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Effects of Neonatal Exposure of Di (n-butyl) Phthalate and Flutamide on Male Reproduction in Rats

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In recent reports, the multiple reproductive defects such as cryptorchidism, hypospadias, epididymal cysts, low sperm counts, and testicular cancers are increased in humans, and these changes were doubted by the chemicals with estrogenic or antiandrogenic activities in our environment. To compare the effects of neonatal exposure of di (n-butyl) phthalate and flutamide on the development of reproductive organs and to identify the specific mechanisms of these abnormalities related to the male reproducton, Sprague-Dawley neonate male rats were injected subcutaneously during 5-14 days after birth with corn oil (control), flutamide (0.05, 0.1, and 0.5 mg/animal) and DBP (5, 10, and 20 mg/animal). Animals were killed at 31 (immature) and 42 (pubertal) days of age respectively and blood was collected from abdominal aorta for serum testosterone analysis. Testes, epididymides, seminal vesicles, ventral prostate, *levator ani plus bulbocavernosus muscle* (LABC), cowpers glands and glans penis were weighed. Expression of steroid hormone receptors (AR and ER) was examined in the testes and ventral prostate. At 31 days of age, ventral prostate, seminal vesicles, LABC, and cowpers glands significantly decreased in the flutamide (0.5 mg/animal) and DBP (20 mg/animal), but serum testosterone levels were not changed. Flutamide slightly delayed the testes descent at the high dose (0.5 mg/animal), but DBP did not show any significant effect on the testes descent at all doses. DBP and flutamide decreased the expression of AR protein in the testes but did not affect the expression of ERa and ER protein in the testes. At 42 days of age, ventral prostate, seminal vesicles, and cowpers glands weights were still significantly decreased at the high dose of flutamide (0.5 mg/animal) and DBP (20 mg/animal), but the weights of testes and epididymides were not different. Serum testosterone decreased significantly in DBP treated animals and slightly, not significantly, in flutamide group. While DBP still significantly decreased the expression of AR protein in testis, flutamide recovered from downregulation of AR protein and did not affect the expression of ERa and ER protein in the testes. Based on these results, flutamide and DBP have shown several similar patterns in reproductive abnormalitis, but some marked differences which may be caused by different acting mechanism.

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