Journal of Andrology, Vol 16, Issue 2 100-107, Copyright © 1995 by The American Society of Andrology

JOURNAL ARTICLE

Anti-androgen effects of the aromatase inhibitor, atamestane

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Prostatic hyperplasia can be induced in both intact and castrated dogs and in intact cynomolgus monkeys by the administration of androgenic steroids. Estrogenic steroids potentiate this effect in dogs. These changes also can be induced by androstenedione, which increases androgen and estrogen levels. Atamestane (ATA; 1-methyl-3,17-dione-androsta-1,4-diene), a potent aromatase inhibitor, inhibits some of the androstendione-induced effects; however, the nonsteroidal aromatase inhibitor, CGS-16949A, has been reported to decrease serum estradiol levels in adult rats but to have no effect on androgen-dependent organ weights. To examine the mechanisms by which ATA affects the rat prostate, in vivo and in vitro studies were conducted using adult rat ventral prostate (VP). Intact Sprague-Dawley rats were injected daily for 14 days with sesame seed oil, ATA (70 mg/kg/day), finasteride (FIN; 5 mg/kg/day), a 5 alpha-reductase inhibitor, or the combination of FIN plus ATA. A fifth group was castrated (CASTR) on day 1. The mean +/- standard error VP weight of the controls was 350 +/- 19 mg. It was reduced 17% ($P < 0.05$) by ATA, 29% ($P < 0.001$) by FIN, 48% ($P < 0.001$) by FIN plus ATA, and 86% ($P < 0.001$) by CASTR. The DNA/VP was reduced 22% (not significant) by ATA, 18% by FIN (not significant), 35% ($P < 0.01$) by FIN plus ATA, and 60% ($P < 0.001$) by CASTR. More significant changes were observed in RNA and protein. The mRNA for prostatein C3 was reduced by each of the treatments, but only CASTR increased the mRNA for TRPM-2, a marker of apoptosis. (ABSTRACT TRUNCATED AT 250 WORDS)