

[P-43]**Effects of ketoconazole on reproductive organs and steroidogenic enzyme**

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Ketoconazole is a well-studied drug that blocks fungal growth and testosterone synthesis in humans and rodents by inhibiting the activity of cytochrome P-450 enzymes. But there were no reports that ketoconazole affects on enzymes related to degradation of testosterone. Aromatase converts testosterone to estradiol. Change of aromatase protein level may destroy hormone homeostasis. So, purpose of this study was to investigate the effect of ketoconazole on aromatase protein levels and to evaluate endocrine disruption effects of ketoconazole. We dosed to 20-day-old, 5-week-old and 7-week-old Sprague-Dawley (SD) male rats with ketoconazole(25, 50, 100mg/kg/day) daily by gavage for 14 days. Ketoconazole significantly decreased the weights of ventral prostate and Cowper's gland in 20-day-old SD male rats. In 5-week-old SD male rats, the weights of seminal vesicle, ventral prostate, LABC and Cowper's gland were decreased. In 7-week-old SD male rats, the weights of ventral prostate, Cowper's gland were decreased. Ketoconazole significantly decreased serum estradiol in 20-day-old and 5-week-old SD male rats, and significantly decreased serum 5 α -dihydrotestosterone (5 α -DHT) and testosterone in 7-week-old SD male rats. In comparison with control group, ketoconazole dose dependently increased aromatase protein levels in 20-day-old rats but decreased in 7-week-old rats. From above results, we found that ketoconazole altered enzymes related to degradation of testosterone. This suggests that these effects may be one of the action mechanisms of endocrine

disruption, but further studies are necessary to investigate hormone levels in testis organ in order to find a relation of aromatase protein levels with hormone levels. This study is supported by NITR/Korea FDA Grant ED 2002-8.