a PImax below 60% of the predicted value. Subjects did not have any other associated medical conditions that might have influenced their weight or respiratory muscle function. Patients with prostate or known cardiac disease were excluded because of the potential side effects of anabolic steroid administration. The protocol was approved by the Human Ethics Committee of the Federal University of São Paulo.

Protocol

After their informed consent was obtained, the subjects were randomized in a double-blind fashion to receive either placebo (control group) or anabolic steroids (study group). Patients in the anabolic steroid group received 250 mg of testosterone IM (Duratetson, a preparation containing phenpropionate, isocaproate, propionate, and caproate of testosterone) at baseline as an “attack” dose; the study group also took oral stanozolol (12 mg/day) for 27 weeks.

The study was divided into three 9-week periods. For the first 9 weeks, the study group received stanozolol and the control group a placebo. Between weeks 9 and 18, both groups received daily inspiratory muscle training (IMT) in addition to stanozolol or placebo. During weeks 18 to 27, exercise training at approximately 80% of maximal work, as determined by a symptom-limited incremental exercise test, was added to this regimen. A cycle ergometer was used for training (Model II; Funbec, São Paulo, Brazil). This was calibrated regularly (physically and electronically) by the manufacturer.

Between weeks 9 and 27, IMT was performed for 20 min, twice a day, at 20 breaths/min using a pressure-loaded device (Resp-Trein; Imebra, São Paulo, Brazil). Training was targeted to be at a pressure equal to 50% of PImax. PImax was measured every 3 weeks using an analogue pressure gauge, and the target pressure was adjusted as necessary. Although most of the IMT sessions were unsupervised, to promote subject compliance patients had one session of supervised IMT every 3 weeks. During these sessions, subjects were provided with feedback on their technique as well as encouragement. Family members were encouraged to assist the subjects with their home rehabilitation program.

Between weeks 18 and 27, patients performed cycle training at the hospital for 30 min three times a week, at a workload equal to 80% of the maximal workload derived from the incremental exercise test; sessions were supervised by a physical therapist. If the patient was unable to perform at that workload, he started with a lower load and increased the load after 1 week. One subject who could not reach this workload trained at the maximal level that he could achieve.

Measurements

At baseline and at 9-week intervals (9, 18, and 27 weeks), dual energy x-ray absorptiometry (DEXA) was performed to determine...
body composition (total lean body mass and percentage of fat mass). Tests of respiratory muscle strength and endurance, the 6-min walk test, and the incremental exercise test also were performed at each of those times. Anthropometric measures and respiratory muscle strength (PImax and maximal expiratory pressure [PEmax]) were measured every 3 weeks.

**Nutritional Assessment**

Weight was measured in the morning using a beam scale, with the patient clothed but not wearing shoes. Ideal body weight was determined from the patient’s weight range and frame size based on the tables from Metropolitan Life Insurance.15

BMI was calculated by dividing the patient’s weight in kg by his height squared (m²). We considered subjects with a BMI of less than 20 kg/m² to be undernourished.16

To measure midarm circumference, the nondominant arm was positioned parallel to the trunk and a nondistensible tape was placed around the midpoint of the arm without compressing the arm tissue, halfway between the tip of the shoulder (acromial process) and the tip of the elbow (olecranon process). Three consecutive measurements were made. If there was agreement between them (within 0.5 cm), the intermediate measurement was accepted as the actual value.

Triceps skinfold thickness was used as an indirect estimate of body fat. It was derived by gathering skin at the midarm point between the thumb and the index finger and measuring its thickness with a skinfold caliper. Three consecutive measurements were made. If there was agreement between them (within 4 mm), the intermediate measurement was accepted as the actual value.

The arm muscle circumference index reflects the amount of muscle or lean tissue in the body. This measurement was derived from the following equation: arm muscle circumference = midarm circumference – (3.14 x triceps skinfold thickness).17

With the patient standing and his weight evenly distributed, the thigh circumference was determined on the nondominant side at half the distance between the inguinal crease and a point midway along the patella. Three consecutive measurements were made. If there was agreement between them (within 0.5 cm), the intermediate measurement was accepted as the actual value.

