Penilaian Antibodi Anti N-Methyl-D-Aspartate-Receptor (NMDAR) Pada Pasien Epilepsi Resistan Obat: Aplikasi Penggunaan Skor Antibody Prevalence in Epilepsy and Encephalopathy 2 (APE2) dan Antibody Contributing to Focal Epilepsy Signs and Symptoms (ACES) = The Assessment of Anti N-Methyl-D-Aspartate-Receptor (NMDAR) Antibody in Drug Resistant Epilepsy Patient: Application of Antibody Prevalence in Epilepsy and Encephalopathy 2(APE2) score and Antibody Contributing to Focal Epilepsy Signs and Symptoms (ACES)

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Abstrak

Pendahuluan: Epilepsi merupakan salah satu kelainan neurologis terbanyak di dunia, kurang lebih 20-30% diantaranya merupakan epilepsi resistan obat. Salah satu penyebab epilepsi resistan obat adalah autoimun, yang diperantari antibodi saraf. Antibodi saraf yang paling sering ditemukan dan diteliti adalah antibodi anti N-Methyl-D-Aspartate (NMDAR). Diagnosis pasti epilepsi autoimun adalah ditemukannya antibodi saraf di serum atau cairan serebrospinal (CSS), namun saat ini ketersediaanya terbatas dan harganya cukup mahal di Indonesia. Skor Antibody Prevalence in Epilepsy and Encephalopathy 2 (APE2) dan Antibody Contributing to Focal Epilepsy Signs and Symptoms (ACES) merupakan dua piranti klinis yang dapat digunakan untuk menduga adanya antibodi saraf, namun belum ada penelitiannnya di Indonesia. Tujuan: Penelitian ini adalah uji diagnostik untuk menilai kemampuan APE2 dan ACES dalam menduga adanya antibodi saraf anti NMDAR di serum pasien epilepsi resisten obat. Metode: Pasien epilepsi resistan obat yang datang ke Poli Neurologi Anak Rumah Sakit Umum Pusat Nasional dr. Cipto Mangunkusumo Jakarta dan Rumah Sakit Umum Daerah dr. Soetomo Surabaya pada bulan Maret hingga Agustus 2023 dinilai menggunakan APE2 dan ACES lalu diperiksa serum antibodi anti NMDAR. Hasil: Didapatkan 90 subyek penelitian yang memenuhi kriteria inklusi dan eksklusi penelitian. Antibodi NMDAR serum ditemukan pada 10 dari mereka. Skor APE2 memiliki sensitivitas 60%, spesifisitas 82,5%, PPV 30%, NPV 94,3%, LR+ 3,43, dan LR- 0,48. Poin skor APE2 yang memiliki nilai bermakna adalah perubahan status mental (p 0,042) dan gejala prodormal sebelum kejang (p 0,005). Skor ACES memiliki sensitivitas 85,71% spesifisitas 72,22%, PPV 37,5%, NPV 96,3%, LR+ 3,08, dan LR- 0,198. Poin skor ACES yang memiliki nilai bermakna adalah gangguan kognitif (p 0,033) dan gangguan bicara (p 0,028). Pada kejang fokal, APE2 memiliki nilai sensitivitas, PPV, NPV dan LR+ yang lebih rendah namun spesifisitas dan LR- yang lebih tinggi dibandingkan dengan ACES. Kesimpulan: Skor APE2 kurang sensitif namun cukup spesifik dengan NPV yang tinggi. Skor ACES cukup sensitif dan spesifik dengan NPV yang tinggi. Keduanya dapat digunakan untuk skrining awal epilepsi terutama bila ada gejala perubahan status mental, gejala prodormal virus, gangguan kognitif dan gangguan bicara sebelum atau saat awal awitan kejang. Diperlukan penelitian lanjutan untuk menilai antibodi saraf lain, dengan pemeriksaan antibodi di CSS dan tidak terbatas pada epilepsi resisten obat saja serta yang awitan kejangnya dibawah 1 tahun. Kata kunci: ACES, APE2, epilepsi autoimun, epilepsi resisten obat, NMDAR

.....Epilepsy is one of the most common neurological disorders in the world, approximately 20-30% of

which are drug-resistant epilepsy. One cause of drug-resistant epilepsy is autoimmune disease, mediated by neural antibodies. The most frequently found and studied neural antibody is the anti-N-Methyl-D-Aspartate (NMDAR) antibody. The definitive diagnosis of autoimmune epilepsy is the discovery of neural antibodies in serum or cerebrospinal fluid (CSF), but currently their availability is limited and the price is quite expensive in Indonesia. The Antibody Prevalence in Epilepsy and Encephalopathy 2 (APE2) score and Antibody Contributing to Focal Epilepsy Signs and Symptoms (ACES) are two clinical tools that can be used to suspect the presence of neural antibodies, but there has been no research in Indonesia. Purpose: This research is a diagnostic test to assess the ability of APE2 and ACES to predict the presence of anti-NMDAR neural antibodies in the serum of drug-resistant epilepsy patients. Methods: Drug-resistant epilepsy patients who seek treatment at the Pediatric Neurology Outpatient clinic at the National Central General Hospital, dr. Cipto Mangunkusumo Jakarta and the Regional General Hospital dr. Soetomo Surabaya from March to August 2023 were assessed using APE2 and ACES, then checked for serum anti NMDAR antibody. Results: There were 90 research subjects who met the research inclusion and exclusion criteria. Serum NMDAR antibodies were found in 10 of them. The APE2 score has a sensitivity of 60%, specificity of 82.5%, PPV of 30%, NPV of 94.3%, LR+ 3.43, and LR- 0.48. In this study, the APE2 score points that had significant values were changes in mental status (p 0.042) and prodromal symptoms before seizures (p 0.005). The ACES score has a sensitivity of 85.71%, a specificity of 72.22%, PPV 37.5%, NPV 96.3%, LR+ 3.08, and LR- 0.198. In this study, the ACES score points that had significant values were cognitive symptoms (p 0.033) and speech problem (p 0.028). In focal seizures, APE2 has lower sensitivity, PPV, NPV and LR+ values but higher specificity and LR- compared to ACES. The APE2 score is less sensitive but quite specific with a high NPV. The ACES score is quite sensitive and specific with a high NPV. Both can be used for initial epilepsy screening, especially if there are symptoms of changes in mental status, viral prodromal symptoms, cognitive symptoms and speech problem before or at the onset of seizures. Further research is needed to assess other neural antibodies, examining neural antibodies in CSF and also including those whose seizure onset is less than 1 year, not limiting to drug-resistant epilepsy only.