LETTER TO THE EDITOR

HEPATIC FUNCTIONS IN EPILEPTICS ON SODIUM VALPROATE MONOTHERAPY

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Sir,

Sodium valproate (VPA) has been advocated as an antiepileptic of first choice in patients of primary generalised seizures (1) because of low risks of serious side effects and negligible neuropsychiatric manifestations. However, it has been clinically and experimentally observed to induce hepatic dysfunction including hepatic failure resulting in fatalities making periodic screening for liver function tests necessary (2). This study was conducted to observe the effect of VPA on hepatic function in epileptics and correlate the changes with dose and serum levels of VPA.

Sixtyeight (46 men and 22 women) patients of primary generalised tonic-clonic seizures corresponding to definition of international classification of ILAE, 1985, in age range of 18-38 years (mean 28.6±4.2) were the subjects of study. They were having seizure since more than one year prior to their inclusion in the study. Clinical evaluation and relevant investigations were done (CT & EEG) to exclude any secondary causes like granuloma or vascular malformation. Thirtyfive healthy individuals on placebo treatment were the control group. The patients had not taken any antiepileptic before and were started on monotherapy of VPA. Initial doses were low (10-20 mg/kg) and they were gradually increased to a dose of 15-30 mg/kg body weight till patient was seizure free, the dose being readjusted at weekly intervals. Two patients each with previous history of jaundice, hepatitis and alcohol and five patients who could not be controlled using monotherapy of VPA have not been included. Patients on drugs, effecting hepatic functions (viz. antitubercular) were not included. Liver function tests were performed in all subjects before the start of therapy and at intervals of 4 months for 18 months. These tests included Van Den Bergh, serum bilirubin, serum alkaline phosphatase, serum glutamate, serum pyruvate transaminase (SGPT) and serum oxaloacetic transaminase (SGOT). Serum VPA was estimated simultaneously at 4 month intervals using Fluorescence Polar Imunoassay Analyser (FPIA). Results were statistically analysed by Wilcoxon method and correlation coefficient accorded.

All patients tolerated VPA well. Occasional epigastric pain was present in 6 patients but it was not sufficient enough to warrant drug stoppage. There was no significant elevation observed in hepatic enzymes as compared to pre-therapy estimation in any of our patients estimated at 4 months intervals, all the liver function tests being normal till the end of study (Table I).

TABLE I: Liver functions on using Sodium Valproate.

<table>
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<tr>
<th></th>
<th>S. Bilirubin (in mg%)</th>
<th>SGPT (KA units)</th>
<th>SGPT. Alk. Phosphatase (KA units)</th>
<th>SGOT (KA units)</th>
<th>Serum Valproate (µg/ml)</th>
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<tbody>
<tr>
<td>Initial evaluation</td>
<td>0.617 ± 0.192</td>
<td>28.70 ± 4.3</td>
<td>9.5 ± 1.509</td>
<td></td>
<td>48.76 ± 134.75</td>
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<tr>
<td>1st visit</td>
<td>0.517 ± 0.198</td>
<td>25.50 ± 4.4</td>
<td>7.7 ± 2.58</td>
<td>12.66 ± 4.5</td>
<td>44.54 ± 20.67</td>
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<tr>
<td>2nd visit</td>
<td>0.39 ± 0.04</td>
<td>21.14 ± 1.08</td>
<td>5.8 ± 2.7</td>
<td>11.91 ± 4.6</td>
<td>34.43 ± 21.49</td>
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<tr>
<td>3rd visit</td>
<td>0.634 ± 0.139</td>
<td>29.73 ± 4.6</td>
<td>10.7 ± 1.418</td>
<td>11.50 ± 6.3</td>
<td>34.43 ± 21.49</td>
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Between visit 1 and 3 P > 0.1 and r < 0.3
Symptomatic (2) and asymptomatic (3) elevation of hepatic enzymes have been reported on usage of sodium valproate, but it has been suspected that the incidence of hepatotoxicity so induced is greater than reported and increased SGPT levels in patients on VPA therapy (4) has been observed. This elevation has been related to dose and serum VPA levels (5), while we did not find any such correlation between them.

In two retrospective studies, one between 1978-84 and second between 1985-86 in USA, a dramatic decrease of hepatic fatality was observed over the year. This has been attributed to better identification of "at risk" patients. Since progress to hepatic coma has been reported (6) in epileptics on VPA therapy, continuous monitoring of liver functions should be done in such cases till they return to normal (7).

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REFERENCES