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JOURNAL ARTICLE

Testosterone-dependent restoration of spermatogenesis in adult rats is impaired by a 5alpha-reductase inhibitor

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Germ cell development (spermiogenesis in particular) in the adult rat is known to be testosterone dependent. Recently we proposed a role for the 5alpha reduction of testosterone to dihydrotestosterone (DHT) in the short-term restoration of round spermatid maturation when testicular testosterone levels are experimentally lowered. The current study aimed to further characterize the involvement of 5alpha-reductase in the restoration of spermatogenesis by investigating the short- and long-term restoration of specific germ cell populations by testosterone in the presence or absence of a 5alpha-reductase inhibitor (L685,273). Spermatogenesis in adult rats was suppressed for 8 weeks using 3-cm testosterone and 0.4-cm estradiol silastic implants (testosterone-estradiol [TE] treatment); spermatogenesis was then restored by administration of increasing doses of testosterone with or without a competitive 5alpha-reductase inhibitor or with the androgen receptor antagonist flutamide. Animals were then killed after either 4 days or 6 weeks of treatment so that we could study the short- and long-term restorations of spermatogenesis. Stereological analysis showed that germ cell development between late pachytene spermatocytes to round spermatids in stage VII during either short- or long-term restoration was not affected by 5alpha-reductase inhibition, but it was affected by flutamide. The conversion of round spermatids between stages VII and VIII was restored by testosterone treatment, but this restoration was prevented by flutamide. Both the short- and long-term restorations of this midspermiogenic event were significantly decreased when 5alpha-reductase was inhibited. After long-term restoration of spermatogenesis, elongated spermatids were restored to 42% of control but were significantly suppressed to 20% of control by coadministration of the 5alpha-reductase inhibitor because of a reduction in the number of round spermatids progressing between stages VII and VIII. The results demonstrate that the 5alpha-reduction of testosterone is particularly important for progression through midspermiogenesis, because this phase of germ cell development is more sensitive to withdrawal of androgens. We suggest that testicular 5alpha-reductase activity is important for the restoration or maintenance of low levels of sperm production in a hormonally based contraceptive setting.

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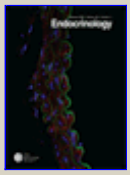

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