

Hubungan polimorfisme CYP2C19*2 dan CYP2C19*3 terhadap inhibisi agregasi trombosit pada pasien sindroma koroner akut yang telah diberikan clopidogrel : aplikasi regresi linier ganda dan regresi logistik ganda = The association of CYP2C19*2 and CYP2C19*3 polymorphisms with platelet aggregation inhibition in acute coronary syndrome

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Abstrak

Latar Belakang: Respon antar-individu yang bervariasi terhadap obat antiplatelet (clopidogrel) telah dilaporkan. Perbedaan tingkat metabolisme clopidogrel untuk metabolit aktif tiol menggambarkan variabilitas antar-individu dalam penghambatan trombosit. Sitokrom P450C19 (CYP2C19) memetabolisme zat metabolit aktif tiol. Carrier polimorfisme yang menyebabkan hilangnya fungsi CYP2C19 * 2 dan * 3 alel pada terapi antiplatelet mengakibatkan berkurangnya penghambatan agregasi trombosit. Informasi mengenai hubungan antara CYP2C19 * 2 dan * 3 dengan inhibisi agregasi trombosit pada pasien Sindroma koroner akut di Indonesia masih terbatas. Tujuan dari penelitian ini adalah untuk mengetahui hubungan antara dua varian, CYP2C19 * 2 (681G>A) dan CYP2C19 * 3 (636G>A) terhadap penurunan fungsi inhibisi agregasi trombosit.

Bahan dan Metode: Desain penelitian cross sectional. Jumlah responden adalah 114 orang (dipilih berdasarkan kriteria inklusi dan kriteria eksklusi). Pemeriksaan polimorfisme CYP2C19 dilakukan dengan menggunakan teknik Real Time-Polymerase Chain Reaction (RT-PCR) TaqMan SNP Genotyping Assays dengan alat dari applied Biosystems 7500 Fast/7900HT Fast Real Time PCR Systems (in standart or 9600 emulation mode). Inhibisi agregasi trombosit diperiksa dengan menggunakan metode Light Transmisi Aggregometry (LTA) dengan alat Helena AggGRAM Analyzer pada penambahan 5umol/L ADP sebagai agregator.

Hasil: Distribusi inhibisi agregasi trombosit menunjukkan perbedaan rerata antara responden non carier polimorfisme dengan responden carier polimorfisme (16,9 CI95%: 12,1-21,6 vs 9,4 CI95%: 2,9 - 15,0). Analisis regresi linier menunjukkan bahwa responden carier polimorfisme memiliki inhibisi agregasi trombosit lebih rendah dibandingkan dengan responden non carier polimorfisme. Analisis regresi logistik menunjukkan bahwa responden carier polimorfisme mempunyai odds untuk merespon kurang baik terhadap clopidogrel sebesar 1,9 kali jika dibandingkan dengan responden yang non carier setelah dikontrol oleh variabel umur dan jenis kelamin, hal tersebut mengindikasikan bahwa carier polimorfisme mempunyai inhibisi yang rendah terhadap agregasi trombosit.

Kesimpulan: Temuan kami membuktikan adanya hubungan antara CYP2C19 * 2 dan * 3 polimorfisme dengan inhibisi agregasi trombosit.

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Background: Inter-individual variability in response to antiplatelet drugs (clopidogrel) has been reported. The difference in the extent of metabolism of clopidogrel to its active metabolite tiol is the most plausible mechanism for the observed inter-individual variability in platelet inhibition. The cytochrome P450C19 (CYP2C19) metabolizes the active metabolite tiol. The carrier polymorphisms of reduced - functions of

CYP2C19*2 and *3 allele on antiplatelet therapy showed diminished platelet aggregation inhibition. There is limited information on the association between CYP2C19 *2 and *3 with platelet aggregation inhibition in ACS patients generally in Indonesia Population. The aim of this study was to determine the association between two variants, CYP2C19*2 (681G>A) and CYP2C19*3 (636G>A) reduced function with platelet aggregation inhibition.

Material & Method: a cross sectional study was done with 114 subjects (selected by inclusions and exclusions criteria). The CYP2C19 polymorphisms were genotype using the PCR method with TaqMan SNP Genotyping Assays from applied Bio systems 7500 Fast/7900HT Fast Real Time PCR Systems (in standard or 9600 emulation mode). The platelet aggregation inhibition was tested using Light Transmission Aggregometry (LTA) by Helena AggGRAM Analyzer with 5umol/L ADP as aggregator.

Results: The distribution of platelet inhibition aggregation showed difference between respondents with non-carrier polymorphisms and carrier polymorphisms (16,9 CI95%: 12,1 -21,6 vs 9,4 CI95%: 2,9 - 15,0). The linier regression analysist indicated that the carrier polymorphisms have lowest platelet aggregation inhibition compared with non-carrier polymorphisms. The logistic regression analysis indicated that carrier polymorphisms respondents has 1,9 odds to be low response to clopidogrel if compared with non-carrier polymorphisms respondents after adjusted with age and sex and it is indicated that it has low platelet aggregation inhibition.

Conclusion: Our present findings the evidence of an association between CYP2C19 *2 and *3 polymorphisms and platelet aggregation inhibition.