The Turkish Journal of Pediatrics 1996; 38: 119-123

HIGH – DOSE INTRAVENOUS IMMUNE GLOBULIN IN THE MANAGEMENT OF SEVERE GUILLAIN – BARRÉ SYNDROME*

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SUMMARY: Baskın E, Türkay S, İçağasıoğlu D, Tanzer F, Cevit Ö. (Department of Pediatrics, Cumhuriyet University Faculty of Medicine, Sivas, Turkey). High-dose intravenous immune globulin in the management of severe Guillain-Barré syndrome. Turk J Pediatr 1986; 38: 119-123.

Guillain-Barré Syndrome (GBS) is the most common cause of acute generalized paralysis. Although the cause and pathogenesis of GBS remain unknown, there is increasing evidence to suggest that this syndrome has an immunological basis. Two children suffering from GBS were treated with high-dose intravenous immune globulin (IVIG) (1 g/kg/day over two consecutive days). Both children showed marked clinical improvement within 48 hours of the onset of treatment. It is suggested, on the basis of recent case reports, that immunoglobulins may have an important role in the treatment of Guillain-Barré Syndrome.
Key words: intravenous immunoglobulin, Guillain-Barré syndrome.

Guillain-Barré Syndrome (GBS) is the most common cause of acute generalized paralysis, with an annual incidence of 0.75 to 2 cases per 100.000 population[1,2]. It is characterized by demyelination of peripheral nerves and causes a flaccid paralysis, autonomic dysfunction and minor sensory symptoms. The mortality rate is approximately five percent. In addition, 10 to 30 percent of patients require artificial ventilation, and three to 10 percent experience relapses. Although functional recovery is the rule, 20 percent of patients have residual disability[3-5]. The likelihood of permanent disability increases with the severity and duration of the disease, and patients may require prolonged hospital care. There is therefore an urgent need for a form of treatment that would decrease the severity of the acute phase of the disease and shorten the recovery period.

There is increasing evidence to suggest that this syndrome has an immunological basis. Recently it has been shown that high-dose intravenous immune globulin (IVIG) may be of benefit in GBS[6-8]. Here we present two cases of GBS who were given high-dose IVIG. Although the usual dose of IVIG is 400 mg/kg/day for five days, we administered 1 g/kg/day over two days as reported in Shahar et al.'s study[7].

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Case Reports

Case 1

An eight-year-old girl who was previously healthy was admitted with a seven-day history of generalized arthralgia and myalgia mainly in the lower limbs following an upper respiratory tract infection. She was unable to stand and could not raise her legs from the bed due to pain. Two days later the weakness in the lower limbs become more marked, and progressed to involve all muscle groups. There was evidence of decreased deep tendon reflexes and cranial nerve involvement with marked facial weakness, decreased pharyngeal reflexes, nasal voice and difficulties in swallowing and breathing. Her forced vital capacity (FVC) was 0.70, which was 32 percent of the predicted value. Arterial blood gases were as follows: pH 7.42, arterial carbon dioxide tension 40 and arterial oxygen tension 60. The cerebrospinal fluid protein content was elevated to 103 mg/dl with no cells. Initial investigations revealed normal hematological and biochemical indices. Results of bacterial and viral studies of blood and cerebrospinal fluid were negative.

A diagnosis of Guillain-Barré syndrome was made according to the criteria of Ausbury and Cornblath[9]. IVIG (Sandoglobulin, Sandoz Pharmaceuticals) was given intravenously at a dose of 1 g/kg/day over two consecutive days. During the infusions the patient was monitored for side effects, including alterations in heart rate, respiratory rate, blood pressure and temperature. There was no treatment added after IVIG. Clinical improvement began 24 hours after the beginning of IVIG therapy with improvement in breathing difficulty, and at 48 hours improvement in facial diplegia and swallowing difficulty were seen. At the end of the fifth day of therapy, the patient was sitting and walking with support. FVC increased to 70 percent of the predicted value on the eighth day.

She was sent home on the 15^{th} day of hospitalization. On her outpatient follow-up visit two months later, complete clinical recovery from illness and no abnormality of the musculoskeletal system were seen.

