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Impact of CYP2C19 Genotype on Escitalopram Exposure and Therapeutic Failure: A Retrospective Study Based on 2,087 Patients

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Abstract

Objective: The antidepressant escitalopram is predominantly metabolized by the polymorphic CYP2C19 enzyme. The authors investigated the effect of CYP2C19 genotype on exposure and therapeutic failure of escitalopram in a large patient population.

Method: A total of 4,228 escitalopram serum concentration measurements from 2,087 CYP2C19-genotyped patients 10-30 hours after drug intake were collected retrospectively from the drug monitoring database at Diakonhjemmet Hospital in Oslo. The patients were divided into subgroups based on CYP2C19 genotype: those carrying inactive (CYP2C19Null) and gain-of-function (CYP2C19*17) variant alleles. The between-subgroup differences in escitalopram exposure (endpoint: dose-harmonized serum concentration) and therapeutic failure (endpoint: switching to another antidepressant within 1 year after the last escitalopram measurement) were evaluated by multivariate mixed model and chi-square analysis, respectively.

Results: Compared with the CYP2C19*1/*1 group, escitalopram serum concentrations were significantly increased 3.3-fold in the CYP2C19Null/Null group, 1.6-fold in the CYP2C19*Null/*1 group, and 1.4-fold in the CYP2C19Null/*17 group, whereas escitalopram serum concentrations were significantly decreased by 10% in the CYP2C19*1/*17 group and 20% in the CYP1C19*17/*17 group. In comparison to the CYP2C19*1/*1 group, switches from escitalopram to another antidepressant within 1 year were 3.3, 1.6, and 3.0 times more frequent among the CYP2C19Null/Null, CYP2C19*1/*17, and CYP1C19*17/*17 groups, respectively.

Conclusions: The CYP2C19 genotype had a substantial impact on exposure and therapeutic failure of escitalopram, as measured by switching of antidepressant therapy. The results support the potential clinical utility of CYP2C19 genotyping for individualization of escitalopram therapy.

Keywords: Antidepressants; CYP2C19; Escitalopram; Genetics; Pharmacokinetics.

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