Total body and soft-tissue composition were measured with dual energy X-ray absorptiometry (DEXA). DEXA measurements were made with a total body scanner (Model DPX; Lunar Radiation Corp; Madison, Wis). Total serum protein and albumin were obtained from venous blood at baseline and every 9 weeks.

**Respiratory Muscle Assessment**

Respiratory muscle strength was assessed by measuring PImax and PEmax (PImax at residual volume and PEmax at total lung capacity) with an analogue pressure gauge using standard methodology.18 Patients were seated and asked to make maximal efforts against an obstructed mouthpiece that had a small leak to prevent patients from closing their glottis during the respiratory maneuver. Patients had to sustain maximal effort for 1 s. The best of five consecutive attempts was used, provided the variability between the best two efforts did not exceed 5%.19

To measure respiratory muscle endurance, subjects breathed through a pressure-dependent inspiratory device set to generate mouth pressures close to 80% of their PImax until they could no longer maintain this pressure target. Endurance time and breathing frequency were recorded. After the subjects practiced at home daily for a week, the baseline endurance was measured. As an approximate measurement of the total work, we calculated the product of pressure, inspiratory time, and number of breaths during the endurance run. Inspiratory time was considered to be 50% of total respiratory time.20

**Exercise Capacity**

Maximal exercise capacity was assessed with a graded, symptom-limited exercise test. The test was performed using the CPX Diagnostic System (Medical Graphics Corp; St. Paul, Minn) linked to a cycle ergometer (CPE 2000; Medical Graphics Corp) with 10-W increments each minute. Maximal oxygen consumption (VO2max) was calculated as a percentage of the predicted value.

Three 6-min walk tests were performed. During the first two tests, patients were encouraged every 2 min. In the third test, they were encouraged and accompanied in order to achieve the best performance.21 The value used was the greatest distance a patient walked in 6 min in any of the three tests.

**Side Effects**

We measured several indices that might reflect toxic effects of anabolic steroids. Venous blood concentrations of testosterone and luteinizing hormone (LH) were measured at baseline and at 9, 18, and 27 weeks. Screening for possible side effects associated with anabolic steroids was carried out according to World Health Organization guidelines.22 Liver function was assessed by measuring levels of serum aspartate aminotransferase, alanineaminotransferase, gamma-glutamyltransferase, total bilirubin, conjugated bilirubin, and alkaline phosphatase. Every 9 weeks, we recorded the international normalized ratio, partial thromboplastin time, fibrinogen level, platelet count, and platelet aggregation to monitor coagulation. Evaluation also included a complete blood count and measurement of prostatic acid phosphatase, triglycerides, total cholesterol, and lipoproteins. In addition, we performed transrectal clinical evaluation of the prostate and transrectal prostatic ultrasound. We also monitored cardiac function by means of ECGs, chest radiographs, and two-dimensional echocardiograms.

**Other Measures**

Calcium, phosphorus, magnesium, sodium, potassium, and glucose levels were measured at baseline and at 9, 18, and 27 weeks.

**Statistical Analysis**

Data are presented as mean±SE. Nonparametric analysis of variance was used to determine the significance of differences between the two groups (Mann-Whitney) and between periods (Friedman). Results were considered statistically significant at p<0.05.

**Results**

The baseline features of the patients are shown in Table 1. There were no significant differences between groups at baseline. Both groups had a mean BMI of 17.3 (below predicted values for their age and sex), severe or moderate airway obstruction,23 24 25 and reduced respiratory muscle strength. Data from six patients were excluded from analysis:
two patients in the control group died of respiratory failure before the study's end; one patient in each group was unable to attend regularly for exercise measures; one member of the study group developed atelectasis associated with a non-small cell lung cancer; and one study patient was withdrawn because of depression. Thus, 17 patients completed the protocol, 10 in the study group and seven in the control group.

