

Polimorfisme dan ekspresi gen multidrug resistant-1 C3435T, serta kadar plasma karbamazepin penderita epilepsi lobus temporal =  
Polymorphism and gene expression of multidrug resistant 1 C3435T and carbamazepine plasma concentration in temporal lobe epilepsy patient

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Abstrak

**ABSTRAK**

Latar belakang: Pada semua sindrom epilepsi, epilepsi lobus temporal ELT memiliki kemungkinan paling besar untuk menjadi resisten terhadap obat. Polimorfisme gen multidrug resistant-1 MDR1 C3435T dicurigai sebagai salah satu penyebabnya. Di RS Cipto Mangunkusumo RSCM, sebagai pusat rujukan nasional, prevalensi ELT potensial resisten obat adalah 84.51 dan duapertiganya dalam terapi karbamazepin KBZ. Tujuan: Mengetahui polimorfisme dan ekspresi gen MDR1 C3435T serta kadar plasma KBZ pada penderita epilepsi yang responsif dan resisten terhadap obat. Metode: Penelitian potong lintang komparatif dilakukan di RSCM dari Juni 2015 sampai Desember 2016. Penderita ELT dipilih secara konsekutif. Kelompok kontrol terdiri dari subjek sehat tanpa riwayat epilepsi. Identifikasi genotipe menggunakan teknik restriction Fragment Length Polymorphism PCR dengan enzim restriksi Mbo1. Pemeriksaan kadar plasma KBZ menggunakan High Performance Liquid Chromatography. Ekspresi mRNA dengan metode sequencing and real time quantitative PCR. Hasil: Didapatkan 61 subjek dan 25 kontrol. Sebaran genotipe TT 71,43 dan alel T genotipe CT dan TT lebih tinggi pada grup resisten  $x = 10,41$ ;  $p = 0,001$ . Terdapat korelasi sangat kuat antara dosis dan kadar plasma KBZ pada grup responsif  $r = 0,75$ ;  $p = 0,000$  dengan rerata dosis 405,21 226,50 mg dan kadar plasma 7,59 2,32 mcg/mL. Ekspresi kuantitatif relatif Rq mRNA paling tinggi pada grup kontrol diikuti resisten dan responsif. Genotipe TT menunjukkan Rq yang berbeda pada tiap grup. Terdapat perbedaan bermakna antara dosis dan kadar plasma KBZ pada masing-masing genotipe tiap grup, terutama antar genotipe CT responsif dengan semua genotipe grup resisten. Kesimpulan: Genotipe TT dan alel T MDR1 C3435T secara statistik berhubungan dengan dosis dan kadar plasma KBZ yang lebih tinggi pada ELT resisten obat.

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**ABSTRACT**

Background Among epilepsy syndrome, temporal lobe epilepsy TLE has the highest probability to become drug resistant. Multidrug resistant 1 MDR1 C3435T polymorphism was suspected to be one of the caused. In Cipto Mangunkusumo hospital RSCM, as the national reference hospital, potential drug resistant epilepsy prevalence was 84.51 and carbamazepine CBZ usage in two third of the patients. Objective This study was performed to learn about MDR1 C3435T polymorphism and expressions, and CBZ plasma concentration in drug responsive and resistant temporal lobe epilepsy patients. Methods A comparative cross sectional study was performed in RSCM. TLE patients were selected consecutively. Healthy people were also selected as the control group. Restriction Fragment Length Polymorphism PCR technique with Mbo1 restriction enzyme was used to identify the genes. High Performance Liquid Chromatography method was used to determine CBZ concentration in plasma. mRNA expressions identification were using sequencing and real time quantitative PCR methods. Result There were 61 subjects in study group and 25 in control group.

Frequency of TT genotype 71.43 and T allele CT and TT genotype were higher in resistant one  $\chi^2$  10.41,  $p$  0.001. There was a very strong correlation between CBZ plasma concentration in drug responsive epilepsy  $r$  0.75,  $p$  0.000 in mean dosage of 405,21 226,50mg and plasma concentration of 7,59 2,32mcg mL. mRNA expressions were highest in control group followed by resistant and responsive ones. TT genotype expression was relatively different in each group. There were significant differences between genotype in each group with CBZ dosage and plasma concentration, especially in CT responsive compare to all genotypes in resistant group. Conclusion TT genotype and T allele of MDR1 C3435T statistically associated with higher CBZ dosage and plasma concentration in drug resistant TLE patients.