ABSTRAK

Epilepsi idiopatik umum (EIU) adalah sindrom epilepsi yang disebabkan oleh faktor genetik dengan pola penurunan *complex inharitence*. Telah dilaporkan beberapa gen yang diduga berperan, di antaranya gen *ME2* yang mengkode enzim malat dehidrogenase berperan pada jalur metabolisme neurotransmiter GABA. Hubungan gen *ME2* sebagai gen predisposisi EIU usia awitan remaja masih belum ada kesesuaian, dan hubungan polimorfisme gen *ME2* dengan EIU usia awitan anak belum terbukti.Valproat terbukti efektif mengatasi bangkitan EIU dengan angka remisi 65–80%, namun sebagian EIU mengalami relaps atau memerlukan obat antiepilepsi seumur hidup. Penelitian ini bertujuan untuk mendeteksi polimorfisme rs585344, rs645088 dan rs642698, gen *ME2* pada EIU dan anak tanpa epilepsi untuk menentukan hubungan polimorfime gen *ME2* dengan EIU; juga untuk menentukan jumlah proporsi hilangnya bangkitan 6 bulan setelah pengobatan valproat untuk menentukan perbedaan hilangnya bangkitan 6 bulan setelah pengobatan valproat pada EIU dengan genotipe mutan dan genotip bukan mutan polimorfisme rs585344, rs645088 dan rs642698 gen *ME2*. Penelitian kasus-kontrol dilakukan selama periode Juli 2010 sampai April 2012 terhadap 92 subjek EIU usia awitan anak dan remaja di RS Dr. Hasan Sadikin Bandung, RS Dr. Cipto Mangunkusumo Jakarta, dan RS St Borromeus Bandung, serta 336 subjek kontrol di RS Dr. Hasan Sadikin Bandung. Hasil penelitian dengan uji *chi*-kuadrat menunjukkan perbedaan bermakna proporsi genotip polimorfisme rs585344 gen *ME2* EIU antara usia awitan anak dan remaja dengan kontrol (p<0,05). Tidak terdapat perbedaan genotip polimorfisme rs645088 dan rs642698 gen *ME2* EIU usia awitan anak dan remaja dengan genotip polimorfisme rs645088 dan rs642698 gen *ME2* kontrol (p>0,05). Didapatkan perbedaan bermakna genotip mutan polimorfisme rs585344, rs645088, dan rs642698 gen *ME2* EIU usia awitan anak <11 tahun dengan genotip mutan polimorfisme rs585344, rs645088 dan rs642698 gen *ME2* EIU usia awitan anak ≥11 tahun *(age-dependent penetrance*). Didapatkan perbedaan bermakna respons terapi valproat <6 bulan antara genotip mutan polimorfisme rs585344 dan rs642698 gen *ME2* EIU usia awitan anak <11 tahun dibandingkan dengan genotip mutan polimorfisme rs585344 dan rs642698 gen *ME2* EIU usia awitan anak ≥11 tahun. Simpulan, polimorfisme rs585344 gen *ME2* berhubungan dengan EIU usia awitan anak dan remaja. Genotip mutan polimorfisme rs585344, rs645088 dan rs642698 gen *ME2* merupakan penentu awitan usia anak EIU. EIU usia awitan anak dengan genotip mutan polimorfisme rs585344 dan rs642698 gen *ME2* menunjukkan respon terapi lebih baik (<6 bulan) setelah pengobatan valproat 6 bulan dibandingkan dengan EIU usia awitan anak tanpa genotip mutan polimorfisme rs585344 dan rs642698 gen *ME2*.

Kata kunci: Epilepsi idiopatik umum (EIU), gen *ME2*, polimorfisme,valproat

ABSTRACT

Idiopathic generalized epilepsy (IGE) is an epileptic syndrome caused by genetic factor by mode of complex inheritance. Many researches had been done to find the underlying genetic factor of IGE. Genes have been reported including the ME2 gene, the coding gene for malate dehydrogenase that functions in the metabolism of GABA neurotransmitter. The correlation of ME2 gene as the predisposing gene in adolescence onset IGE still has no conformity, and the relationship between ME2 gene polymorphism and childhood onset IGE has not proven a significant evidence. Valproic acid has been proven effective to relieve IGE seizure with 65–80% rate for remission, but some IGE will go into relapse or need a lifetime of antiepileptic drug. This research intends to detect polymorphism rs585344, rs 645088, and rs 642698, ME2 gene in IGE and children without epilepsy to determine the relationship between ME2 gene polymorphism and IGE, and also to analyze the proportion of the seizure-free within six months after valproic acid treatment is less than the IGE with mutant genotype compared to IGE without mutant genotype rs585344, rs642698, and rs645088 gene ME2 The case-control study was done between the periode of July 2010 to April 2012 in 92 childhood and adolescence onset IGE patients at Dr Hasan Sadikin Hospital Bandung, Dr. Cipto Mangunkusumo Hospital Jakarta, and St. Borromeus Hospital Bandung, 336 control subjects at Dr. Hasan Sadikin Hospital Bandung. The result of this study with chi-square method shows significant difference of genotype polymorphism rs585344 ME2 gene proportion between childhood and adolescence onset IGE to control ($p<0,05$). There was no difference between genotype polymorphism rs645088 and rs642698 ME2 gene in childhood and adolescence onset IGE and genotype polymorphism rs645088 and rs642698 ME2 gene in control ($p>0,05$). Significant difference was obtained in mutant genotype polymorphism rs5853454, rs645088 and rs642698 ME2 gene in childhood onset IGE <11 years old with mutant genotype polymorphism rs585344, rs645088, and rs642698 ME2 gene in childhood onset IGE >11 years old (age-dependent penetrance). Significant difference was found in valproic acid response therapy <6 months between mutant genotype polymorphism rs585344 and rs642698 ME2 gene in childhood onset IGE <11 years old compared to mutant genotype polymorphism rs585344 and rs642698 ME2 gene in childhood onset IGE ≥11 years old. Taken together the result can be concluded that polymorphism rs585344 ME2 gene is related to childhood and adolescence onset IGE. Polymorphism rs585344, rs645088 and rs642698 ME2 gene is the determining gene for age of onset in IGE children. Childhood onset of IGE with polymorphism rs585344 and rs642698 ME2 gene shows better therapy response (<6 months) after 6 months of valproic acid treatment compared to childhood onset of IGE without polymorphism rs585344 and rs642698 ME2 gene.

***Key words**: Idiopathic generalized epilepsy (EIU), ME2 gene, polymorphism, valproate*