**THE EFFECT OF INTRAHEPATIC CHOLESTASIS OF PREGNANCY ON THE EXPRESSION AND FUNCTIONALITY OF PLACENTAL P-GLYCOPROTEIN IN MICE: IMPLICATIONS IN THE INDIVIDUALIZED TRANSPLACENTAL DIGOXIN TREATMENT FOR FETAL HEART FAILURE**

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*Introduction*: Placental P-glycoprotein (P-gp) plays a significant role in controlling digoxin transplacental rate. Investigations on P-gp regulation in placenta of women with different pregnant pathology are of great significance to individualized transplacental digoxin treatment for fetal heart failure (FHF). This study aimed to explore the effect of intrahepatic cholestasis of pregnancy (ICP) on the expression and functionality of placental P-gp in mice.

*Methods*: Pregnant dams in ICP group (n=8) and control group (n=8) received 17a-ethynylestradiol and propylene glycol by subcutaneous injection once daily from E12.5-E16.5, respectively. Maternal plasma ALT, AST, TB, DBIL, IDIL, γ-GT, LDH, ALP and TBA concentrations were detected. HE staining was applied for the observation of liver cells degeneration, necrosis and intrahepatic cholestasis. Placental *Abcb1a/Abcb1b/HIF-1α* mRNA and P-gp/HIF-1α protein expression were determined by real-time quantitative PCR and western-blot. Maternal plasma and fetal-unit digoxin concentrations were detected by a commercial kit assay.

*Results*: The ICP group showed higher levels of maternal plasma ALT, AST, TB, DBIL, IDIL, γ-GT, LDH, ALP and TBA concentrations, higher fetal still-birth/abortion rates, lower placental and fetal weights, and typical liver cells degeneration, necrosis and intrahepatic cholestasis. The placental *Abcb1a* mRNA and P-gp expression of ICP group were significantly increased, while digoxin transplacental rates were significantly decreased. Both placental *HIF-1α* mRNA and protein expression was significantly elevated in ICP group, and there was a positive correlation between *Abcb1a* mRNA and *HIF-1α* mRNA.

*Conclusions*: ICP could up-regulate placental P-gp expression and functionality in mice, which might be partially associated with higher expression of HIF-1α.