Polimorfisme Gen Sitokrom P450 2C8, Sitokrom P450 1A1, Sitokrom P450 1B1 pada Kasus Gagal Obat Artemisinin-based Combination Therapy (Artesunat-Amodiakuin) di Sumba, Indonesia = Polymorphisms of Cytochrome P450 2C8, Cytochrome P4501A1, Cytochrome P450 1B1 Genes in the Treatment Failure of Artemisinin-based Combination Therapy (Artesunate-Amodiaquine) in Sumba, Indonesia

Fitriah, author

Abstrak

[Pendahuluan
Artesunat amodiakuin (AS-AQ) merupakan artemisinin-based combination therapy (ACT) yang digunakan sebagai lini pertama di berbagai daerah endemik di Indonesia. Studi sebelumnya pada pasien malaria falsiparum tanpa komplikasi di Sumba Indonesia menunjukkan gagal terapi sebesar 11,1%. Diduga salah satu penyebab kegagalan terapi adalah polimorfisme gen sitokrom P450 2C8 (CYP2C8), CYP1A1 dan CYP1B1. Penelitian ini bertujuan untuk mempelajari peran polimorfisme pada gen pemetabolisme artesunat amodiakuin terhadap kegagalan terapi amodiakuin.
Metodologi
Analisis polimorfisme CYP2C8*2, CYP2C8*3, CYP1A1*2, CYP1B1*2 dan CYP1B1*3 dilakukan pada pasien malaria falsiparum yang mendapatkan AS-AQ di Sumba Indonesia (N=110). Single nucleotide polymorphisms (SNPs) dianalisis menggunakan polymerase chain reaction (PCR) dilanjutkan dengan retriction-fragment length polymorphism (RFLP) dan sekuensing.
Hasil
Tidak ditemukan alel CYP2C8*2 dan alel CYP2C8*3 pada sampel penelitian (N=110). Frekuensi alel CYP1A1*2, CYP1B1*2 dan CYP1B1*3 berturut-turut sebanyak 5%, 23,6% dan 4,1%. Tidak ditemukan kemaknaan pada analisis haplotipe CYP1B1*2 (p=0,13, 95% CI: 0,11 – 1,34) dan CYP1B1*3 (p=0,34, 95% CI: 0,44 – 11,34). Hanya ditemukan tipe heterozigot pada alel CYP1A1*2 dan CYP1B1*3.
Kesimpulan
Tidak ditemukan hubungan antara alel CYP2C8*2, CYP2C8*3, CYP1A1*2, CYP1B1*2 dan CYP1B1*3 dengan kegagalan terapi amodiakuin di Sumba, Indonesia.;Introduction
Artesunate amodiaquine (AS-AQ) is one of the ACT used in many endemic areas in Indonesia. Previous study in Sumba showed that there were 11,1% treatment failure with AS-AQ in uncomplicated malaria falciparum patients. Polymorphisms in cytochrome P450 2C8 (CYP2C8), CYP1A1 and CYP1B1 genes are thought to be the major factors in the treatment failure of amodiaquine. The aim of this study was to analyze the role of polymorphisms in the genes encoding amodiaquine metabolizing enzymes (CYP2C8, CYP1A1, CYP1B1) in the treatment failure of amodiaquine.
Methodology
Polymorphisms of CYP2C8*2, CYP2C8*3, CYP1A1*2, CYP1B1*2 and CYP1B1*3 were studied in patients with malaria falciparum treated with AS-AQ in Sumba Indonesia (N=110). Single nucleotide polymorphisms (SNPs) were analyzed using polymerase chain reaction (PCR) continued with restriction-

fragment length polymorphism (RFLP) and sequencing.
Results
There were no CYP2C8*2 and CYP2C8*3 alleles found in the samples (N=110). The frequency of CYP1A1*2, CYP1B1*2 and CYP1B1*3 alleles were 5%, 23,6% and 4,1%, respectively. There were no significant difference in haplotype analysis of CYP1B1*2 (p value=0,13, 95% confidence interval=0,11 – 1,34) and CYP1B1*3 (p value=0,34, 95% confidence interval=0,44 – 11,34). Heterozygote types were found in CYP1A1*2 and CYP1B1*3 alleles.
Conclusions
There were no associations between CYP2C8*2, CYP2C8*3, CYP1A1*2, CYP1B1*2 and CYP1B1*3 alleles with treatment failure of amodiaquine in Sumba, Indonesia., Introduction
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