ADVANTAGES OF INTRAVENOUS GAMMA GLOBULIN THERAPY IN GUILLAIN BARRE'S SYNDROME (IN EIGHT CHILDREN)

Kıvılcım GÜCÜYENER*, M.D., Üstün EZER, M.D., Ufuk BEYAZOVA, M.D., Canan TÜRKYILMAZ, M.D.

Gazi University, Faculty of Medicine, Departments of Paediatrics and Paediatric Neurology*, Ankara, Turkey
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SUMMARY : IVGG can improve the clinical course of several immune mediated diseases such as idiopathic thrombocytopenic purpura, multiple selerosis and Rh/rh incompatibility in newborn. The aetiology of GBS has not been established but immunological mechanisms are involved. We report the results of IVGG therapy in eight children diagnosed as GBS, and their prognosis.

***Key Words :** Intravenous Gammaglobulin Therapy, Guillain Barrẻ Syndome, Children.*

INTRODUCTION

Guillain-Barrẻ Syndrome (GBS) is an inflammatory demyelinating disease of the peripheral nerve and may be associated with extensive axonal and even anterior cell degeneration (2). Antecedent events include infections, immunization, malign disease and surgery (1) Cardinal features of the syndrome are characterized by a symmetrical, rapidly progressive quadriparesis frequently involving bulbar and respiratory muscles, associated with absent deep tendon reflexes and elevated CSF protein (1, 2). Although many patients with GBS make a satisfactory recovery, there is a mortality rate of about 5%, 10 to 23% require artificial respiration, and 10 to 15% remain disabled (2). The aetiology of GBS has not been established but immunological mechanisms almost certainly are involved (3, 6, 12) .

Intravenous gamma globulin (IVGG) can improve the clinical course of several immune mediated diseases. We investigated the effectiveness of such treatment on the course of GBS and report the results of eight patients.

MATERIALS AND METHODS

Eight patients who fulfilled the criteria for the diagnosis of were investigated GBS (2) . In all patients treated the diagnosis was supported by neurophysiological studies that showed decreased nerve conduction velocity or conduction block. IVGG sandoglobulin (SANDOZ) was given in a dose of 0.5 g/kg/d for 5 consecutive days.

Clinical and laboratory data of the patients and the response to treatment are shown in table (1).

RESULTS

In five of the 8 patients IVGG seems to have been effective. This effect was most marked if the therapy was started within the first three days after the onset of weakness(patients 4, 7, 8 and maybe 3). However in all patients the recovery of EMG was slow and incomplete. Four patients died; one due to the primary disease; non-Hodgkin lymphoma and the other three had severe cardiac dysrhythmia hypo-hypertension attacks and severe respiratory problems (Table 1).

Case	1	2	3	4	5	6	7	8
Age	2.5 m	1 y	2.5 y	12 y	12 y	9 y	6 y	8 y
Sex	F	M	M	F	M	F	F	M
Interval between preceding illness	7days	-	1days	10days	6days	10days	7days	12days
Duration of weakness on admission	6d	10d	1d	3d	11d	4d	2d	2d
LP day done	d 7	-	d 1	d 7	d 12	d 11	d 2	d 2
Protein level	70mg/dl	10mg/dl	70mg/dl	185mg/dl	200mg/dl	84mg/dl	480mg/dl	340mg/dl
Cranial nerve	-	VII	-	VII	VII,VI	VII,VI,IX	-	-
Autonomic symptoms	hypertension	-	urinary incontinence	-	hypertension urinary hypertension	hypertension	-	-
Respiratory symptoms	Bulbar problems	Bulbar problems	Minimal bulbar problems	Bulbar problems	Bulbar problems	Bulbar problems	Bulbar problems	Bulbar problems
Pain	+	-	+	+	+	+	+	+
Muscle weakness	+	+	+	+	+	+	+	+
Paresthesia	+	-	+	+	+	+	+	+
Abnormal EMG consistent with GBS	+	+	+	+	+	+	+	+
Time from onset of GBS to IVGG(dose 0.5g/kg/5d)	7d	10d	1d	3d	12d	3d	2d	2d
Time from IVGG initial improvement	no improvement	after 5th treatment upper extremity movement improved	after 3rd treatment upper extremity movement improved	After 2nd treatment upper extremity movement improved	No improvement	No improvement	After 3rd dose upper extremity improved with mild lower extremity movement	After 2nd dose minimal extremity movement started
Length of hospital stay	11 d	15 d	45 d	15 d	15 d	30 d	15 d	18 d
Follow up	Severe autonomic symptoms cardiac arhythmia Exitus	Clumsy at 4 mos normal at 13 mos EMG improved	Later diagnosed to have Non-Hodgkin Lymphoma and died	Walked with aid after 3 mos, normal at 7 mos EMG improved	Severe autonomic symptoms with cardiac arhythmia Exitus	Severe autonomic symptoms Exitus	Clumsy at 2 mos normal at 4 mos EMG improved	Walking with aid after 3 mos normal at 7 mos EMG improved

Table 1 : Clinical and laboratory data of the patients and the response to treatment.

