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Comparison of Tamoxifen and Testosterone Propionate in Male Rats: Differential Prevention of Orchidectomy Effects on Sex Organs, Bone Mass, Growth, and the Growth Hormone–IGF-I Axis

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Testis dysfunction can weaken bone and reduce muscle mass as well as impair sexual function. Testosterone (T) therapy has useful effects on sex organs, bone, and muscle in T-deficient males, but prostate concerns can preclude T use in some men. Although estrogens or other drugs can protect bone in men, gynecomastia makes estrogens unappealing, and other drugs may also be undesirable in some cases. Selective estrogen receptor modulators (SERMs) inhibit estrogen-evoked sex organ growth but mimic estrogen effects on bone and cholesterol and are advantageous for some women. SERMs may also be useful in men who must avoid androgens. As a preclinical test of this idea, tamoxifen (a SERM) and testosterone propionate (TP, a classic androgen) were compared for their efficacy in preventing varied effects of orchidectomy (ORX) in adult male rats. ORX led to ventral prostate and seminal vesicle atrophy and decreases in somatic growth, proximal tibia bone mineral density (BMD), and serum growth hormone (GH) and insulin-like growth factor I (IGF-I). ORX also increased anterior pituitary glandular kallikrein, serum cholesterol, and body temperature. Pituitary prolactin (PRL) content was unaltered. ORX effects on sex organs, somatic growth, IGF-I, cholesterol, body temperature, and pituitary kallikrein were prevented by TP at 1 mg/kg (3 doses per week), but BMD and GH were unresponsive. ORX effects on BMD and GH were prevented by TP at 10 mg/kg, but this dose evoked supraphysiologic increases in sex organs and PRL, failed to restore somatic growth, and further reduced IGF-I. Tamoxifen (1 mg/kg daily) prevented ORX effects on BMD, GH, and cholesterol without altering basal or TP-induced sex organ growth and further reduced IGF-I and somatic growth. Tamoxifen did not alter basal PRL but blocked increases caused by TP at 10 mg/kg. In summary, tamoxifen prevented ORX effects on bone and cholesterol in male rats without affecting sex organs or PRL and might be useful for men who must avoid androgens. Unexpectedly, a TP dose that replicated testis effects on sex organs and other targets had no effect on BMD or GH, and a larger TP dose that restored BMD and GH was worse at replicating normal male physiology. In addition, correlation/regression results suggested that the GH–IGF-I axis contributes to changes in BMD.

Key words: Testis, androgens, estrogens, aromatase, osteoporosis, prostate, seminal vesicle

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