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Muscle Gain From Testosterone Not Hampered by Dutasteride

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March 6, 2012 — A recent study has shown that in patients receiving testosterone, dutasteride (*Avodart*, GlaxoSmithKline) did not blunt the hormone's effects on muscle mass.

Shalender Bhasin, MD, professor of medicine at Boston University School of Medicine in Massachusetts, and colleagues report the results of their study in the March 7 issue of *JAMA*.

Dutasteride is a 5-α reductase inhibitor that is used to treat benign prostatic hypertrophy and androgenic alopecia. It works by inhibiting the conversion of testosterone to α-dihydrotestosterone (DHT).

Dr. Bhasin and colleagues conducted the 5α-Reductase Trial, a parallel-group, double-blind, randomized placebo-controlled trial of 139 healthy men, aged 18 to 50 years, with normal testosterone levels.

Patients either were assigned to receive 1 of 4 testosterone enanthate doses (50, 125, 300, or 600 mg/week) plus dutasteride or were assigned to 1 of 4 groups that were given 1 of 4 testosterone enanthate doses (50, 125, 300, or 600 mg/week) plus placebo for 20 weeks.

Change in fat-free mass from baseline, as measured by dual-energy X-ray absorptiometry, was the primary outcome. The researchers also measured testosterone levels, muscle strength, sexual function, and sebum production and acne.

"The investigators performed a meticulously designed and executed study to answer an almost 5-decades-old question: are testosterone, DHT, or both in physiological and supraphysiological levels important in the gain of lean body mass?" writes Ugis Gruntmanis, MD, from the University of Texas, Southwestern Medical Center, in Dallas, and the Dallas Veterans Affairs Medical Center, Texas, in an accompanying editorial.

Testosterone Levels

Total and free testosterone increased with testosterone administration in all groups, and there were no statistically significant differences between the groups. Among participants in the testosterone enanthate plus dutasteride groups, the mean testosterone level was 519 ng/dL (95% confidence interval [CI], 378 - 660 ng/dL) for 50 mg/week, 895 ng/dL (95% CI, 616 - 1173 ng/dL) for 125 mg/week, 1706 ng/dL (95% CI, 1341 - 2071 ng/dL) for 300 mg/week, and 3898 ng/dL (95% CI, 3089 - 4708 ng/dL) for 600 mg/week.

Among participants in the testosterone enanthate plus placebo groups, the mean testosterone level was 385 ng/dL (95% CI, 261 - 508 ng/dL) for 50 mg/week, 822 ng/dL (95% CI, 658 - 986 ng/dL) for 125 mg/week, 1702 ng/dL (95% CI, 1201 - 2203 ng/dL) for 300 mg/week, and 3578 ng/dL (95% CI, 2876 - 4279 ng/dL) for 600 mg/week.

Fat-Free Mass

There was a dose-dependent increase in fat-free mass and lean body mass in the dutasteride and placebo groups. Fat-free mass changes were related to testosterone dose and changes in testosterone concentrations in the dutasteride and placebo groups, but there were no differences between groups. The changes in fat-free mass were related to testosterone dose and changes in testosterone concentrations in the placebo and dutasteride groups, but did not differ between groups; the dose-adjusted mean difference (placebo minus dutasteride) in fat-free mass was 0.50 kg (95% CI, −0.22 to 1.22 kg; P = .18).

There was a negative relationship between changes in fat mass and testosterone dose and concentrations, but there

were no significant differences between the placebo and dutasteride groups in the relationship between change in fat mass and dose (*P* = .41).

Muscle Strength

In the placebo and dutasteride groups, there was a dose-dependent increase in leg-press and chest-press strength. These increases were greater with larger doses and higher concentrations of testosterone, with no differences in relationships found between the placebo and dutasteride groups.

Sexual Function

Sexual function was not significantly related to testosterone dose or testosterone concentrations during treatment, and did not differ significantly between placebo and dutasteride groups.

Prostate Volumes and Prostate-Specific Antigen (PSA) Level

There was no significant relationship between prostate volumes and PSA level and either testosterone dose or concentration, and there were no significant differences in prostate volume and PSA level between the placebo and dutasteride groups.

Sebum Production and Acne

Only serum production in the forehead area (not on the nose or back) was related to testosterone dose, and there were no differences between the placebo and dutasteride groups.

Laboratory Tests

Hemoglobin and hematocrit levels increased dose-dependently in the placebo and dutasteride groups. Changes in hemoglobin and hematocrit levels were significantly related to changes in testosterone concentrations, but did not differ significantly between the groups.

Total cholesterol and high-density lipoprotein cholesterol changes were negatively related to dose, but there were no significant differences between the groups.

Serum NTx (collagen-type I N-telopeptides) and osteocalcin levels did not change in either the placebo or the dutasteride groups.

The overall frequency of adverse events was similar in both the placebo and dutasteride groups.

Dutasteride Okay to Take With Testosterone

"[T]he inhibition of testosterone's conversion to DHT by dutasteride had no significant effect on the ability of testosterone to exert its effects on muscle mass and strength, sexual function, erythropoiesis, plasma lipid levels, prostate volume, and sebum production," write the authors. "Instead, over the range of testosterone concentrations that were achieved (and which spanned the entire physiological male range and extended well into the subphysiological and supraphysiological range for men), testosterone was able to subserve all androgen-dependent functions that were studied herein, including maintenance of prostate volumes, PSA levels, and sebum production."

They add, "Even under these conditions of suppressed circulating and intraprostatic DHT concentrations induced by a high-dose dutasteride regimen, prostate volumes and PSA levels were maintained by testosterone doses administered in this trial."

"The main clinical message...is that for patients receiving exogenous testosterone, the gain in muscle mass was not

affected by concurrent 5α-reductase inhibition," writes Dr. Gruntmanis in the editorial. "Because the study was not powered to detect differences in other clinically important outcomes, conclusions regarding changes in fat mass, muscle strength, hematocrit level, sebum production, or serum lipid levels resulting from these drugs cannot be definitively made. Future studies should address these important secondary outcomes, and by doing so, will provide clinicians with additional useful information to better understand the risks and benefits of 5α-reductase inhibition and testosterone replacement therapy," he concludes.

The study was supported by the National Institute of Child Health and Human Development, the Boston University Clinical and Translational Science Institute, the Boston Claude D. Pepper Older Americans Independence Center, and the National Institute on Aging. Glaxo-SmithKline Inc provided dutasteride and placebo, and ENDO Pharmaceuticals provided testosterone enanthate. Dr. Bhasin has served on the board for Novartis; has worked as a consultant to GlaxoSmithKline; has grants pending with Solvay Pharmaceuticals, Merck & Co, and Ligand Pharmaceuticals Inc; has received reimbursement for travel expenses from GlaxoSmithKline, Novartis, Lilly & Co, and Ligand Pharmaceuticals; and has received compensation for serving as the chair for 2 Endocrine Society expert panels. The other authors and Dr. Gruntmanis have disclosed no relevant financial relationships.

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