Testosterone Replacement and Resistance Training Improve Muscle and Physical Function in Men With COPD

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Abstract

Skeletal muscle dysfunction contributes substantially to exercise intolerance seen in chronic obstructive pulmonary disease (COPD). In addition, testosterone (T) concentrations in men with COPD are often low, contributing to abnormal muscle size and strength. ***PURPOSE:*** To examine the singular and combined effects of a physiologic replacement dose of T and resistance exercise training (R) on muscle performance and physical function in men with COPD. ***METHODS:*** Fifty-two men with severe COPD (mean FEV_1=40% pred) were randomized to receive no R and placebo (NRP), no R and T (NRT), R and placebo (RP), or R and T (RT). R consisted of five lower extremity exercises performed 3 d/wk for 10 wks. Training was progressive with loads ranging from 60-80% 1-RM performed in 3-4 sets of 8-12 repetitions. T was administered intramuscularly 100 mg/wk for 10 wk. ***RESULTS:*** Subjects receiving T doubled nadir T levels to values that were in the mid-range of normal for young men. Significant (P<0.001) improvements in leg press strength (by 1-RM) were noted for NRT, RP, and RT. The 17%, 16%, and 23% increases, respectively, were greater than the 2% change in NRP. The change in +X/+T was also significantly greater than the change in -X/+T. Leg press repetitions to failure (80% initial 1-RM) increased significantly (P<0.02) only in the RP (15 to 23) and RT (13 to 24) groups. The 87% increase noted in the RT group was significantly greater than the 0% and –14% changes in NRP and NRT, respectively. There were no significant changes in leg power, assessed by Bassey leg rig. Stair climb performance improved significantly (by 19%, P<0.01) only in RT. No improvements from baseline or among groups were noted for timed up-and-go or 10-meter walk performance. ***CONCLUSION:*** Physiologic T replacement and progressive R training alone or in combination improves muscle strength and fatigability in men with COPD. However the combination of Tplus R was required to improve stair climb time.

Introduction

Exercise intolerance invariably accompanies chronic pulmonary disease. Pulmonary rehabilitation, with exercise training considered as the most important component, has been found to improve exercise tolerance. However, exercise regimens have traditionally focused on the pulmonary system since patients are ventilatory limited. Accumulating evidence suggests that muscle dysfunction contributes significantly to the exercise intolerance seen in chronic pulmonary disease. Possible mechanisms explaining this muscle dysfunction include deconditioning resulting in muscle atrophy, a specific myopathy (especially corticosteroid-induced myopathy), malnutrition, chronic hypoxia, and low levels of anabolic hormones leading to muscle wasting. Consequently, attention has been directed to anabolic strategies that improve skeletal muscle function, reverse disuse atrophy, and improve exercise tolerance. The purpose of this study was to examine the singular and combined effects of a physiologic replacement dose of testosterone and resistance exercise training on muscle performance and physical function in men with COPD and low levels of endogenous testosterone.

Methods

STUDYDESIGN: Randomized, double-blind, placebo controlled.

SUBJECTS: Fifty-two male volunteers aged 55-80 yr with moderate to severe, but stable Chronic Obstructive Pulmonary Disease (COPD) and low testosterone levels randomized to one of four groups (Figure 1).

RESISTANCE EXERCISE TRAINING: Five lower extremity exercises (seated leg press, seated leg curl, seated leg extension, seated calf press, seated ankle dorsi-flexion) performed 3 d/wk for 10 wks. Training was progressive with loads ranging from 60-80% of the one-repetition maximum (1-RM) performed in 3-4 sets of 8-12 repetitions.

TESTOSTERONE REPLACEMENT: Testosterone enanthate administered intramuscularly 100 mg/wk for 10 wk.

OUTCOME MEASURES: Changes in maximal voluntary strength assessed by 1-RM in the leg press exercise, peak leg power (watts) with the Bassey Leg Rig, leg press repetitions to failure using 80% of the baseline 1-RM leg press strength score, and time (to 0.01 sec by photoelectric cells and timers) to ascend a standardized four-step stair climb.

STATISTICAL ANALYSES: Analysis of variance (ANOVA) on change scores with Newman Keuls post hoc analyses for significant ANOVAs.

