Abstract

Aims. P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) are efflux transporters expressed in the placenta, limiting their substrates from reaching the fetus. Our aim was to investigate if concomitant prenatal exposure to several substrates or inhibitors of these transporters increases the risk of congenital anomalies.

Methods. The national 'Drugs and Pregnancy' database, years 1996-2014, was utilized in this population-based birth cohort study. In the database, the Medical Birth Register, the Register on Induced Abortions, the Malformation register and the Register on Reimbursed Drug Purchases have been linked. The University of Washington Metabolism and Transport Drug Interaction Database was used to identify substrates and inhibitors of P-gp and BCRP. We included singleton pregnancies ending in birth or elective termination of pregnancy due to fetal anomaly. Known teratogens were excluded. We identified women exposed one month before pregnancy or during the first trimester to P-gp/BCRP polytherapy (n=21,186); P-gp/BRCP monotherapy (n=97,906); non-P-gp/BCRP polytherapy (n=78,636), and unexposed (n=728,870). We investigated the association between the exposure groups and major congenital anomalies using logistic regression adjusting for several confounders.

Results. The prevalence of congenital anomalies was higher in the P-gp/BCRP polytherapy group (5.5%) compared to the P-gp/BCRP monotherapy (4.7 %, OR 1.13; 95% CI 1.05-1.21), the non-P-gp/BCRP polytherapy (4.9%, OR 1.14; 95% CI 1.06-1.22), and to the unexposed group (4.2 %, OR 1.23; 95 % CI 1.15-1.31).

Summary / Conclusions. The results suggest a role of placental transporter-mediated drug interactions in teratogenesis.

Keywords: drug transporters, P-glycoprotein, pregnancy, birth defects, placenta