There were numerous respiratory exacerbations, including flulike illnesses (two control and five study subjects), tracheobronchitis (12 control and 11 study subjects), and pneumonia (one subject in each group). All subjects with tracheobronchitis received antibiotics. Corticosteroids were administered for 5 to 7 days in 11 subjects (five control and six study subjects). During exacerbations, subjects missed 1 week of exercise. They then restarted at a lower workload, gradually returning to their previous level over 1 week. Measures of exercise tolerance were postponed for 1 week and measures of respiratory muscle strength and endurance were postponed for 2 weeks. One control subject and two patients from the treatment group missed the last test because of respiratory exacerbations; their data for that test was excluded from analysis.

The changes in anthropometric measurements in study and control subjects during the 27-week period are summarized in Figure 1. For changes in BMI, differences between groups were statistically significant at 3 weeks and were sustained throughout the 27 weeks (p<0.05; Fig 1, left). The arm muscle circumference increased consistently among the study subjects; at 21 weeks, the increase was significantly greater in the study group compared with the control group (p<0.05; Fig 1, center). Between-group differences in thigh circumference were detectable at 3 weeks and increased progressively during the study (p<0.05; Fig 1, right).

Weight increased in 9 out of 10 subjects who received anabolic steroids (mean, +1.8±0.5 kg; p<0.05), whereas the control group lost weight (mean, −0.4±0.2 kg) after 6 months. At baseline, 

<table>
<thead>
<tr>
<th>Table 1—Anthropometric and Pulmonary Function Data at Baseline*</th>
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<tr>
<td>Control Group (n=7)</td>
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<tr>
<td>Age, yr</td>
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<tr>
<td>Weight, kg</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
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<tr>
<td>% of ideal weight</td>
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<tr>
<td>FEV₁, % pred</td>
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<tr>
<td>FEV₁/FVC, %</td>
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<tr>
<td>Pmax, cm H₂O</td>
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<tr>
<td>Pmax, cm H₂O</td>
</tr>
<tr>
<td>PaO₂, mm Hg</td>
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<tr>
<td>PaCO₂, mm Hg</td>
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*Data presented as mean (SEM). There were no significant differences between the control and study groups.

![Figure 1](image-url)
lean body mass as measured by DEXA was similar in both groups. In subjects who received anabolic steroids, lean body mass increased significantly at 9 weeks compared with baseline (p<0.05; Fig 2, left), whereas control subjects showed no increase. The increase in the study group was sustained at 18 weeks. There were no statistically significant changes in fat mass over time or differences between groups (Fig 2, right).

All subjects reported compliance with the training regimen. Both groups demonstrated increased respiratory muscle strength at 27 weeks (20.0±11.0% in the control group, 41.0±9.4% in the study group), although the increases were not significant; between-group differences were also not significant (Fig 3, left). There were no changes in PEmax (Fig 3, right).

Changes in functional exercise capacity (6 MW) and $\dot{V}O_2$ max were not significant in either group (Table 2).

There were no significant differences in biochemical measures (electrolytes, glucose, calcium, phosphorus, magnesium), total protein, albumin, blood cell count, prostatic acid phosphatase, or prostate size within groups, between groups, or across time. Baseline levels of prostatic acid phosphatase were 2.7 IU/L and 2.5 IU/L in the control and study groups, respectively, compared with 2.3 IU/L (control group) and 2.2 IU/L (study group) after 27 weeks. The baseline prostate size was 25.8 and 28.0 cm$^3$ in the control and study groups, respectively, compared with 24.2 and 29.4 cm$^3$ after 27 weeks. Levels of LH and testosterone were similar in both groups at baseline but showed significant decreases in those receiving anabolic steroids (Table 3). The between-group differences for LH were evident at 9 weeks and through 27 weeks. Testosterone levels were significantly lower in the study group compared with the control group at 9 and 18 weeks. The results of all other screening tests for side effects of anabolic steroids did not change.

**Discussion**

We undertook this randomized controlled trial in order to evaluate the potential benefits of anabolic steroids in malnourished individuals with COPD whose BMI was less than 20 kg/m$^2$ and whose PImax was below 60% of the predicted value. Such individuals have been noted to have a reduced body fat content, skinfold thickness, and arm circumference. At the end of the 6-month study, the control and treatment groups’ weights differed, with subjects who received anabolic steroids weighing an average of 2 kg more than control subjects. This weight gain was associated with significant increases in arm muscle and thigh circumference and in lean body mass as measured by DEXA.