DISCUSSION

The response of patients suggests IVGG has a beneficial effect on the clinical course of GBS, thus the need for such a treatment which will influence the clinical course is obvious. Comparison between our patients and other trials GBS of treated with IVGG of is demonstrated in Table II. In a small number of children IVGG with a dose ranging from 0.4-1g/kg/d has been reported to be helpfull (7,10). Recently a randomized Dutch trial demonstrated the efficacy of daily infusions of IVGG(0.4g/d) in the first two weeks of the disease (11). Moreover treatment with IVGG especially in small children has several advantages. IVGG-treated patients improve faster, so spend less time in hospital, have a lower incidence of mechanical ventilation and the mean intubation period is reduced. With less days spent in the intensive care unit, the hospital cost of the IVGG treated patient is less than for patients treated by other modalities. IVGG is easily

	Total patients with IVGG	Favourable response to IVGG	Incomplete slow recovery	IVGG treatment after another treatment
Klegweg 1988	6 (%100)	4 (%67)	2 (%33)	2 (%33)
Eli Shahar 1990	3(%100)	3(%100)		
Dutch trial 1992		%53		
Pearce		3 (%100)		3(%100)
Our patients	8 (%100)	5 (%63)		

Abbrevations: Intravenous gamma globulin (IVGG) Guillain Barre' (GBS)
Electromyography= EMG

Table 2 : Comparison between our patients and other trials of GBS treated with IVGG

administered without retard and is widely available (12, 11). There are barely any contraindications, it is easily applicable in all hospitals, has no serious complications and has proved to be safe (9).

During the acute illness an abnormal immune response, presumably a primary lymphocytic T cell mechanism for the inflammation as an aberrant response to a precipitating infection or other immunological stimulus, has been implicated in the pathogenesis of GBS. During the acute illness some circulating lymphocytes are sensitized to P-2 a major peripheral nerve myelin antigen but the cause-effect relationship with regard to myelin destruction is unclear. Pathological studies led to the hypothesis that an early antibody attack on myelin occurs in some cases and an inflammatory process in others, both leading to myelin destruction by macrophage response (12). Circulating antineural antibodies against P-2 cerebroside have been demonstrated in GBS (14) and FgM antibodies against ganglioside GM-1 have been found after campylobacter infection (15). Experimental allergic neuritis, an animal model of GBS is produced (15) by sensitizing animals to the P-2 myelin antigen or its fragments by inoculation and a species-specific antigen response can be elicited (13). A model of humoral non inflammatory demyelination is produced by the intraneural injection of galactocerebroside or by anti-cerebroside antibody (8). A conclusion can be drawn that both arms of the immune system can participate in the macrophage induced demyelination with the humoral response occurring in a small group of patients but inflammation dominating in most cases.

IVGG contains anti-idiotypes against cross reactive idiotypes expressed by disease associated autoantibodies (4). An interesting anology can be drawn between therapeutic recovery from autoimmune diseases induced by IVGG and the spontaneous remission from autoimmune diseases which occurs in association with generation of auto-anti idiotypic anti-bodies against prerecovery autoantibodies. Antiidiotypic antibodies against autoantibodies have been found in remission sera of patients with GBS (12).Also F(ab')2 fragments of GB patients' post recovery IgG inhibits autoantibody activity in F(ab')2 fragments of autologous IgG obtained during the acute phase of the disease (9, 12). F(ab')2 fragments of IVGG neutralize the functional activity of autoantibodies and /or inhibit the binding of autoantibody to antigen. IVGG is very effective in preventing the binding of complement to targets and will prevent the immunopathological effects of complement (5). In GBS when macrophage-associated demyelination occurs directly operating by complement fixation and generation of the membrane attack complex, IVGG may prevent the immunopathological events in this antibody mediated mechanism.

The immune system has a large mosaic of interactions among its various components and the differing pathogenesis in GBS depends on the relative contributions of those components, and IVGG by interfering to some extent blocks the ongoing pathology and results in clinical improvement.

Correspondence to : Dr.Kıvılcım GÜCÜYENER
Gazi Üniversitesi Tıp Fakültesi
Pediatrik Nöroloji Anabilim Dalı
Beşevler
06500 ANKARA - TÜRKİYE
Phone : 312 - 214 10 00 / 6007

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