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Effects of in Utero Exposure of Di(n-butyl)phthalate and Flutamide on the Development of Reproductive Organs in Male Rats

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The aims of present study were to compare the effects of in utero exposure of several chemicals which have antiandrogenic characteristics on the development of reproductive organs and to investigate the specific mechanisms related to the abnormalities observed in the male reproductive system. During gestation days 10-19, pregnant Sprague-Dawley (SD) female rats were administered orally with corn oil (control), flutamide (1, 12.5, or 25 mg/kg/day) or Di(n-butyl)phthalate (DBP) (250, 500, or 700 mg/kg/day). Male offspring rats were killed at 31 and 42 days of age. At 31 and 42 days of age, the male reproductive tract abnormalities (hypospadias, cryptorchidism) were dose-dependently increased in the DBP or flutamide treated groups. The weights of testes and accessory sex organs (epididymides, seminal vesicles, ventral prostate, LABC, Cowper's glands) were significantly decreased in the DBP or flutamide group when compared to those of control. Epididymides cauda agenesis and ventral prostate atrophy were observed in the DBP (700 mg/kg/day) or flutamide (25 mg/kg/day) treated groups. At 31 days of age, the serum testosterone level significantly decreased in the DBP (700 mg/kg/day) treated group but slightly increased in the flutamide (25 mg/kg/day) treated group. At 42 days of age the serum testosterone and LH levels significantly decreased in the DBP (500 or 700mg/kg/day) treated groups but increased in the flutamide (25 mg/kg/day) treated group. The expression of AR in the penis decreased in the DBP (700 mg/kg/day) or flutamide (25 mg/kg/day) treated groups. These results demonstrate that exposure to antiandrogen during gestation days 10-19 causes changes in the endocrine system resulting in abnormal development of male reproductive organs.

Keyword : Endocrine disruptors, flutamide, di(n-butyl) phthalate (DBP), hypospadias