

Effect of Ethane Dimethane Sulfonate(EDS) on the Gene Expression Profiles in Hypothalamic-Pituitary-Testis(HPT) Hormonal Axis in Rat

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Ethane dimethane sulfonate(EDS), a Leydig cell specific toxicant, has been widely used to create the reversible testosterone withdrawal rat model. In this model, reproductive parameters such as sperm counting are dramatically altered after EDS injection. As supplement of fresh Leydig cells proceeds, the parameters progressively go back to those of preinjection state. The aim of present study was to monitor the gene expression profiles in hypothalamic-pituitary-testis (HPT) hormonal axis up to 7 weeks after EDS injection.

Adult male Sprague-Dawley rats(350~400g B.W.) were injected with a single dose of EDS(75mg/kg i.p.) and sacrificed on weeks 0, 1, 2, 3, 4, 5, 6 and 7. Serum LH level was determined by specific radioimmunoassay. The change in Leydig cell population was determined by luteinizing hormone receptor(LHR) immunohistochemistry. The transcriptional activities of the genes related to reproductive hormonal axis were evaluated by semi-quantitative RT-PCRs.

The mRNA levels of hypothalamic gonadotropin-releasing hormone(GnRH) and KiSS-1 increased significantly during 1~3 weeks, then return to control level on week 5. In the anterior pituitary, the levels of message for common alpha subunit($C\alpha$) and LH beta subunit($LH\beta$) increased sharply during weeks 1~4, then return to normal on week 5. In contrast, expression of steroidogenic acute regulatory protein(StAR) and 3 beta-hydroxysteroid dehydrogenase(3β HSD) in testis decreased significantly during weeks 1~3, then recovered to normal levels after week 4. Serum LH level was sharply elevated on week 2, then gradually decreased during weeks 3~5.

The present study indicated that EDS treatment induced reversible alterations in the transcriptional activities of some crucial reproduction-related genes and the effects were reversible as expected. EDS injection model might be useful to understand the mechanism of hormonal regulation of male reproduction.

Key words) *Ethane Dimethane Sulfonate(EDS), Hypothalamic-pituitary-testis(HPT) hormonal axis, Gene expression profiles*