

Detection of a relationship between multidrug resistance and over-expression of P-glycoprotein gene in peripheral blood lymphocytes of epilepsy patients

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Background and Objective: The diagnosis and treatment of intractable epilepsy remains a difficult problem. Solution to the problem is crucial to improvement in epilepsy prognosis. Previous studies have shown that overexpression of MDR1 gene is a mechanism of intractable epilepsy and antiepileptic drugs (AEDs) can induce the overexpression of P-glycoprotein (P-GP).^{1,2} We believe it is possible for AEDs to induce P-GP overexpression in blood and brain to result in drug resistance. This is a study of the P-GP in the peripheral blood of the patients with intractable epilepsy to find an effective marker in drug resistance.

Methods: This is a prospective, observational study. Eighty-five patients from the epilepsy center of this hospital were chosen for the study. The subjects consisted of 39 males, 46 females with average age of 24 years (17 to 54 years). All the patients had typical seizures and EEG changes, and the seizures were resistant to 2 or 3 first line AEDs. The expression of P-GP in peripheral blood lymphocytes of the 85 patients were investigated using immunocytochemistry or flow cytometry. Patients were then given a single or a combination of 2-3 first line AEDs, including carbamazepine, valproic acid, phenobarbital and phenytoin, which were not previously used by the patients. If a single drug was not effective, multiple drugs (2-3 AEDs) were used. AED was replaced when the highest drug-serum concentration was achieved without clinical efficacy, or significant side effects were seen. Fifty percent or more decrease in seizures is considered effective treatment.

Results: P-GP was determined by flow cytometry in 49 patients. It was positive in 11 patients (23%), negative in 32 patients (65%), and borderline in 6 patients. All the 11 patients with positive P-GP did not response to the AEDs in the trial. The seizures in the 18 patients negative for P-GP reduced markedly. The 2 patients with doubtful level of P-GP also responded to the AEDs trial. PGP was determined by immunocytochemistry in 34 patients. It was positive in 22 patients (65%), and negative in 12 patients (35%). Only 2 out of 22 patients with positive P-GP responded to the AED trial. Seven out of 12 patients with negative P-GP were responsive to AED. Two patients withdrew from the AED trial.

Conclusion: Measurement of P-GP in the peripheral blood can be a marker of drug resistance in intractable epilepsy. Immunocytochemistry may be more sensitive in detecting P-GP gene, but flow cytometry may be a more specific method.

References

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