Polimorfisme dan ekspresi gen multidrug resistant-1 C3435T, serta kadar plasma karbamazepin penderita epilepsi lobus temporal = Polimorphism 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 salahsatu penyebabnya. Di RS Cipto Mangunkusumo RSCM , sebagai pusat rujukannasional, prevalensi ELT potensial resisten obat adalah 84.51 dan duapertiganya dalam terapi karbamazepin KBZ .Tujuan: Mengetahui polimorfisme dan ekspresi gen MDR1 C3435T serta kadarplasma KBZ pada penderita epilepsi yang responsif dan resisten terhadap obat.Metode: Penelitian potong lintang komparatif dilakukan di RSCM dari Juni 2015sampai Desember 2016. Penderita ELT dipilih secara konsekutif. Kelompokkontrol terdiri dari subjek sehat tanpa riwayat epilepsi. Identifikasi genotipemenggunakan teknik restriction Fragment Length Polymorphism PCR denganenzim restriksi Mbo1. Pemeriksaan kadar plasma KBZ menggunakan HighPerformance Liquid Chromatography. Ekspresi mRNA dengan metodesequencing and real time quantitative PCR.Hasil: Didapatkan 61 subjek dan 25 kontrol. Sebaran genotipe TT 71,43 danalel 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 padagrup responsif r = 0,75; p = 0,000 dengan rerata dosis 405,21 226,50mg dankadar plasma 7,59 2,32mcg/mL. Ekspresi kuantitatif relatif Rq mRNA palingtinggi pada grup kontrol diikuti resisten dan responsif. Genotipe TT menunjukkanRq yang berbeda pada tiap grup. Terdapat perbedaan bermakna antara dosis dankadar plasma KBZ pada masing-masing genotipe tiap grup, terutama antaragenotipe CT reponsif dengan semua genotipe grup resisten.Kesimpulan: Genotipe TT dan alel T MDR1 C3435T secara statistik berhubungandengan 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 thehighest probability to become drug resistant. Multidrug resistant 1 MDR1 C3435T polymorphism was suspected to be one of the caused. In CiptoMangunkusumo hospital RSCM , as the national reference hospital, potentialdrug resistant epilepsy prevalence was 84.51 and carbamazepine CBZ usagein two third of the patients.Objective This study was performed to learn about MDR1 C3435T polymorphismand expressions, and CBZ plasma concentration in drug responsive and resistanttemporal lobe epilepsy patients.Methods A comparative cross sectional study was performed in RSCM. TLEpatients were selected consecutively. Healthy people were also selected as thecontrol group. Restriction Fragment Length Polymorphism PCR technique withMbo1 restriction enzyme was used to identify the genes. High Performance LiquidChromatography method was used to determine CBZ concentration in plasma.mRNA expressions identification were using sequencing and real timequantitative PCR methods.Result There were 61 subjects in study group and 25 in control group.

Frequencyof TT genotype 71.43 and T allele CT and TT genotype were higher inresistant one x2 10.41, p 0.001 . There was a very strong correlationsbetween 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 byresistant and responsive ones. TT genotype expression was relatively different ineach group. There were signifant differences between genotype in each groupwith CBZ dosage and plasma concentration, especially in CT responsivecompare to all genotypes in resistant group.Conclusion TT genotype and T allele of MDR1 C3435T statistically associatedwith higher CBZ dosage and plasma concentration in drug resistant TLE patients.