BENZO(A)PYRENE PERTURBS OVARIAN FUNCTION BY SUPPRESSING E₂ SYNTHESIS

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Abstract: Epidemiological data suggest that smokers have delayed conception, premature ovarian failure leading to early menopause. Furthermore, these subjects have lower success rates when attempting pregnancy through IVF. However, the toxic agents in cigarette smoke, and their mechanisms of action responsible for the adverse effects of cigarette smoke on ovarian function have yet to be determined. Approximately 4000 chemicals, including polycyclic aromatic hydrocarbons (PAHs) are present in cigarette smoke. One of the PAHs, benzo(a)pyrene (BaP), a ubiquitous environmental pollutant found in cigarette smoke perturbs fertility. The mechanism by which BaP perturbs ovarian function is investigated in this study. Cycling female F-344 rats were given BaP (5mg/kg; exposure group) or vehicle (tricaprilyn) by oral gavage for 30 days. A week after the onset gavaging, daily vaginal histologies were used to determine the ability of BaP-exposed rat to continue cycling as well as the length of each cycle. At the second proestrus, blood samples were collected from anesthetized exposed and control rats for the determination of serum estrogen, LH and FSH concentrations by radioimmunoassay. Ovaries were harvested post CO₂ asphyxiation for determining the expression of pro-inflammatory bio-markers by RT-PCR. Estrogen and LH concentrations at proestrus were decreased (P<0.05) by BaP (estrogen, 51.0 ± 4; LH, 3.5 ± 0.15 pg/ml) versus control rats (estrogen, 70.2 ± 3.0; LH, 62. ± 0.2 ng/ml). On the contrary, serum FSH concentrations at proestrus were increased (P<0.05) in BaP-exposed (27.1 ± 2.9 ng/ml) rats compared with their control counterparts (9.3 ± 1.9 ng/ml). Furthermore, some pro-inflammatory biomarkers were significantly elevated in Bap-exposed versus control rats. We conclude that the reduced response of the ovaries to pituitary FSH stimulation, based on reduced estrogen synthesis and secretion at proestrus, is influenced by pro-inflammatory cytokines. As a consequence, increases in estrogen-stimulated LH secretion could not be realized.

Key words: Benzo(a)pyrene; estrous cycle; Proestrus; Estrogen; FSH; LH; Cytokines.

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