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Abstracts

Articles appearing in the April 2019 issue

Poor glycemic control and posterior circulation ischemic stroke

Background This study aimed at determining whether diabetes or glucose metabolism is associated with ischemic stroke in the posterior circulation.

Methods We included 10,245 patients with acute ischemic stroke (mean age 72.7 ± 12.5 years, men 59.5%) who were enrolled in a multicenter hospital-based stroke registry in Fukuoka, Japan, between June 2007 and August 2016. Posterior circulation ischemic stroke (PCIS) was defined as brain infarction in the territory of the posterior cerebral artery and vertebro-basilar arteries. We investigated the associations between diabetes or glycemic parameters, including plasma glucose concentrations, hemoglobin A1c, and the homeostatic model assessment of insulin resistance (HOMA-IR), and PCIS using logistic regression analysis. To improve covariate imbalance, we further evaluated associations after propensity score matching using 1:1 nearest neighbor matching and inverse probability weighting.

Results Diabetes was significantly associated with PCIS even after adjusting for multiple confounding factors (odds ratio—OR [95% CI], 1.37 [1.25–1.50]). Similarly, fasting (1.07 [1.02–1.12]/SD), casual plasma glucose (1.16 [1.11–1.20]/SD) concentrations, and hemoglobin A1c (1.12 [1.08–1.17]/SD), but not HOMA-IR (1.02 [0.97–1.07]/SD), were associated with PCIS. These associations were maintained in patients with ischemic stroke because of thrombotic etiology and were unchanged even after the propensity score matching methods. In patients with diabetes, the ORs of PCIS further increased with an increase in hemoglobin A1c and the presence of microvascular complications.

Conclusions Poor glycemic control may be associated with an increased risk of thrombotic infarction that occurs preferentially in the posterior circulation of the brain.

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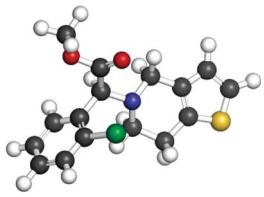
Role of CYP2C19 alleles in the management of recurrent ischemic stroke



Purpose of review CYP2C19 is the primary enzyme involved in the activation of clopidogrel, an antiplatelet agent used for secondary stroke prevention. An individual's *CYP2C19* alleles are used to understand their *CYP2C19*-clopidogrel metabolizer phenotype. Single nucleotide polymorphisms of the *CYP2C19* gene result in altered metabolism of this prodrug.

Recent findings Three ischemic stroke cases were treated with clopidogrel. Despite confirming adequate drug exposure, medication adherence, and ruling out drug-drug interactions, all had recurrent ischemic stroke. Each case had a *CYP2C19* *2/*17 genotype, categorizing them as intermediate clopidogrel metabolizers. Even with the gain-of-function allele, the loss-of-function allele resulted in lack of prodrug activation, leading to decreased efficacy in platelet inhibition.

Summary These cases illustrate the importance of a thoughtful approach to secondary stroke prevention and demonstrate the utility of pharmacogenomic testing in clopidogrel hyporesponders. Recognition of the importance of *CYP2C19* genotyping has the potential to enable better selection of appropriate secondary prevention strategies.

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