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JOURNAL ARTICLE

The effect of ketoconazole on endocrine and reproductive parameters in male mice and rats

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Ketoconazole has been shown to reduce steroidogenesis by inhibiting the cytochrome P-450 enzymes in these pathways. This finding, along with the observation that the compound reduces sperm motility, led us to study the effectiveness of ketoconazole as a male contraceptive agent administered in acute and chronic studies of both rats and mice. Four hours after a single administration, male rats showed significant reductions in both serum testosterone and corticosterone levels that completely recovered (testosterone) or nearly recovered (corticosterone) 24 hours after administration. Chronic administration of ketoconazole to male rats and mice resulted in steroid levels comparable with those of control animals. Epididymal sperm motility was only slightly reduced in male mice 4 hours after administration of the drug. No effect on sperm motility was noted after chronic administration in either species studied. In vitro exposure of epididymal sperm to ketoconazole resulted in a significant reduction of sperm motility. Breeding trials after ketoconazole administration resulted in normal fertility and fecundity even at the highest dosage studied. The lack of correlation between steroid levels and sperm immobilization, along with rapid in vivo and in vitro effects on sperm motility, suggests that the reduction in sperm motility is not related to a decrease in steroid levels. From these data, the authors conclude that ketoconazole is probably not a viable approach to the development of a male contraceptive.

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