ABSTRACT

Introduction : Individuals' responses to certain AEDs are differed according to various acquired and genetic factors. Understanding the pharmacogenetic aspect and its interaction with associated clinical factors play a key role in predicting drug response, making a tailored treatment for every individual possible. SCN1A gene encodes NaV1.1 sodium channel in the central nervous system that serves as the target for many antiepileptic drugs (AEDs) including phenytoin. Our study aimed to investigate the association of SCN1A polymorphism (SNP rs3812718, rs2298771) with phenytoin response.

METHODS: This study included 120 patients attending the Neurology Clinic at three general hospitals in Yogyakarta, Indonesia: Sardjito General Hospital, PKU Gamping Hospital, and Bantul General Hospital between December 2019 until March 2021. Data regarding clinical parameters were collected prior to genotyping, and all patients were genotyped using acustom designed TaqMan based allelic discrimination assay and PCR restriction fragment length polymorphism. Statistical analysis was performed using *chi-square*, *fisher exact test* and Haplo.stats.

RESULTS: A total of 120 patients were enrolled to this study (male = 68, 54.4%). The patients were classified as responsive (n = 62, 48.3%) and unresponsive (n = 58, 51.7 %) to phenytoin. The genotype rs3812718 frequencies were 15% (n= 18) for AA, 42.5% (n=52) for AG, and 41.7% (n=50) for GG. The genotype rs2298771 frequencies were 47.5% (n= 57) for AA, 52.5% (n=63) for AG, and 0% (n=0) for GG. There was no significant relationship between the genotype rs2298771, rs3812718 and the response to phenytoin. However, haplotype analysis showed that rs3812718A-rs2298771G tended to be unresponsive to phenytoin 3.33 times compared to rs3812718G-rs2298771A (p=0.038).

CONCLUSION: The haplotype analysis showed that the combination of SCN1A rs3812718-rs2298771 had a significant relationship with the response to treatment of epilepsy patients with Phenytoin, although there was no relationship between the SCN1A genes rs3812718 and rs2298771 with the response to treatment of epilepsy patients with Phenytoin when analyzed respectively.

Keyword : *gene polymorphism, SCN1A, phenytoin, responsiveness*.

INTISARI

PENDAHULUAN : Respons pasien terhadap Obat Anti-epilepsi (OAE) bervariasi dipengaruhi berbagai faktor, baik faktor yang didapat maupun genetik. Farmakogenetik berperan dalam memprediksi perbedaan respons obat pada setiap individu. Gen SCN1A mengkode saluran natrium NaV1.1 pada sistem saraf pusat yang berfungsi sebagai target beberapa OAE termasuk fenitoin. Penelitian ini bertujuan untuk mengetahui hubungan polimorfisme SCN1A (SNP rs3812718, rs2298771) dengan respons fenitoin.

METODE: Penelitian ini melibatkan 120 pasien di poliklinik Saraf di Yogyakarta, yaitu di RSUP Sardjito, RS PKU Gamping, dan RS Bantul pada Desember 2019 sampai Maret 2021. Semua pasien dilakukan pengambilan data klinis serta darah untuk dilakukan pemeriksaan genotipe TaqMan dan PCR RFLP. Analisis statistik dilakukan dengan menggunakan metode chi-square. fisher exact test, analisis regresi dan Haplo.stats.

HASIL: Subjek penelitian sebanyak 120 pasien (laki-laki, n = 68). Pasien responsif (n= 62) dan tidak responsif (n = 58). Frekuensi genotipe rs3812718 AA adalah 15% (n= 18), AG sebanyak 42,5% (n=52), dan GG sebanyak 41,7% (n=50). Frekuensi genotipe rs2298771 AA adalah 47,5% (n= 57), AG sebanyak 52,5% (n=63) dan GG sebanyak 0% (n=0). Tidak terdapat hubungan bermakna antara genotipe rs2298771, rs3812718 dengan respons fenitoin, namun setelah dilakukan analisis haplotipe menunjukkan bahwa rs3812718A-rs2298771G cenderung tidak responsif terhadap fenitoin 3,33 kali dibandingkan dengan rs3812718G-rs2298771A (p=0,038).

KESIMPULAN: Analisis haplotipe menunjukkan bahwa kombinasi SCN1A rs3812718-rs2298771 memiliki hubungan bermakna dengan respons fenitoin, walaupun tidak terdapat hubungan antara masing-masing gen SCN1A rs3812718 dan rs2298771 dengan respons fenitoin pada pasien epilepsi.

Kata kunci: *polimorfsime gen, SCN1A, fenitoin, respons*