

JCK Oral

JCK Oral 1 (II-JCKO1)

Basic/New Insights

Chair:Hiryoyuki Yamagishi(Department of Pediatrics, Keio University School of Medicine, Japan)

Chair:Yimin Hua(Department of Pediatric Cardiology, West China Second University Hosiptal, China)

Chair:Chung Il Noh(Department of Pediatrics, Seoul National University Hospital, Korea)

Sat. Jul 8, 2017 8:30 AM - 9:20 AM ROOM 3 (Exhibition and Event Hall Room 3)

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[II-JCKO1-04]Placental P-glycoprotein inhibition enhances susceptibility toDi(2-ethyhexyl)phthalateinduced cardiac malformations in mice

○Kaiyu Zhou, Wang Chuan, Yi Zhang, Yifei Li, Yimin Hua (Department of Pediatric Cardiology, West China Second University Hospital, Sichuan University, Chengdu, Sichuan, China)

Purpose:This study aims to explore whether inhibition of placental P-gp function with verapamil could enhance susceptibility to DEHP induced cardiac malformations in mice or not. **Methods:** The pregnant C57BL mice were randomized into the vehicle group (n=10), the DEHP group (n=20, 1g/Kg), the verapamil group (n=10, 3mg/Kg) and the DEHP+verapamil group (n=20). Pregnant dams in different groups received respective interventions by gavage once daily from E6.5-E14.5. Maternal weights were monitored everyday and samples were collected at E15.5. HE staining was used to examine fetal cardiac malformations. Fetal cardiac development-related genes (Nkx2.5/Gata4/Tbx5/Mef2c/Chf1) mRNA and protein expression were determined by quantitative real-timePCR (qRT-PCR) andwestern blot (WB), respectively. Maternal modality, maternal complete stillbirth/ abortion rates and fetal cardiac malformations rates were also calculated. **Results:** Maternal modality, maternal complete stillbirth/abortion rates and fetal cardiac malformations rates of DEHP+verapamil group were significantly higher than that of DEHP group, verapamil group and vehicle group. Compared with DEHP group, verapamil group and vehicle group, fetal cardiac Gata4/Mef2c/Chf1 expression was significantly down regulated in DEHP+verapamil group. There were no differences in above parameters between verapamil group and vehicle group.

Conclusions:Placental P-glycoprotein inhibition could enhance susceptibility to DEHP induced cardiac malformations in mice.