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Frekuensi distribusi alel mutan Gen CYP2C8 pada suku Nias = Frequency distribution of CYP2C8 gene mutant alleles in Nias ethnic group

Instiaty, author

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Abstrak

ABSTRAK
Gen CYP2C8 mempunyai beberapa alel mutan yang menyandi enzim CYP2C8 dengan kapasitas metabolisme yang rendah. Enzim CYP2C8 berperanan penting dalam metabolisme antimalaria amodiakuin menjadi metabolit aktifnya desetilamodiakuin sehingga mutasi pada gen CYP2C8 diduga berpotensi menyebabkan kegagalan terapi maupun kejadian efek samping agranulositosis yang dipicu oleh metabolit nonenzimatiknya amodiakuinkuinonimin.

Penelitian observasional ini bertujuan untuk mengetahui frekuensi distribusi alel mutan gen CYP2C8 yaitu CYP2C8*2, CYP2C8*3, dan CYP2C8*4 pada salah satu kelompok etnik yang tinggal di daerah endemik malaria, yaitu suku Nias. Analisis PCR-RFLP untuk identifikasi alel gen CYP2C8 yang dilakukan pada 214 sampel berupa tetes darah di kertas saring (dot blot) dan subjek suku Nias memperlihatkan bahwa semua sampel membawa alel normal (wild type). Dengan tidak ditemukannya alel mutan gen CYP2C8 pada suku Nias, kita dapat berharap bahwa kemungkinan kegagalan terapi amodiakuin dan efek samping obat akibat metabolit nonenzimatiknya pada suku Nias tidak berkaitan dengan polimorfisme gen CYP2C8.
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ABSTRACT
The CYP2C8 gene has been documented to have several alleles encoding enzyme with low metabolic capacity. Since CYP2C8 plays a major role in metabolizing antimalarial drug amodiaquine to its active metabolite desethylamodiaquine, it is assumed that mutation in CYP2C8 gene may potentially lead to treatment failure or to occurrence of adverse drug reactions such as agranulocytosis induced by its nonenzymatic metabolite amodiaquinequinoneimine.

The aim of this study was to determine the frequency distribution of CYP2C8 mutant alleles particularly CYP2C8*2, CYP2C8*3 and CYP2C8*4 in one of the ethnic group that resides in malaria endemic area, Nias. PCR-RFLP analysis of 214 dot blot samples from Nias ethnic group subjects revealed that all of the samples carried the wild type allele of the CYP2C8 gene. In the absence of mutant alleles of CYP2C8 among Nias ethnic group, one can expect that treatment failure in amodiaquine therapy and adverse drug reactions associated with reactive metabolite of the drug are not related with CYP2C8 genetic polymorphisms.</i>