The improved nutritional status that we observed was confined to those who received anabolic steroids. Although the absolute weight gain among those receiving anabolic steroids in the study by Schols et al$^{14}$ was not influenced by the nutritional supplement, the fat-free mass was significantly
greater in those receiving both steroids and nutritional supplements. Their placebo group lost 0.4 kg, as did our control subjects. The increase in lean body mass that we observed without a nutritional supplement (2.5 kg at 9 weeks and 1.9 kg at 27 weeks) was similar in magnitude to that reported by Schols et al14 (1.4 kg at 8 weeks in nondepleted subjects and 1.9 kg in depleted subjects), despite the use of different measurement techniques; Schols et al14 used bioelectrical resistance. In our study, lean body mass did not change in control subjects, but increased in treatment subjects. Although statistical significance was not reached at 27 weeks, the trend for the increase was still evident (Figure 2). Fat mass did not change in either group.

Although Schols et al14 also measured body composition and respiratory muscle strength in subjects with COPD, our study differed in several ways. First, because we wanted to separate the influence of the anabolic steroid from that of nutritional supplementation, we did not modify subjects’ nutritional intake. Second, we included IMT, which was not part of the study by Schols et al.14 Third, we chose to study an oral anabolic steroid rather than a parenterally administered steroid and administered it for 27 weeks in order to approximate an outpatient clinical approach to those with COPD; Schols et al14 gave subjects a parenteral steroid for 8 weeks. Fourth, we were concerned about side effects and performed detailed monitoring of biochemical, hormonal, and hematologic measures, as well as both clinical and ultrasound assessment of prostatic function.

Although our subjects did undergo cycle training, this training was not associated with increases in measurements of maximal or functional exercise capacity. We selected malnourished, severely impaired individuals with COPD who had high target exercise levels. Whereas a less impaired cohort may have improved more than our study subjects, the literature suggests that improvements in exercise tolerance can be achieved among severely impaired individuals. In their well-designed study, Schols et al14 succeeded in obtaining reliable measures of functional exercise (12-min walk distances) in only 62% of nutritionally depleted individuals. These

**Table 2—Distance Walked in 6 Min and $\dot{V}O_2$ max in Control and Study Groups**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Study</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Week 9</td>
</tr>
<tr>
<td>Six-min walk, m</td>
<td>540 (24)</td>
<td>545 (29)</td>
</tr>
<tr>
<td>$\dot{V}O_2$ max, % pred</td>
<td>54.6 (6)</td>
<td>57.5 (7)</td>
</tr>
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*Data presented as mean (SEM). % pred=percentage of predicted value.
authors did not identify any increase in 12-min walk distances in their subjects.

We observed clear trends in the measures of respiratory muscle strength (increases of 20.0% and 41.0% in the control and treatment groups, respectively). However, the differences between the two groups did not reach statistical significance. In the Schols et al.14 study, nutritionally depleted individuals who received both anabolic steroids and nutritional supplementation achieved a significant increase in PImax at 8 weeks. Conceivably, a larger sample size might have allowed us to detect a statistically significant change. Alternatively, the subjects in our study may have been too impaired to experience a significant response to the training regimen. Another factor contributing to the lack of change in respiratory muscle function may have been the absence of supervision during IMT sessions. This is consistent with rehabilitation literature suggesting that unsupervised training interventions are less effective than supervised interventions.28 Finally, the role of IMT in this population is questionable; even among well-nourished individuals with COPD who underwent training at highly controlled and supervised centers, the evidence of improvement in dyspnea or exercise capacity is equivocal.29

