28 CAN PHTHALATES DISRUPT OOCYTE MEIOTIC MATURATION IN MOUSE MODEL?

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Background and aims: Phthalates, which are commonly used to render plastics into soft and flexible materials, have also determined as developmental and reproductive toxicants in human and animals. The purpose of this study was to evaluate the effect of mono-(2-ethylhexyl) phthalate (MEHP) and di-(2-ethylhexyl) phthalate (DEHP) oral administration on maturation of mouse oocytes, apoptosis and gene transcription levels.

Methods: Immature oocytes recovered from NMRI mouse strain (6–8 weeks) were divided into seven different experimental and control groups. Control group oocytes were retrieved from mice that received only normal saline. Experimental groups I, II or III oocytes were retrieved from mice treated with 50, 100 or 200 μl DEHP (2.56 μM) solution, respectively. Experimental groups IV, V or VI oocytes were retrieved from mouse exposed to 50, 100 or 200 μl MEHP (2.56 μM) solution, respectively. Fertilization and embryonic development were carried out in OMM and T6 medium. Apoptosis was assessed by annexin V-FITC/Dead Cell Apoptosis Kit with PI staining. In addition, the mRNA levels of *Pou5f1*, *Ccna1* and *Asah1* were examined in oocytes.

Results: The proportion of oocytes that progressed up to metaphase II (MII) and 2-cells embryo formation stage was significantly decreased by exposure to MEHP or DEHP, in a dose related pattern. Annexin V and PI positive oocytes showed greater quantity in treated mice than control. Quantitative RT-PCR revealed that expression levels of *Pou5f1*, *Asah1* and *Ccna1* were significantly lower in treated mouse oocytes than control.

Conclusion: These results indicate that oral administration of MEHP and DEHP could negatively affect mouse oocyte meiotic maturation and development *in vivo*, suggesting that phthalates could be risk factors for mammalians' reproductive health. Phthalate-induced changes in *Pou5f1*, *Asah1* and *Ccna1* transcription level explain in part the reduced developmental ability of mouse-treated oocytes.