Hubungan Polimorfisme Gen ABCB1 Terhadap Variabilitas Respons Clopidogrel pada Stroke Iskemik = The Association between ABCB1 Gene Polymorphism and Clopidogrel Response Variability in Ischemic Stroke

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Abstrak

Latar Belakang. Clopidogrel adalah salah satu pilihan antiplatelet pada kasus stroke iskemik yang bekerja dengan menghambat ikatan adenosine diphosphate (ADP) dengan reseptor P2Y12. Gen ABCB1 diketahui mengkode transporter P-glikoprotein (P-gp) multidrug resistance-1 (MDR1) yang mempengaruhi absorpsi clopidogrel di usus, sehingga mempengaruhi efektivitasnya dalam mencegah agregasi trombosit. Penelitian ini bertujuan untuk menilai peran polimorfisme gen ABCB1 terhadap variabilitas respons clopidogrel yang dilihat dari agregasi trombosit serta mengetahui frekuensi genotip ABCB1 pada populasi.
Metode. Studi potong lintang dilakukan pada pasien stroke iskemik yang mengkonsumsi clopidogrel di RSUI/RSCM pada 2020-2023. Dilakukan pemeriksaan polimorfisme ABCB1 C3435T dan C1236T serta agregasi trombosit dengan VerifyNow PRU. Variabilitas respons clopidogrel dikelompokkan menjadi tidak respons (>208 PRU), respons (95-208 PRU), dan risiko perdarahan (<95 PRU).
Hasil. Sebanyak 124 subjek direkrut dalam penelitian, dengan 12,9% subjek tidak respons, 45,9% respons, dan 41,9% lainnya memiliki risiko perdarahan terhadap pemberian clopidogrel. Genotip homozigot wildtype (CC) pada ABCB1 C1236T memiliki kemungkinan risiko perdarahan pada konsumsi clopidogrel 3,76 kali lebih tinggi (p=0,008; 95%CI 1,41-10,07) dibandingkan varian lainnya (CT/TT). Frekuensi genotip ABCB1 C3435T subjek pada kelompok homozigot wildtype, heterozigot, dan homozigot varian berturut-turut sebesar 35,9%, 43,5% dan 16,9%. Sementara itu, pada genotip C1236T berturut-turut sebesar 17,8%, 39,5%, dan 42,7%.
Kesimpulan. Genotip ABCB1 C1236T varian homozigot wildtype memiliki kemungkinan risiko perdarahan 3,76 kali lebih tinggi pada pemberian clopidogrel. Frekuensi genotip terbanyak pada ABCB1 C1236T adalah homozigot varian, sementara pada ABCB1 C3435T adalah heterozigot.
.....Background. Clopidogrel has been the primary choice of antiplatelet in ischemic stroke that inhibits adenosine diphosphate (ADP)-induced platelet aggregation. P-glycoprotein (P-gp) multidrug resistance-1 (MDR1) is a transmembrane efflux transporter in intestinal cells that plays a significant role in clopidogrel absorption, therefore may affect platelet aggregation. P-gp is encoded by the ABCB1 gene. This study aims to evaluate the effect of ABCB1 polymorphism on clopidogrel response variability in ischemic stroke patients and its genotype frequency.
Methods. A cross-sectional study was conducted in ischemic stroke patients who received clopidogrel between 2020-2023 in RSUI/RSCM. All subjects were assessed for ABCB1 polymorphisms C3435T and C1236T. Platelet aggregation were measured using VerifyNow PRU. Clopidogrel response variability was classified into unresponsive (>208 PRU), responsive (95-208 PRU), and bleeding risk (<95 PRU).
Results. 124 subjects enrolled in this study, with 12,9% of subjects classified as non-responsive/resistant, 49,5% as responsive, and 41,9% as bleeding risk. ABCB1 C1236T homozygote wildtype (CC) was associated with 3,76 times higher bleeding risk than other variants (p=0,008; 95%CI 1,41-10,07). Genotype

frequency of ABCB1 C3435T homozygote wildtype, heterozygote, and homozygote variants were 35,9%, 43,5% and 16,9%, respectively; while the genotype frequency of ABCB1 C1236T were 17,8%, 39,5%, and 42,7%, respectively.
Conclusion. ABCB1 C1236T homozygote wildtype was associated with 3,76 times higher bleeding risk than other variants. The most common genotype frequency of ABCB1 C1236T was homozygote variant; while for ABCB1 C3435T was heterozygote.