Malnutrition impairs skeletal muscle function among healthy individuals and those with respiratory conditions. By affecting both ventilatory6,30,31 and peripheral muscles,32 malnutrition increases impairment and likely adds to the disability of individuals with COPD. Malnourished subjects have been shown in at least one report33 to have worse scores for the impact and activity domains of a specific respiratory quality-of-life questionnaire. Reductions in muscle mass, especially in the lower limbs, are common in elderly men.34,35 this has been linked to deconditioning as well as decreased production of growth hormone and testosterone levels.36,37 In some men, the levels of testosterone, dehydroepiandrosterone, and dehydroepiandrosterone sulphate decrease slowly, but in others, these hormones remain within the normal range.38 In a study of 36 individuals with COPD, Roth et al.39 noted that in those who had experienced a weight loss of more than 4.5 kg in the preceding 6 months or those in whom weight was below 90% of the predicted value, the incidence of hypogonadism was higher than in those with normal weights. Although both an animal study40 and an uncontrolled clinical study41 have suggested that growth hormone may be of benefit, growth hormone is expensive and has side effects; in elderly men, growth hormone was no better than a placebo when evaluated in conjunction with physical training.42 When administered to 12 subjects with COPD, growth hormone plus exercise training resulted in greater increases in lean body mass and muscle cross-sectional area than either placebo plus training (12 subjects) or placebo alone (five subjects), with no measurable between-group differences in exercise tolerance.43

A wide range of responses to anabolic steroids has been reported. Anabolic steroids have been claimed to increase muscle mass and performance among athletes by inducing an anabolic effect on proteins via androgenic receptors as well as by inhibiting protein catabolism via glucocorticoid receptors.11 Testosterone stimulates muscle growth via its effects on somatomedin,8 influences actin and myosin to increase strength,44-46 and might even act centrally to stimulate athletes to strive for higher training intensities.9,47,48 Unfortunately, accurate reports on the effects of anabolic steroids have been difficult to obtain; there have been wide variations in dosages and methods of administration, as well as a relative paucity of well-designed outcome studies.13 A well-designed study by Bhasin et al.13 supraphysiologic doses of testosterone were administered to healthy male volunteers, some of whom also received supervised weight training three times per week. The authors reported significant improvements in muscle size and strength between placebo and testosterone in nonexercising groups and greater increases in fat-free mass, muscle size, and strength among those receiving testosterone in the exercising groups.

Table 3—LH and Testosterone Levels in Control and Study Groups*

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 9</th>
<th>Week 18</th>
<th>Week 27</th>
</tr>
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<tbody>
<tr>
<td>LH, IU/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>5.7 (1.7)</td>
<td>7.2 (2.3)</td>
<td>7.1 (1.8)</td>
<td>7.4 (2.0)</td>
</tr>
<tr>
<td>Study group</td>
<td>3.3 (0.6)</td>
<td>0.66†‡ (0.2)</td>
<td>1.8†‡ (0.7)</td>
<td>2.1† (0.8)</td>
</tr>
<tr>
<td>Testosterone, ng/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>496 (117)</td>
<td>452 (43)</td>
<td>463 (31)</td>
<td>402 (89)</td>
</tr>
<tr>
<td>Study group</td>
<td>415 (34)</td>
<td>157†‡ (28)</td>
<td>135†‡ (14)</td>
<td>220† (61)</td>
</tr>
</tbody>
</table>

*Data presented as mean (SEM).
†p<0.05 compared with baseline.
‡p<0.05 compared with control group.
There were no side effects in mood or behavior attributable to testosterone.13

The effects of anabolic steroids on the athlete and athletic performance remain controversial. There appears to be a consensus, however, regarding the effects of anabolic steroids on aerobic metabolism: no beneficial effect of anabolic steroids has ever been shown on aerobic metabolism or an individual’s \( V_{O_{2}} \text{max} \).10

The clinical applications of anabolic steroids have been acknowledged for some time. They have been administered as adjuvants in the management of protein deficiency states, after major surgery or severe trauma, for malabsorption during radiotherapy, and in conjunction with cytotoxic chemotherapy.29 Anabolic steroids have also been included with parenteral nutrition and have been shown to have a markedly beneficial effect.30 The response to anabolic steroids has been most favorable among those in negative nitrogen balance. Undernourished elderly people respond to steroids with marked nitrogen retention and significant weight gain.51

