Guillain-Barré syndrome clinical profile and the efficacy of immunoglobulin therapy

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ABSTRACT

Objectives: A retrospective study was performed to report the results obtained with intravenous immunoglobulin therapy in patients with Guillain-Barré syndrome, and to look at the clinical profile and outcome of those patients.

Methods: The clinical profile of 26 patients with proved Guillain-Barré syndrome were reviewed, all were admitted to the Pediatric Department at King Hussein Medical Center, Amman, Jordan over the period from June 1988 - June 1997. The presenting complaints, neurological examination, cerebrospinal fluid and neurophysiological studies and follow up assessment were analyzed.

Results: It has been shown that the male to female ratio is 1.6:1.0, all patients presented with flaccid symmetrical ascending paralysis with loss of deep tendon reflexes. Twelve patients (46.1%) had sensory manifestations, 10 patients (38.4%) developed cranial nerves palsy, and 6 patients (23%) had autonomic involvement. CSF measurement of protein in the first 10 days of the illness was high in 17 patients (65.3%) and normal in 9 patients (34.6%). Nerve conduction of all patients showed demyelinating polyneuropathy of varying severity, 3 patients (11.5%) developed permanent motor neurological deficit, one patient (3.8%) died. Immunoglobulin was given to 12 patients (46.1%) and it showed their efficacy at a dosage of 0.4 gm/kg/day for 5 days.

Conclusion: Guillain-Barré syndrome has a good prognosis and mortality and morbidity rates are comparative to rates in other studies. Treatment with immunoglobulins is easy, safe and morbidity is lower.

Keywords: Guillain-Barré syndrome, intravenous immunoglobulin.


The Guillain-Barré syndrome (GBS), a subacute inflammatory demyelinating polyneuropathy, leads to severe quadripareis and requires artificial ventilation in about 20% of patients. Although functional recovery is the rule, 15% of patients have residual deficits. GBS is an acute inflammatory demyelinating neuropathy characterized by progressive symmetric loss of motor strength, reflexes, and variable sensory loss. There is strong evidence that demyelination in the peripheral nerves and consequent neurologic deficit in GBS is the result of an immunologic attack on the peripheral nervous system myelin or possibly schwann cells. The diagnostic criteria of Guillain-Barré syndrome after Asbury and Cornblath3 is shown in Table 1. The worldwide incidence of the GBS ranges from 0.7-1.9 per 100,000.4 High dose intravenous immunoglobulin has been reported to be effective in numerous potentially immune-mediated diseases such as Guillain-Barré syndrome.4,54,7 In 1988 Kleeweg reported treating GBS with high doses of immunoglobulins and thereafter more reports

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immunoglobulin in severe pediatric GBS patients with dramatic responses.¹¹

In acute GBS, treatment with intravenous immunoglobulin is at least as effective as plasma exchange and may be superior.¹² The early use of immunoglobulin in this disorder may prevent further progression of the disease and accelerate short term recovery with resulting medical, social and financial implications.¹³

**Methods.** The files of patients with GBS who were admitted to the Pediatric Department at King Hussein Medical Center, Amman, Jordan over the period from June 1988 - June 1997 were collected and reviewed. Patients conformed to the internationally accepted diagnostic criteria for acute GBS as published by Asbury and Cornblath (Table 1).² The age range of patients included in the study was between 17 months to 13 years and this is the age group who have been admitted to the Pediatric Department. The signs and symptoms at admission to hospital and at the height of the disease were recorded in a structured way (Table 2). The degree of disability at admission and maximum weakness was coded in 10 levels as indicated in Table 3, this has been referred to the disability scale used by R Korinthenberg.¹⁴

The clinical data including history of previous infections, present illness and the neurological examination of the patients was analyzed, the CSF result and neuropsychological studies were reviewed as well. The neurological follow up and outcome of the patients were reviewed, and the patients who had neurological deficits were called and examined.

**Results.** The number of males was 16 and females was 10 in a ratio of 1.6 : 1.0 the age range was from 17 months to 13 years. Age distribution is shown in Figure 1.

All patients had ascending flaccid symmetrical
Table 3 - Degree of disability

<table>
<thead>
<tr>
<th>Degree</th>
<th>Definition</th>
<th>At admission (%)</th>
<th>At maximum disability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
<td>1.4</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>Slight gait disturbance</td>
<td>24.4</td>
<td>7.8</td>
</tr>
<tr>
<td>2</td>
<td>Moderate gait disturbance</td>
<td>26.4</td>
<td>16.6</td>
</tr>
<tr>
<td>3</td>
<td>Walks holding on to furniture</td>
<td>8.6</td>
<td>3.8</td>
</tr>
<tr>
<td>4</td>
<td>Walks with help by person</td>
<td>14.2</td>
<td>11.2</td>
</tr>
<tr>
<td>5</td>
<td>Not able to walk</td>
<td>8.9</td>
<td>14.4</td>
</tr>
<tr>
<td>6</td>
<td>Not able to sit upright</td>
<td>4.2</td>
<td>9.8</td>
</tr>
<tr>
<td>7</td>
<td>Tetraparesis</td>
<td>3.6</td>
<td>11.2</td>
</tr>
<tr>
<td>8</td>
<td>Tetraplegia</td>
<td>0</td>
<td>3.2</td>
</tr>
<tr>
<td>9</td>
<td>Artificial ventilation</td>
<td>0</td>
<td>7.69</td>
</tr>
</tbody>
</table>

Paralysis of both lower and upper limbs with absent deep tendon reflexes. Twelve (46%) patients had sensory involvement, 6 patients had pain, 2 patients had numbness and 4 had a combination of both, 6 (23%) patients had autonomic manifestations (urination and defecation disturbances). Ten (38.4%) patients had cranial nerve involvement and the nerves involved were the 6th, 7th, 9th, and 10th, facial nerves were the most common nerves affected and this was seen in 6 (23%) patients. The clinical features are shown in Table 4.

Three patients (11.53%) had residual motor deficit, one of them had motor deficit along with mental retardation and this was the patient who had the presentation of encephalomyelitis. The peak period of paralysis was ranged from 2 days to 3 weeks from onset of illness. Ten patients (38.4%) got their maximum weakness at 2 weeks time. History of previous infection was seen in 12 patients (46.1%), 8 had upper respiratory tract infection (30.76%) and 2 had gastroenteritis (7.69%) of viral cause, one had shigellosis (3.8%) and one had mycoplasma infection (3.8%) and this is illustrated in Table 5.

CSF protein was high in 17 patients (65.3%) and all patients had their lumbar puncture in the first 10 days of illness, one patient had cells of 50 and all were lymphocytes and this is the patient who had the picture of encephalomyelitis and he continued to have residual motor paralysis with mental retardation. Neurophysiological studies were done for all patients and all of them showed demyelination process of varying severity ranging from absent response to conduction delay and conduction block.

The duration of improvement in those who recovered completely ranged from 4 weeks to 5 months. The patient who died was a 6 year old male patient, his weakness reached it’s maximum 3 weeks after the onset, he had history of gastroenteritis 10 days prior to the weakness, his CSF protein was 40 mg/dL, and this patient was among the group of patients who did not receive immunoglobulin. The 2 patients who had residual weakness did not show any correlation with any specific presentation or laboratory findings, although those who needed ventilator support had poor prognosis (one died and one had residual motor paralysis). One of the patients had both residual motor deficit and mental retardation. Twelve patients (46.1%) received immunoglobulin in a dose of 0.4 gm/kg/day for 5 days and all improved after 14 days of treatment. Almost all the IVIG treated patients were able to sit and walk within 14-21 days and not one of them had any complication or any residual deficits, whereas this took at least 4 weeks to 5 months for the group which did not take immunoglobulin. The outcome of the patients in the two groups is shown in Table 6.

The P-value was 0.022 which indicates that the treatment with IVIG is significantly effective at the
Table 6 - The outcome of disease in the treatment groups

<table>
<thead>
<tr>
<th>Prognosis</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who received IVIG immunoglobulin</td>
<td>12</td>
<td>46.1%</td>
</tr>
<tr>
<td>Complete recovery</td>
<td>12</td>
<td>46.1%</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients who received supportive care only and did not take IVIG</td>
<td>14</td>
<td>54.9%</td>
</tr>
<tr>
<td>Complete recovery</td>
<td>10</td>
<td>38.4%</td>
</tr>
<tr>
<td>Residual motor paralysis</td>
<td>3</td>
<td>11.53%</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>3.84%</td>
</tr>
</tbody>
</table>

5% significant level. The statistical method used was the comparison of proportions to the binomial distribution. The follow up period of patients was for one year from the start of illness, 3 patients were missed for follow up.

Discussion. Although in many patients GBS is a self limiting illness, it can be associated with severe morbidity and mortality. In our series of 26 patients, the male to female ratio was 1.6 : 1 and the mean age was 5.8 years. There were 2 peaks of incidence one below 3 years of age and the other one in adolescence, there is no clear explanation for this age predilection but those 2 age groups are more susceptible to infection than others.\textsuperscript{15}

History of previous infection was seen in about 12 patients (46.1%), upper respiratory tract infection was the most common, 8 patients (30.76%). In other studies upper respiratory tract infection was also the most common.\textsuperscript{16} All patients had flaccid ascending symmetrical paralysis which is the usual features of GBS.\textsuperscript{3}

Sensory and cranial nerve involvement were common in our patients, the facial nerve was the most common one to be involved. One patient had a picture of encephalitis, he had altered levels of consciousness and mental changes beside motor disability, this patient was left with residual deficits in the form of motor disability and mental retardation, this condition, is reported in GBS/ (Gamstrop 1974).\textsuperscript{17} This patient had 50 lymphocytes in his CSF and this is a possibility in GBS where it is accepted that up to 150 cells can be found in the CSF but all cells should be lymphocytes.\textsuperscript{18,19,20} The period of progression from onset to maximum weakness ranged from 2 days to 3 weeks, but most of the patients got their maximum weakness 2 weeks time. High protein in CSF was seen in 17 patients (65.3%), and this issue had no relation to the severity of the disease or the chronic sequelae of it. Although normal CSF protein is possible, however the lumber puncture being carried out in the first 10 days of the onset of the disease, and not repeated, will make the raised protein go undetected.

Nerve conduction and electromyography was carried out for all patients, all patients showed evidence of motor demyelination with variable severity and 6 patients (23%) had evidence of delayed sensory responses.

Most of the patients who recovered completely started to improve within the first 2 weeks after reaching maximum weakness, and this is the group of patients who were treated with IVIG.

The longest period of improvement was 5 months. Twelve patients received immunoglobulin and all improved after 14 days of treatment. All the IVIG treated patients were able to sit and walk within 14-21 days and not one of them had any complication or residual deficit, all of them recovered completely. Fourteen patients did not receive immunoglobulin because either they were referred late to our hospital or because some of them had the disease before the approval of immunoglobulin treatment in GBS.

The one patient who died did not receive immunoglobulin because he came late, and immunoglobulin is only effective if it is given in the 1st 2 weeks of the paralysis.\textsuperscript{21,22,23,24}

Our study emphasizes the faster rate of recovery following IVIG therapy and it also shows diminished mortality rate in the IVIG treated patients.

Three patients had residual motor deficit, one had mental retardation as well, and those patients were followed for more than 2 years after the onset of the disease, this made our morbidity to be 11.53% while our mortality rate was 3.8%. The patient who died was stable on mechanical ventilation besides other supportive measures, but he arrested suddenly and died which was due to cardiac arrhythmia and sudden cardiac arrest, which is a known complication in patients with GBS. Our morbidity and mortality rates are very close to the international figures which are 16% and 5% in correspondence.\textsuperscript{25,26,27}

Comparison of the outcome of IVIG treated and

Table 7 - Comparison of the outcome of IVIG treated group and non-IVIG treated group.

<table>
<thead>
<tr>
<th>Duration in days</th>
<th>IVIG treated group</th>
<th>Non IVIG treated group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval from symptoms to hospitalization</td>
<td>(2-7) days</td>
<td>(4-16) days</td>
</tr>
<tr>
<td>Interval from onset to maximum symptoms</td>
<td>(8-11) days</td>
<td>(9-17) days</td>
</tr>
<tr>
<td>Interval from maximum weakness to improvement</td>
<td>(8-14) days</td>
<td>(9-20) days</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td>(12-18) days</td>
<td>(14-24) days</td>
</tr>
</tbody>
</table>

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untreated children with GBS is shown in Table 7.

We did not find any definite correlation, between the prognosis of the disease and the clinical or laboratory characteristics of the condition, however those 2 patients who needed ventilator support had poor prognosis, one died and one had residual weakness.

The possible consequences of giving high dose immunoglobulins have to be kept in mind, these have been reported as severe immunological reaction in IgA deficiency, increased intracranial pressure, aseptic meningitis, thromboembolic strokes and renal failure. 27-28,29,30,31

In conclusion, we have demonstrated that the patients with GBS treated with IVIG have a faster rate of recovery than children only treated with supportive measures. Furthermore, it can be inferred from our study and from the reports in the literature, that IVIG treatment diminishes the mortality rates in childhood GBS, although we must emphasize that this was a retrospective study, GBS in our children has a good prognosis and mortality and morbidity rates are comparative to rates in other studies. Treatment with immunoglobulin is easy, safe and morbidity is lower. However larger and more comprehensive studies are needed to confirm the benefit of IVIG for routine use in the treatment of GBS in childhood.

References


