P43 Effect of Ethane Dimethane Sulfonate (EDS) on the Epididymal Sperm Counts and LH-related Gene Expressions in Rat

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Objectives: The maintenance of epididymal structure and function is dependent on testosterone. Ethane Dimethane sulfonate (EDS), a Leydig cell toxicant, has been widely used to create the reversible testosterone withdrawal rat model. The present study was carried out to test the effect of EDS administration on the restoration of epididymis and exert any specific effect on reproductive hormonal axis.

Materials and Methods: Adult male Sprague-Dawley rats (350~400 g B.W.) were injected with a single dose of EDS (75 mg/kg, i.p.) and sacrificed on days 0, 7, 14, 21, 28, 35, 42 and 49. Tissue weights (testis, epididymis and seminal vesicle) were measured, and serum LH levels were determined by specific radioimmunoassay. The destruction of Leydig cell was confirmed by semi-quantitative RT PCR and immunohistochemical studies (LH receptor). The transcriptional activities of common alpha subunit (Cα), LH beta subunit (LHβ) and hypothalamic KiSS-1 genes were evaluated by semi-quantitative RT-PCR.

Results: Weights of the reproductive and accessory organs declined progressively after the EDS treatment (days 7, 14, 21). After this, the decrease stopped, with a gradual return towards normal. Only 70% of recovery was found in epididymis during weeks 5-7. More dramatic drop was observed in cauda epididymal sperm counting, and the maximum recovery was 40% on week 7. Serum LH levels increased significantly on week 2 after EDS treatment, then gradually decreased during weeks 3-5. Change of Leydig cells and expression of LH receptor (LH-R) in testis declined sharply during weeks 1-2, then returned to normal on week 4. The transcripts for the Cα gene in epididymis increased sharply during weeks 1-2, then returned to normal on week 3. The transcripts for the KiSS-1 gene in hypothalamus and Cα gene in pituitary also increased sharply during weeks 1-2, then returned to normal on week 5.

Conclusions: The present results demonstrated the EDS might directly induce more severe damages such as tissue destruction and decline of sperm count in epididymis compared to those in testis and seminal vesicle. The expression of extragonadal LH might suggest that apoptosis and differentiation of sperm associated with LH control. Taken together, EDS injection model might be useful to understand not only the mechanism of differentiation of somatic and germ cells in male reproductive organs but the function of epididymis in aging process.

Key words: Ethane Dimethane sulfonate(EDS), Leydig cell, epididym's, LH-related genes

P44 Endocrine Disruptors, Genistein and Phthalate, on the Onset of Puberty in the Immature Female Rat

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Objectives: Genistein (GS) and di (2-ethyl hexyl)phthalate (DEHP) are well-known endocrine disruptors (EDs) that interfere with the endocrine system, leading to beneficial or detrimental effect not only in the reproductive process but in aging process. The purpose of this study was to elucidate whether GS or DEHP exert any effect on the onset of puberty in the immature female rat.

Materials and Methods: The testing drugs, GS (100 mg/kg/day) or DEHP (100 mg/kg/day), was administrated daily from postnatal day 25 (PND 25) to vaginal opening day of immature rats. Body weight was measured daily at 10 AM, and the rats were sacrificed on the day after vaginal opening (VO) occurred. Gross anatomy and wet weight of the ovary and uterus were compared between the vehicle-treated group and EDs-treated group. Furthermore, histological studies using paraffin section/hematoxylin & eosin staining were performed to identify the structural alterations in tissue and cellular levels. Specific radioimmunoassay (RIA) were carried out to measure serum LH levels. To determine the transcriptional changes in major reproductive parameters such as LH receptor (LHR) and steroid hormone receptors (of ER-α, ER-β and PR), total RNAs were extracted from ovary and uterus and were applied to semi-quantitative reverse transcription polymerase chain reaction (RT-PCR).

Results: Advanced VO (PND 31.2 ± 0.6) was shown in GS group while significantly delayed VO (PND 37.3 ± 0.7) was shown in DEHP group compared to vehicle group (PND 35.3 ± 0.7). The wet weights of ovary and uterus from GS group were significantly higher than those from vehicle group. Inversely, DEHP treatment decreased tissue weights and resulted in somewhat detrimental follicular structure. As expected, increased serum LH levels were shown in GS group. In the semi RT-PCR studies, the transcriptional activities of ER-α, ER-β, LHR, PR in both ovary and uterus from GS group were higher than those from vehicle group. Inversely, DEHP treatment decreased expression of those receptor genes.

Conclusions: The present studies demonstrated that GS and DEHP inversely act on reproductive system in immature female rats inducing precocious or delayed puberty, respectively.

Key words: genistein, phthalate, endocrine disruptors, puberty