Non-equivalence of bioavailability between generic and branded form of Sodium valproate

Sir

In the open market, an anticonvulsant drug is available by different brand names promoted by the respective pharmaceutical companies. However, the hospital pharmacies, including in the developed European countries stock and supply the generic forms (Chemical compound) purchased through the tender system. Differences in the bioavailability of different brands of the same antiepileptic and rarely different batches of the same anticonvulsant belonging to the same company have also been reported.1,2

Two mentally retarded adults suffering from a combination of myoclonic and generalized tonic clonic seizures since childhood were treated with a generic form of sodium valproate. Initially the generalized tonic clonic seizure was occurring in a frequency of 2 - 6 / week in the first and about 1 / week in the second patient. The myoclonic seizure was occurring daily in a varying frequency in both. The patients were staying in a Home and were looked after by ‘caretakers’. To start with, the generic form of sodium valproate was administered in a dose of 200 mg bid and gradually stepped up to 1600 mg / day and 1400 mg / day in three divided doses over a period of 1½ years. The drug was administered orally by the ‘caretakers’ and the seizure count was recorded in a diary. For two consecutive months, they were maintained on the same dose. The myoclonic seizures being fully controlled and the generalized tonic clonic seizure was occurring in a frequency of 4 / month and 2 / month respectively. The serum level of the free valproic acid was estimated by Fluorescent Polarisation Immuno Assay (FPIA) technique. Blood samples were drawn by 8 am, prior to that day’s drug intake. The biochemist was blinded to the patient and the form of the drug. The serum level was 67.87 µg/ml and 71.16 µg/ml respectively. A branded form of sodium valproate was substituted for the generic form in the same dose and interval for a period of one month. At the end of one month, the seizure frequency was 2 and 1 per month and the repeat serum level of free valproic acid (blood sample taken at 8 a.m.) was 118.40 µg/ml and 80.58 µg/ml respectively. No adverse effects were noticed.

The bioavailability of a drug is the quantum of the drug available in the systemic circulation for its action after absorption.4 In the management of epilepsy which requires a long-term treatment for years, the bioavailability of the antiepileptic drug should not fluctuate from time to time. If the level goes up, it may lead to intoxication and if it lowers down, seizure may relapse. Recently, non-equivalence in the bioavailability of carbamazepine of two different brands has been observed. An epidemic of phenytoin intoxication among epileptic patients taking the same brand of phenytoin but different batches has been reported from an Australian city. Change in the excipient in the phenytoin capsule was responsible for the higher serum level of the drug. Thus, the same antiepileptic belonging to the same brand can produce changes in the bioavailability. Even in -developed countries hospital pharmacies issue the generic form of the drugs because they are cheaper, the generic name avoids delay in recognizing toxic effects and the doctor can know immediately what his colleague has prescribed. But different pharmaceutical companies may supply the same generic drug whose bioavailability is likely to vary.1

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References


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