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BPH

5α-Reductase inhibition does not adversely affect muscle mass

Results newly reported in *JAMA* show that the muscle mass of men is not affected by inhibition of 5α-reductase, the enzyme that produces the androgen 5α-dihydrotestosterone (DHT) from testosterone. DHT is a potent testosterone metabolite that has a number of roles in male physiology, including in the embryonic development of the prostate. Inhibitors of 5α-reductase are often prescribed for BPH, as blockade of DHT is known to shrink the hyperplastic prostate tissue. However, the roles of testosterone and DHT in regulating lean body mass have hitherto been difficult to disentangle from the multitude of other complex hormonal interactions that occur. Indeed, the roles of testosterone and DHT in other tissues, such as bone, are also unclear.

The 20-week study of 102 healthy men examined the effects of high-dose (2.5 mg per day) dutasteride (a 5α-reductase inhibitor) and testosterone enanthate compared with placebo and testosterone enanthate. All participants were given a long-acting gonadotropin releasing hormone agonist to suppress endogenous testosterone. Each arm was also subdivided into four dosage branches based on the testosterone dose given (50–600 mg per week). In doing so, the subgroups of patients were comparable with respect to their testosterone and DHT levels.

The fat-free mass and lean body mass in the two arms increased dose-dependently with respect to testosterone and were not significantly different between the dutasteride and placebo groups. Additionally, inhibiting DHT production did not alter the ability of testosterone to modulate muscle strength, sexual function or prostate volume.

From a therapeutic perspective, inhibitors of 5α-reductase to treat BPH have long been suspected of causing many adverse effects including reduced muscle mass, reduced bone density and sexual dysfunction. The results of this trial suggest these fears are perhaps overstated. "These findings bode well for the safety of 5α-reductase inhibitors with respect to their effects on muscle, because they indicate that these drugs will not induce muscle loss," says lead investigator Shalender Bhasin of Boston University School of Medicine. Indeed, the common adverse effects might be related to the age of the patients—approximately 40% of men aged 51–60 years have BPH—rather than the therapeutic regimen.

Importantly, these results support the hypothesis that in men with adequate circulating levels of testosterone, DHT simply enhances the androgen effect rather than being instrumental in regulating function of the prostate, bone and muscle. However, in men who have low levels of testosterone, DHT becomes important for maintaining prostate growth. Therefore, 5α-reductase inhibition might only be a useful strategy for treating men with BPH who have low levels of circulating testosterone.

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Original article Bhasin, S. *et al.* Effect of testosterone supplementation with and without dual 5α-reductase inhibitor on fat-free mass in men with suppressed testosterone production. *JAMA* **307**, 931–939 (2012)