**Justification of Methods**

Testosterone cannot be effectively administered by mouth, as it is rapidly absorbed into the portal blood stream for degradation by the liver. Thus, only a small amount reaches the systemic circulation. When administered parenterally, effective levels are not sustained in the plasma because anabolic steroids are promptly degraded.11 We chose to use stanozolol (a synthetic substance derived from testosterone), which can be orally administered. Synthetic derivatives have the added advantage of having more anabolic and less androgenic effects than natural testosterone. The dosage we selected, 12 mg per day, is twice the replacement dosage10 and is the dosage conventionally used by athletes.11 We used one dose of IM testosterone at the start of the study as an “attack” dose, in keeping with the approach preferred by athletes. Generally, athletes use either a pyramidal administration schedule, starting with low daily dosage and building to higher dosages, or they use a “stacking” schedule in which several different preparations are taken simultaneously (oral and parenteral).38,47

During the administration of stanozolol, testosterone levels decreased significantly at weeks 9, 18, and 27. At week 27, the differences between groups were not statistically significant even though the levels of testosterone in the anabolic steroid group were comparable to prepubertal levels.52

We used DEXA to measure body composition. This method has been shown to be accurate to within 1.5% for measurements of total body mass as well as fat and lean mass percentages.53 The advantage of DEXA for composition studies is that it requires only 10 to 20 min to complete, involves minimal exposure to radiation, and gives regional values as well as total body values. The reproducibility is such that serial measurements are routinely used in estimates of calcium intake and are accurate to within 0.8%.53 We used Lunar DPX, which is a precise and accurate tool for the assessment of whole body composition.54 Since there is no method available to measure body cell mass in clinical practice, it is generally acknowledged that in absence of fluid shifts, the fat-free mass provides an acceptable estimate.55 In our study, the increase in lean body weight cannot be equated unequivocally to an increase in muscle or tissue mass because fluid retention could not be absolutely ruled out. However, regular clinical evaluation by the same physician did not reveal clinical evidence of fluid retention nor any change in BP. In addition, DEXA scanning was standardized to be performed at the same time of the day (late morning, before lunch) and by the same technician.

In our study, the dietary intake of our subjects remained open, without any attempt at standardization or supplementation. Supplementation has been shown to be useful when provided to patients with COPD in conjunction with anabolic steroids.14 Many of our study subjects spontaneously reported an increase in their appetite, consistent with reports on the influence of anabolic steroids on appetite.38 However, even in the absence of supplementation, BMI and muscle circumference increased among those who received anabolic steroids.

Our relatively small sample size may have influenced the power of our measurements. For example, there appeared to be a clinical effect of anabolic steroids on PImax but this did not reach statistical significance, possibly because of the lack of power in a small sample. Further studies on the influence of anabolic steroids should examine a larger sample and should also evaluate their influence on health-related quality of life.

In summary, anabolic steroids administered to severely impaired, malnourished men with COPD were associated with a greater increase in weight, fat-free mass, and arm and thigh muscle circumference than was placebo. There was a trend for an increase in inspiratory muscle strength in both groups. These changes occurred in the absence of clinical or biochemical side effects.

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REFERENCES


4. Rosa E, Pereira CAC. Dyspnea and functional findings in poorly nourished COPD and well nourished COPD. J Pneumol 1992; 18:105-10


21. Cavalheiro LV, Cendon SP, Ferreira IM, et al. Six-minute walking test by a physiotherapist assess better the physical capacity of patients with COPD [abstract]. Am J Respir Crit Care Med 1997; 155:A167


43. Casaburi R, Carithers E, Tosolini J, et al. Randomized
placebo controlled trial of growth hormone in severe COPD patients undergoing endurance exercise training [abstract]. Am J Respir Crit Care Med 1997; 155:A498


46 Forbes GB. The effects of anabolic steroids on lean body mass: the dose-response curve. Metabolism 1985; 34:571-72

47 Wilson JD, Griffin JE. The use and misuse of androgens. Metabolism 1980; 29:1278-95


50 Shizgal HM. Anabolic steroids and total parenteral nutrition. Wien Med Wochenschr 1993; 143:375-80

51 van Wayjen RG. Metabolic effects of anabolic steroids. Wien Med Wochenschr 1993; 143:368-75


55 Wouters EFM, Schols AMWJ. Nutritional depletion in COPD. Eur Respir Rev 1997; 7:60-65