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Selection of proper antiepileptic drugs

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1. Introduction

Epilepsy affects 0.6% of Japanese population, and monotherapy has been the gold standard in epilepsy treatment in the past two decades. However, up to one third of patients do not achieve sufficient seizure control with antiepileptic (AED) monotherapy. Further, in case of patients with partial seizures, 25% of them are not rendered seizure free with 3 AEDs combination therapy. In spite of these facts, AEDs are the mainstay of treatment, and monotherapy should be remain the treatment of choice for newly diagnosed epilepsy. Recently, new AEDs such as gabapentin (GBP), topiramate (TPM) and lamotrigine (LTG) have been introduced in Japan, and levetiracetam will be introduced within this year. Some of them are better tolerated and less prone to complex pharmacokinetic drug interactions than their older counterparts, consequently AED therapy has entered a new stage.

2. Current AED selection

Currently, AED is selected according to seizure phenotype. LTG is prescribed to generalized and partial seizures, and GBP and TPM are prescribed to partial seizures. GBP and TPM respond to a part of generalized seizures but these new AEDs are not approved to use for the treatment of generalized seizures in Japan. None of them has not been ap-

proved to use as a monotherapy yet. As a single AED, the degree of antiepileptic efficacy and of unwanted effects is thought to be TPM > LTG > GBP. Current first choice for most forms of generalized seizures is valproate, and that for partial seizure is carbamazepine or zonisamide. The selection of AED polytherapy based on mechanisms of action and kind of unwanted effects may enhance effectiveness without an increase of toxicity. Combining a Na⁺ channel blocker with a drug enhancing GABAergic inhibition appears to be advantageous. Combining two GABA mimetic drugs or combining an AMPA antagonist with an NMDA antagonist may enhance efficacy, but tolerability is sometimes reduced. Combining two sodium channel blocker may be less promising. Among newly introduced AEDs specifically noticed effects are mood stabilizing effects of LTG and TPM, Bulimia Nervosa ameliorative effects of TPM, and anxiolytic effects of GBP.

3. Selection of AEDs in the near future

The molecular revolution in epilepsy research during the last two decades is beginning to have a significant impact on diagnosis of epilepsy and AED treatment including drug choice. In the near future, the selection of AED and dosage will be made mostly based upon genetic background of each patient together with his/her epilepsy phenotype.