Results

Forty-seven of the 52 subjects randomized completed the study as depicted in *Figure 1*. Changes in nadir serum testosterone levels are presented in *Table 1*, revealing that nadir testosterone levels remained low in the placebo groups but doubled to values that were in the mid-range of normal for young men in groups receiving replacement does of testosterone. Significant (P<0.001) improvements in leg press strength were noted for –X/+T, +X/-T, and +X/+T (*Figure 2*). The 17%, 16%, and 23% increases, respectively, were greater than the 2% change in –X/+T. The change in +X/+T was also significantly greater than the change in -X/+T, (P<0.05). Leg press repetitions to failure (80% initial 1-RM) increased significantly (P<0.02) only in the +X/-T (15 to 23) and +X/+T (13 to 24) groups (Figure 3). The 87% increase noted in the +X/+Tgroup was significantly greater than the 0% and –14% changes in –X/-T and –X/+T, respectively. There were no significant changes within or between groups for leg power. Stair climb performance improved significantly (by 19%, P<0.01) only in +X/+T (*Figure 4*). No changes from baseline within or between groups were noted for timed up-and-go or 10-meter walk performance.

Table 1. Mean (± SD) nadir testosterone levels (ng·dL-1) before and after the 10-week intervention.

	No Exercise, No Testosterone	No Exercise, Testosterone	Exercise, No Testosterone	Exercise, Testosterone
Pre	302 ± 154	301 ± 89	377 ± 142	408 ± 139
Post	353 ± 190	595 ± 161	401 ± 177	656 ± 264

Figure 1. Number of subjects randomized to each group that completed the study

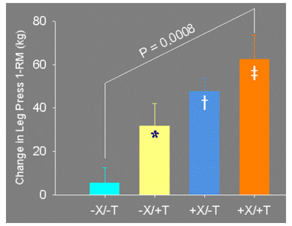

*Figure 2. Change in leg press 1-RM (kg) after 10 weeks of training in men with COPD. ‡ = +X/+T significantly greater change than both –X/-T and –X/+T, p<0.05. † = +X/-T significantly greater change than –X/-T, P<0.05. *= -X/+T significantly greater change than –X/-T, P<0.05. Group abbreviations on X-axis as follows. –X/-T is no resistance exercise training, no testosterone (i.e., placebo); -X/+T is no resistance exercise training, testosterone; +X/-T is resistance exercise training, no testosterone; +X/+T is resistance exercise training, testosterone.*

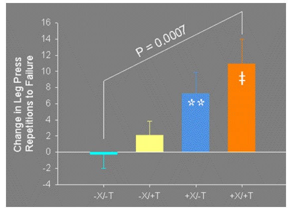

*Figure 3. Change in leg press repetitions to failure after 10 weeks of training in men with COPD. ‡ = +X/+T significantly greater change than both –X/-T and –X/+T, p<0.05. ** = +X/-T significantly greater change than both –X/-T and –X/+T, p<0.05. Group abbreviations on X-axis as follows. –X/-T is no resistance exercise training, no testos - terone (i.e., placebo); -X/+T is no resist - ance exercise training, testosterone; +X/-T is resistance exercise training, no testos - terone; +X/+T is resistance exercise train - ing, testosterone.*

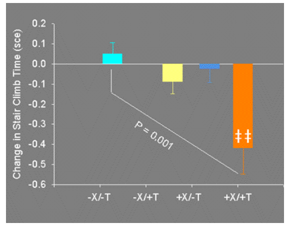

Figure 4. Improvements in four-step stair climb time (sec) after 10 weeks in men with COPD. ‡‡ = +X/+T significantly greater change than all other groups, p<0.05. Group abbreviations on X-axis as follows. –X/-T is no resistance exercise training, no testosterone (i.e., placebo); -X/+T is no resistance exercise training, testosterone; +X/-T is resistance exercise training, no testosterone; +X/+T is resistance exercise training, testosterone.

Figure 5. Representative subject performing leg press exercise

Figure 6. Representative subject performing leg power test.

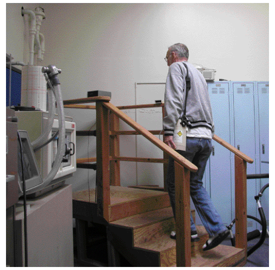

Figure 7. Representative subject performing four-step stair climb.

Summary

Physiologic testosterone replacement and progressive resistance training alone or in combination improves muscle strength and fatigability, but not leg power in men with COPD. The combination of testosterone plus resistance exercise training was required to improve stair climb time.

Conclusion

Both testosterone supplementation and strength training, alone or in combination, significantly improve maximal voluntary muscle strength and fatigability of the muscles of ambulation in men with COPD. Time to ascend a standardized four step stair climb significantly improves with the combination of replacement doses of testosterone and progressive resistance exercise training. These interventions should be practical additions to programs of pulmonary rehabilitation.

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