

AUA ABSTRACT

Effects of Testosterone Administration on Prostate Tissues In Men with ADAM Syndrome

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Introduction and Objective

Prostate safety is a major concern when aging men receive supplemental testosterone (T). However, effects of T on prostate tissues are largely unknown, and T treatment of aging men is increasing. Thus, we performed a randomized clinical trial (RCT) studying effects of T on prostate tissues in men with ADAM syndrome (androgen decline of aging male).

Methods

48 men, ages 50-75 y.o., with ADAM (+ Morley score and morning T < 300 ng/dl at screen) were enrolled. At baseline, all men underwent 14-core TRUS-guided biopsy of prostate peripheral zone (PZ); 4 had cancer (CaP) and were excluded. The remaining 44 were randomized to a 6-month trial of T enanthate 150 mg IM q2weeks or PBO, with repeat biopsy at end of study. Two biopsy cores were snap-frozen for tissue hormone levels; 12 cores were used for detailed histology and biomarker studies for cell proliferation (Ki-67, MIB-1), stroma-epithelial ratio (SER), androgen receptor (AR), angiogenesis (CD34), and gene-expression profiling using a microarray of prostate cDNAs. Prostate volume (PV) was measured by MRI. The study was powered to detect a 25% increase in dihydrotestosterone (DHT) in prostate tissue (Urology 57:999, 2001).

Results

41 men completed both baseline & 6-month biopsies: 21 on T, 20 on PBO. The groups were comparable at baseline for age (65.4 ± 9.0); serum T (299 ± 98 ng/dl) and DHT (29.4 ± 10.4); PSA (median 1.3 ng/ml); PV (46.9 ± 26.0 cc); and median prostate levels of T (1.1 ng/g) and DHT (7.1 ng/g).

T treatment raised serum T levels (7 days after last injection) to 693 ± 250 ng/dl and DHT to 51.7 ± 24.4 ng/dl (both $p < 0.01$); hematocrit increased by 4.7 ± 2.9 % ($p < 0.05$). However, prostate levels of T and DHT did not change from baseline in either group. PSA, PV, tissue biomarkers, and histologic indices for % atrophy and inflammation were also unchanged. Gene expression profiles of prostate epithelial cells before and after T replacement showed no treatment effect. At 6-month biopsy, CaP was found in 4 men on PBO and 2 on T.

Conclusions

Surprisingly, no prostate tissue changes attributable to testosterone (T) supplementation were found in this RCT. Despite marked increases in serum levels, prostate levels of T & DHT were unchanged after 6 months of treatment. Furthermore, gene expression was not altered, cell proliferation was not accelerated, and histologic cancers were not increased. While a large RCT is needed to assess long-term risks, in the short term (6 months) T supplementation appears to exert no adverse effects in prostate tissues of men with ADAM syndrome.

Source of Funding: Watson Laboratories and Solvay Pharmaceuticals

Session Type: Podium

Session Title: Sexual Function/Dysfunction/Andrology: Medical & Non-Surgical Therapy (I)

Session Start: 5/22/2006 10:00:00 AM

Session End: 5/22/2006 12:00:00 PM

Location: