A RANDOMIZED TRIAL COMPARING INTRAVENOUS IMMUNE GLOBULIN AND PLASMA EXCHANGE IN GULLAIN–BARRE SYNDROME

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ABSTRACTS:

BACKGROUND: The sub acute demyelinating polyneuropathy known as Gullian–Barre syndrome improves more rapidly with plasma exchange. We conducted study of 50 patients to compare response of plasma exchange vs IVIG.

METHODS: we have enrolled patients who had been diagnosed as gullian–barre syndrome, which include clinical laboratory and electrophysiological diagnostic features. They were randomly assigned to receive either five plasma exchanges (50 ml/kg) on five separate sitting over 1-2 weeks or five doses of IVIg (0.4g/kg per day). The predefined outcome measure was improvement at four weeks by at least one grade of motor function.

RESULTS: Median time to start recovery after plasma exchange was 6 days compare to 5 days of IVIG. 70% of patients improve more than one grade at 4 weeks compare to 69.23% of IVIG.

CONCLUSION: In the acute Gullian-Barre syndrome, treatment with IVIg is at least as effective as plasma exchange.

KEY WORDS: gullian barre syndrom. Plasma exchange, IVIG.

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INTRODUCTION: Guillain-Barré syndrome (GBS) is an acute, frequently severe and fulminant polyradiculoneuropathy that is autoimmune in nature, most commonly characterized by a rapidly progressive, essentially symmetric, ascending flaccid paresis, weakness and areflexia. Multifocal segmental demyelination is the main underlying pathology of the disease. Molecular mimicry and a cross-reactive immune response play a crucial part in its pathogenesis, at least in those cases with a preceding Campylobacter jejuni infection and with antibodies to gangliosides. Intravenous immunoglobulin (IVIg) and plasma exchange are effective treatments in GBS. Despite medical treatment, GBS often remains a severe disease; 3–10% of patients die and 20% are still unable to walk after 6 months. In addition, many patients have pain and fatigue that can persist for months or years.

MATERIAL AND METHODS: A In The Present Study The Diagnosis Was Established By Criteria Of National Institute Of Neurological And Communicable Disorders And Stroke (NINCDS).
CRITERIA FOR DIAGNOSIS:
In Classic Cases Diagnosis Is Easy. But In Few Cases It Becomes Difficult. The Following Criteria, Laid By NINCDS in 1978 Help in the Diagnosis, Which Include Clinical Laboratory and Electrophysiological Diagnostic Features.

(A) Features Required For Diagnosis
- Progressive Weakness of More Than One Limb Due To Neuropathy.
- Areflexia or Marked Hyporeflexia.

(B) Features Strongly Supportive Of Diagnosis

I. Clinical Features
- Progression of Symptoms and Signs over Days Up to 4 Weeks.
- Relative Symmetry of Symptoms.
- Mild Sensory Symptoms or Signs.
- Cranial Nerve Involvement Especially Facial Diplegia.
- Recovery Beginning 2-4 Weeks After the Progression Ceases.
- Autonomic Dysfunction.
- Absence of Fever At The Onset Of Illness.

II. CSF Picture
- Elevated CSF Protein After 1 Week Of Symptoms.
- Cell Counts Of <10 Mononuclear Leucocytes per Mm of CSF.

III. Electro diagnostic Studies
- Evidence Of Nerve Conduction Slowing Or Block.

(C) Features Making the Diagnosis Doubtful
- Marked Persistent Asymmetry of Weakness.
- Marked Bladder or Bowel Dysfunction At The Onset or Its Persistence There on.
- Presence of Polymorphonuclear Leucocytes or > 50 Mononuclear Leucocytes Per C. Mrn of SF.
- Sharp Sensory Level.

(D) Features Excluding the Diagnosis
1. Diagnosis of Acute Intermittent Porphyria or Recent Diptheria
2. Diagnosis of Botulism, Poliomyelitis, Hysterical Paralysis, Toxic Neuropathy (Lead, Nitrofurantoin, Dapsone) or History of Hexacarbon Abuse.
3. Purely Sensory Syndrome

50 Patients Who Fulfilled The Clinical Criteria Of NINCDS For Guillain-Barre Syndrome During Period From August, 2010 To August, 2012 Were Included In The Study. Patients <12 Years of Age, Patients with Severe Unrelated Medical Illness. Patients with Duration of Illness More Than 4 Weeks Were Excluded From Study. Detailed Clinical History Recording And Examinations Were Carried Out In Each Patient. Routine Laboratory Investigations I.E. Hemogram, Urine Analysis, Blood Sugar, Blood Urea, Serum Creatinine, Electrolytes, ECG,
X-Ray-Chest, Were-Done In All Cases. CSF Was Examined Biochemically And Cytologically in Majority of Patients.

**Mode of Treatment**

After Knowing The Clinical Profile, Patients Were Divided 'Into Three Groups Considering The Line of Management.

1. Those who underwent Plasma Exchange with Supportive Measures.
2. Those who Received IV Gamma Globulin Along With Supportive Measures.
3. Those who received supportive care.

Plasma Exchange Was Done In IHBT Department, CHA With Baxter Plasmapheresis Machine (Continuous Flow). 5 Cycle Of 50ml/Kg Exchange Was Done Over 8-13 Days. Replacement Fluid Was Either “Albumin & Normal Saline” Or “Fresh Frozen Plasma”.

In IVlg Group Of Patients, IVlg Was Given In Dose Of 0. For 5 Days 4 G/Kg Daily

**ASSESSMENT**:

For all patients, clinical assessment was done using Hughes GBS disability score at admission, at starting treatment, at maximum worsening of illness, at 4 weeks of end of treatment.

Hughes scale was used for assessment. Guillain-Barre syndrome disability scale (Hughes et al., 1978)

0. Healthy
1. Minor symptoms or signs of neuropathy but capable of manual work/capable of running
2. Able to walk without support of a stick (5 m across an open space) but incapable of manual work/running.
3. Able to walk with a stick, appliance or support
4. Confined to bed or chair bound
5. Requiring assisted ventilation (for any part of the day or night)
6. Death

Outcome was measured in terms of median time to start recovery after treatment, no. of patients with improvement in disability grade at 4 weeks of treatment, mean improvement in disability grade at 4 weeks of treatment, median days to improve 1 grade of treatment

**DISCUSSION**

50 Patients, who fulfilled the clinical criteria of NINCDS for Guillain-Barre syndrome during period from august, 2010 to August, 2012 were included in the study.
Table – I response to treatment

<table>
<thead>
<tr>
<th>Course</th>
<th>PE (n=30)</th>
<th>IVIg (n=13)</th>
<th>Supportive (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median time to start recovery after treatment</td>
<td>6 days</td>
<td>5 days</td>
<td>9 days</td>
</tr>
<tr>
<td>No. of patients with improvement ≥1 grade at 4 weeks of treatment</td>
<td>21(70%)</td>
<td>9(69.2%)</td>
<td>2(28.57%)</td>
</tr>
<tr>
<td>Mean improvement in disability grade at 4 weeks of treatment</td>
<td>1.1</td>
<td>1</td>
<td>0.28</td>
</tr>
<tr>
<td>Median days to improve 1 grade of treatment</td>
<td>12 days</td>
<td>13 days</td>
<td>20 days</td>
</tr>
</tbody>
</table>

There is significant difference in number of patient's improved one grade at 4 weeks of treatment in plasma exchange group 70% & IVIg 69.2%, compared to supportive group 28.57%.

Median days for onset of recovery from start of treatment were comparable in plasma exchange group (6 days) and IVIg groups (5 days) while it is more in conventional group 9 days. Median days taken to improve one grade was comparable in plasma exchange group (12 days) & IVIg group (13 days) while more in conventional group (20 days).

There was no significant difference in mean improvement of disability grade at 4 weeks between PE (1.1) & IVIg (1.0) group.

Table –II : Comparison of Plasma Exchange & Supportive group

<table>
<thead>
<tr>
<th>Study</th>
<th>% Of patients improved ≥1 grade at 4 weeks in PE group</th>
<th>% Of patients improved ≥ grade at 4 weeks in supportive group</th>
</tr>
</thead>
<tbody>
<tr>
<td>The GBS study group,1985</td>
<td>59%</td>
<td>39%</td>
</tr>
<tr>
<td>Osterman et al,1984</td>
<td>77.7%</td>
<td>30%</td>
</tr>
<tr>
<td>Present study</td>
<td>70%</td>
<td>28.7%</td>
</tr>
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</table>

Present study has comparable result to The GBS study group & Osterman et al so far as percentage of patients improved ≥1 grade at 4 weeks from start of treatment is considered. 70% of patients undergoing PE improved ≥1 grade as compare to only 28.7% in supportive group. So there is significant improvement in outcome of patients undergoing PE as compared to patients taking supportive care only.
Table-III Comparison of mean improvement of disability scale at 4 weeks between PE & IVIg group.

<table>
<thead>
<tr>
<th>Study</th>
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<th>IVIg</th>
</tr>
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<tr>
<td>Plasma Exchange/Sandoglobulin Guillain-Barre Syndrome Trial Group, 1997</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Present Study</td>
<td>1.1</td>
<td>1</td>
</tr>
</tbody>
</table>

There is no significant difference in mean improvement of disability scale among patients taking IVIg & undergoing PE. Thus, PE and IVIg had equivalent efficacy.

Table-IV Comparison of other outcome between IVIg & PE

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There is no significant difference between IVIg & PE in terms of median time to start recovery, no. of patients improved ≥1 grade & median days to improve 1 grade.

We reviewed previous studies comparing outcome between IVIg & PE, most of them show no significant difference. Diener et al., 2001, Garcia et al., 1985, Nomura et al., 2000, Plasma Exchange/ Sandoglobulin Guillain-Barre Syndrome Trial Group, 1997.
This study cannot carry the same weight as a prospective randomized clinical trial, but the results are comparable. Thus supports the role of plasma exchange or IVIg in acute GBS.

Table-V Comparison of other outcome between IVIg & PE

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**CONCLUSION:** 50 patients of GBS were studied. 30 patients treated with plasma exchange were compared with 13 patients who received high dose IV gamma globulin & 7 patients who received supportive treatment only.

Immunotherapy definitely makes a difference in the recovery of GBS patients. PE and IVIg are equally effective. Although IVIg has advantage of ease to administer & lesser side effects, but, it is costly. PE is less costly than IVIg, but its main limitations would be availability of the technical expertise and support. So decision regarding use of either PE or IVIg should depend upon availability of resources and patient’s affordability.

Supportive care in addition to Immunotherapy are also important. Proper nursing care, nutrition, management of dysautonomia, prevention of infection, DVT prophylaxis & physiotherapy are valuable.

**REFERENCES :**