Case 2

A previously well 12-year-old boy was admitted with a four-day history of progressive weakness and pain in his feet and legs following mild gastroenteritis. On examination he had flaccid paralysis and hyporeflexia affecting all four limbs symmetrically with reduced strength. His proximal muscle groups were affected most severely. Decreased pharyngeal reflexes, diplopia and difficulty in breathing were seen. Vital capacity declined to 20 percent of predicted value, and arterial blood gases were as follows: pH: 7.43, $PaCO_2$ 35, PaO_2 76. The cerebrospinal fluid was cellular with the protein concentration elevated to 182 mg/dl. The hematological and biochemical results were within normal limits. Bacterial and

viral studies of blood and cerebrospinal fluid were done, and only the cytomegalovirus serologic test was found to be positive.

The patient's clinical presentation and laboratory parameters led to the diagnosis of Guillain-Barré syndrome[9]. He was intubated and ventilated. Treatment with IVIG was given at a dose of 1 g/kg/day over two consecutive days. No side effects occurred during IVIG therapy. Fourty-eight hours after treatment, he was extubated and was able to sit with support. Within eight days of the start of IVIG infusion, he was able to walk more than five meters with assistance. Improvement continued gradually, and 10 days after the completion of therapy FVC returned to normal.

The patient was sent home on the 30th day of hospitalization with complete clinical recovery. No recurrence of symptoms was observed during the subsequent one-year follow-up period.

Discussion

The acute polyneuropathy of GBS often affects peripheral nerves. Typically a nonspecific prodromal illness is followed one to 28 days later by the onset of weakness which progresses over the next seven to 14 days, generally reaching a peak by day 10. A plateau period lasting 5 to 46 days (mean 10.5 days) precedes the onset of recovery, which is complete by 2.5 to 15 months[4]. Difficulty in swallowing and impaired respiration are the most serious symptoms. Mechanical ventilation may be needed for as long as eight weeks, with subsequent possible complications such as pneumonia and pneumothorax[7].

Although the cause and pathogenesis of GBS remain unknown, it has been proposed that anti-peripheral nerve myelin antibodies may account for the segmental demyelination of the peripheral nerves occurring in this syndrome. Rising titers of complement-fixing anti-peripheral-nerve myelin antibodies have been found during the acute phase, and declining titers during convalescence[10]. The association of these antibodies with damage to myelin has been determined[10, 11].

Various methods of treatment have been advocated to modify the course of the disease. Supportive and symptomatic measures are still considered the mainstay of therapy. Steroid use was popular for many years, but controlled trials have found no benefit and corticosteroids can no longer be considered useful therapy[1]. For severe GBS plasmapheresis and high-dose intravenous immunoglobulin are other therapy methods. Plasmapheresis can shorten the duration of the disease and reduce the risk of respiratory failure if given early in the disease process. However, plasmapheresis is technically difficult to perform in children and may be contraindicated at any age because of cardiac instability, particularly for children less than two years old, and can be performed only in a few centers that have both the appropriate equipment and trained personnel[12]. When IVIG

therapy and plasmapheresis were compared in controlled trials, the functional recovery in the IVIG group was found to be more rapid and complete than in the plasmapheresis group. In addition, the mean period of intubation and hospitalization were found to be seven to 14 days less in the immunoglobulin group. These earlier studies showed that IVIG therapy is widely available, less aggressive, safe regarding viral transmission and adverse reactions, and less expensive[13, 14]. The rapid recovery of our patients was probably related to IVIG treatment.

The mode of action of IVIG remains uncertain, although several mechanisms have been proposed. Some evidence suggests that IVIG contains antiidiotype antibodies against the auto-antibodies present in patients with autoimmune diseases[15]. A similar action in GBS could be suspected, blocking the auto-antibodies against myelin present in these patients[10]. Alternatively, IVIG might improve neuronal damage by another mechanism. Approximately two-thirds of GBS cases follow an infection, and a virus or a bacterial toxin may be an etiologic factor. The IVIG may have provided neutralizing antibodies or antitoxin[1, 7].

Recently it has been reported that relapses may occur in GBS after treatment with IVIG. It is suggested that the active phase of the disease is longer than the duration of treatment in these individuals. In these patients longer treatment regimens might provide better results than current regimens[16, 17].

We conclude that immune globulin is a practical, safe and effective treatment for GBS. Because the condition is uncommon, multicenter, controlled studies are needed to evaluate this new method of treatment.

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