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JOURNAL ARTICLE

The antigonadotropic action of testosterone but not 7alpha-methyl-19-nortestosterone is attenuated through the 5alpha-reductase pathway in the castrated male rat pituitary gland

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The enzyme 5alpha-reductase plays a significant role in the prostate to amplify the action of testosterone (T) by converting it to a more potent androgen, dihydrotestosterone (DHT). The role of 5alpha-reductase in the testosterone feedback inhibition of gonadotropin secretion from the pituitary has not been elucidated. Therefore, we investigated the role of 5alpha-reductase on T action in in vitro and in vivo models. Castration has been reported to increase the 5alpha-reductase activity in pituitary glands. Hence, the effect of castration duration on the conversion of T to DHT by pituitary homogenates and the responsiveness of pituitary monolayer cell cultures to gonadotropin-releasing hormone (GnRH) challenge exposure were investigated. Incubation of [3H]-T with pituitary homogenates showed that the conversion of T to 5alpha-reduced metabolites was two- to threefold greater in pituitaries from rats who had been castrated for 14 days compared with those castrated for 1 day. In addition, the GnRH-stimulated release of LH from monolayer cell cultures of pituitaries from rats castrated for 1 day was twofold greater, whereas that from rats castrated for 2 weeks was six- to sevenfold greater compared with basal luteinizing hormone (LH) release. Hence we used rats castrated for 2 weeks to elucidate the role of 5alpha-reductase in T feedback inhibition. The inhibitory effects of the androgens T, 19-nortestosterone (19-NT), and 7alpha-methyl-19-nortestosterone (MENT) at 3 different concentrations (10(-9), 10(-7), and 10(-5) mol/L) on GnRH-stimulated LH release from monolayer cell cultures of pituitaries from rats castrated for 2 weeks were examined. All 3 androgens showed dose-dependent inhibition of LH release. MENT showed the greatest inhibition, followed by 19-NT and T. In the presence of finasteride (a 5alpha-reductase inhibitor), the inhibition of LH released by T and 19-NT were significantly greater. The inhibitory effect of MENT, which does not undergo 5alpha-reduction, was not altered by finasteride. In an in vivo study, rats castrated for 2 weeks received T with or without finasteride. There was a significantly greater suppression of serum LH in rats receiving T plus finasteride compared with those receiving T alone. These results suggested that 5alpha-reductase in the pituitary is not obligatory for the inhibitory action of T on gonadotropin secretion in the castrated rat. The action of MENT, a nonreducible androgen, on the pituitary is not affected by 5alpha-reductase.

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