Serum Immunoglobulins and complement subfactors levels in sodium valproate treated epileptic patients

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ABSTRACT

Objectives: To assess, the serum levels of immunoglobulins (IgG, IgA, IgM) and complement subfactors (C₃, C₄) in newly diagnosed epileptic patients in the pre-therapy stage and ٣ months after valproate therapy, in comparison with controls.

Methods: This study was conducted at Iben-Seena Hospital and the College of Medicine- University of Mosul from January to December ٩٠٠٢. Forty-two newly diagnosed epileptic patients were selected and included in this study. Fifty apparently healthy subjects, age and sex matched to the patients group also included and taken as a control. Initially from both the patients and controls, blood samples were taken and assessment of sera levels of immunoglobulins and complement subfactors were done by single radial immuno diffusion method, using commercial kits. Then patients were put on valporate therapy for ٣ months and a blood sample were taken from the patients and assay of the same parameters mentioned above were done using the same technique and the same kits.

Results: There were insignificant differences between patients in pre-therapy stage and controls with regard serum immunoglobulin levels (and complement subfactors). Also there were insignificant differences between epileptic patients before and ٣ months after therapy with valproate.

Conclusion: valproate as an anticonvulsant have no influence on serum immunoglobulin (IgG, IgA, IgM) and complement subfactors (C₃, C₄) after ٣ months of therapy.

Key Words: newly diagnosed epileptic, valproate therapy, immunoglobulin and complements subfactors levels.
Epilepsy is a common neurological problem which has occupied clinicians for many centuries. However little is known about the aetiology of the disease, but among many mechanisms proposed, the immunological one have been implicated as an aetiological factor of epilepsy, especially in children with intractable epilepsy. Certain clinical studies suggested that aberrations of the immunologic system may be associated with untreated epilepsy and with the use of anticonvulsant therapies.

Immunoglobulin A (IgA) deficiency has been detected in up to 52% of patients with epilepsy, and the most frequent abnormality is a reduction in serum and salivary IgA concentration which occurs in about one-fifth of epileptic patients receiving diphenhydantoin. On the other hand, disturbances of immunoglobulin G and M (IgG, IgM) levels have also been reported, but the results are conflicting since both increased and decreased concentrations have been found. The complements are cascading series of plasma enzymes and effector proteins whose function is to lyse pathogens and or target them to be phagocytized by phagocytic cells of the reticuloendothelial system.

The aim of this study is to assess the immunoglobulin levels and complement subfactors in newly diagnosed epileptic patients before therapy and 3 months after valproate therapy in comparison to control.

Patients and methods
This study was conducted from January to December 2002. Approval have been obtained from ethical committee (the main health centre in Mosul and Mosul College of Medicine, University of Mosul, Iraq). Patients were selected according to certain criteria.

Criteria for selection
1. Newly diagnosed patients with epilepsy (clinical diagnosis was made by neurologist).
2. Selected for valproate monotherapy for the initial 3 months.
3. No coexisting renal, hepatic, thyroid dysfunction, nor diabetes or any disease of suspected immunological basis.

Of the patients interviewed only 84 were eligible for enrollment in the study according to the criteria mentioned above and only 24 completed the study. They were 21 females and 3 males with a mean ± SD age 62.08 ± 5.11 years (ranged between 81 and 83 years). Also included (6) apparently healthy subjects as a control group. They were (18) females and (36) males with a mean ± SD age 72.60 ± 5.50 years (ranged between 81 and 83 years). Initially from both the patients and controls, 5 ml venous blood samples were taken and assessment of immunoglobulin levels (IgG, IgA, IgM) and complement subfactors (C3, C4) were done by single radial immunodiffusion method using kits from Sanofi diagnostics Pasteur (France). For the patients group, they were put on valproate therapy in a mean ± SD dose 754.41 ± 0.33 mg/dL (ranged between 94.7 mg and 983 mg/dl) for 3 months, by the end of which another blood samples were taken and assessment of the same parameters mentioned above were done.

Standard statistical methods were used to determine the mean, standard deviation (SD) and the range. Paired t-test was used to compare the results of
the patients in the pre and post-therapy stage. Unpaired t-test was used to compare the results of the patients in the pre-therapy stage and the controls. \( P < 0.5 \) was considered to be statistically significant.

