THE EFFECTS OF CANDIDATE GENE IN PKPD PATHWAY ON ANTIPSYCHOTICS-INDUCED AMENORRHEA IN FEMALE SCHIZOPHRENIA PATIENTS

Phuong T. T Nguyen¹, Ho-Sook Kim¹ ², Jung-Jun Moon², Eun-Young Kim¹ ², Joo-Cheol Shim², Jong-Lyul Ghim¹ ², Jae-Gook Shin¹ ²

¹Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of Medicine, Korea, ²Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Korea

BACKGROUND: The aim of this study was to explore the genetic effects of candidate single nucleotide polymorphisms (SNPs) in pharmacokinetics and pharmacodynamics (PKPD) pathway of AP on AP-induced amenorrhea in female schizophrenia patients.

METHODS: Eighty nine female schizophrenic patients (age range from 18 to 40) taking the same AP for more than 3 months were enrolled. Amenorrhea was defined as the absence of menses for three months or three periods in a row. The serum levels of prolactin, estradiol (E2), Follicle-stimulating hormone (FSH), Luteinizing hormone (LH), and thyroid-stimulating hormone (TSH) were measured. Cytochrome P450 2D6 (CYP2D6), dopamine receptor D2 (DRD2) and estrogen receptor 1 (ESR1) were genotyped.

RESULTS: Compared to the patients without amenorrhea (n=67), prolactin levels was higher (71.5 vs. 94.1 ng/mL; p=0.044) and E2 was lower (46.7 vs. 27.0; p=0.007) in the patients with amenorrhea (n=22). There was no difference in other hormones and baseline characteristics between the patient with and without amenorrhea. Amisulpiride, chlorpromazine, haloperidol, paliperidone, and risperidone were observed to highly increase prolactin level and categorized to drugs increasing prolactin level.

DRD2 -141insC (OR=0.59, 95% CI=0.34-0.99; p=0.049) and drugs increasing prolactin level (OR=6.17, 95% CI=1.28-29.64; p=0.023) were identified as predictors for AP-induced amenorrhea using multiple logistic regression analysis identified.

CONCLUSION: This finding is the first evidence suggesting that DRD2 -141insC might be a possible protective biomarker for AP-induced amenorrhea. Further studies to confirm the DRD2 -141insC as a biomarker for AP-induced amenorrhea are needed in larger female antipsychotic patients.