**Results**

There were insignificant differences between epileptic patients in the pre-therapy stage and the controls with regard serum immunoglobulin levels (IgG, IgA, IgM) and complement subfactors (C³, C⁴) as shown in Table 1.

Table 1. Comparison of immunological classes and complement subfactors in pre-therapy epileptic patients and control.

<table>
<thead>
<tr>
<th>Parameter Immunoglobulins and complements g/L</th>
<th>Patients pre-therapy No=24 mean±SD</th>
<th>Controls No=50 mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>10.47 ± 1.44</td>
<td>10.42 ± 1.23</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>IgA</td>
<td>2.27 ± 0.44</td>
<td>2.12 ± 0.27</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>IgM</td>
<td>1.89 ± 0.44</td>
<td>1.81 ± 0.31</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>C³</td>
<td>2.07 ± 0.19</td>
<td>2.06 ± 0.42</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>C⁴</td>
<td>0.35 ± 0.09</td>
<td>0.36 ± 0.07</td>
<td>&gt; 0.5</td>
</tr>
</tbody>
</table>

There were insignificant differences between patients in the pretherapy and post-therapy stages with regard serum levels of immunoglobulin levels (IgG, IgA, IgM) and complement subfactors (C³, C⁴). Table (2)

Table 2. Comparison of immunological classes and complement subfactors in epileptic patients in the pre and post-therapy stage.

<table>
<thead>
<tr>
<th>Parameter Immunoglobulins and Complements g/L</th>
<th>Patients pre-therapy mean±SD</th>
<th>Patients post-therapy stage mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>10.47 ± 1.17</td>
<td>10.35 ± 1.44</td>
<td>NS</td>
</tr>
<tr>
<td>IgA</td>
<td>2.27 ± 0.54</td>
<td>2.30 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>IgM</td>
<td>1.89 ± 0.14</td>
<td>1.56 ± 0.21</td>
<td>NS</td>
</tr>
<tr>
<td>C³</td>
<td>2.07 ± 0.19</td>
<td>2.48 ± 0.19</td>
<td>NS</td>
</tr>
<tr>
<td>C⁴</td>
<td>0.35 ± 0.09</td>
<td>0.36 ± 0.06</td>
<td>NS&gt;0.5</td>
</tr>
</tbody>
</table>
Discussion

Our study revealed insignificant differences between newly diagnosed epileptic patients before starting therapy and the control with regard serum levels of immunoglobulins (IgG, IgA, IgM) and complement subfactors (C₃, C₄), also there was insignificant differences between patients in pre-therapy and post-therapy stages with regard serum levels of immunoglobulin (IgG, IgA, IgM) and complements (C₃, C₄).

In Joubert et al, reported that epileptic patients on valproate therapy had mean serum IgA levels significantly lower than non-users of valproate. In agreement with our study Lenti et al. evaluated serum immunoglobulins in epileptic children treated with anticonvulsants (carbamazepine and valproic acid), untreated patients and healthy subjects. The treated and untreated patients did not differ significantly from the controls with respect to the mean IgA, IgG and IgM serum levels, and concluded that there were no major changes in immune status related to clinical type of epilepsy or to carbamazepine or valproate therapy.

Bostantjopoulo et al. studied epileptic patients (without medication, on carbamazepine and on valproic acid) and healthy controls. They reported that the untreated epileptic group had increased levels of IgA and IgG, patients on carbamazepine showed increased IgG and IgM levels, while patients on valproate had increased levels of IgM. Basaran et al. studied the humoral and cellular immune parameters in untreated and phenytoin or carbamazepine treated epileptic patients and noticed that patients on phenytoin had decreased serum IgA and IgG levels, while those on carbamazepine had decreased serum IgM levels and untreated epileptic showed immune profiles significantly different from healthy subjects suggesting that epilepsy per se may be associated with certain immune aberrations induced by antiepileptic drugs. The complement system and immunoglobulins are the main components of humoral immunity. The activation of complement is known to be involved in a number of forms of cardiovascular disease, such as exacerbation of myocardial defect following ischaemic injury and may be involved in the degeneration of spontaneous atherosclerotic lesions. This might be the first study concerning levels of complements(C₃, C₄) in epileptic patients before and after valporate therapy.

In conclusion, our study concluded that valproate as an antiepileptic drug did not have a significant effect on serum immunoglobulins (IgG, IgA, IgM) and complement subfactors (C₃, C₄) levels in epileptic patients.

References
