

## MANAGEMENT OF GUILLAIN-BARRÉ SYNDROME-AN AUTOIMMUNE DISORDER: A REVIEW

Raghvendra<sup>1\*</sup>, Satyanand Tyagi<sup>2</sup>, Pramod Yadav<sup>2</sup> and Sunanda Saxena<sup>2</sup>

<sup>1</sup>Aligarh College of Pharmacy, Aligarh, Uttar Pradesh, India -202001.

<sup>2</sup>K.N.G.D Modi Institute of Pharmaceutical Education & Research, Modinagar, Ghaziabad, Uttar Pradesh, India -201204.

**ABSTRACT:** Guillain-Barré syndrome is a disorder in which the body's immune system attacks part of the peripheral nervous system. The first symptoms of this disorder include varying degrees of weakness or tingling sensations in the legs. In many instances, the weakness and abnormal sensations spread to the arms and upper body. There is no known cure for Guillain-Barré syndrome, but therapies can lessen the severity of the illness and accelerate the recovery in most patients. There are also a number of ways to treat the complications of the disease. Currently, plasmapheresis and high-dose immunoglobulin therapy are used. Plasmapheresis seems to reduce the severity and duration of the Guillain-Barré episode. In high-dose immunoglobulin therapy, doctors give intravenous injections of the proteins that in small quantities, the immune system uses naturally to attack invading organism. The most critical part of the treatment for this syndrome consists of keeping the patient's body functioning during recovery of the nervous system. This can sometimes require placing the patient on a respirator, a heart monitor, or other machines that assist body function. The aim of present article is to provide in depth knowledge about Guillain-Barré syndrome which is no doubt, a rare autoimmune disorder. In this article the author has explained all the clinical aspects related to Guillain-Barré syndrome. This article presents a brief review of Guillain-Barré syndrome with an emphasis on its possible management and therapies.

**Key words:** Autoimmune Disorder, Guillain-Barré syndrome, GBS, AIDP, Landry's paralysis, peripheral neuropathies.

Guillain-Barré syndrome (GBS) is an acute inflammatory demyelinating polyneuropathy (AIDP), an autoimmune disorder affecting the peripheral nervous system, usually triggered by an acute infectious process. The syndrome was named after the French physicians Guillain, Barré and Strohl, who were the first to describe it in 1916. It is sometimes called Landry's paralysis, after the French physician who first described a variant of it in 1859. It is included in the wider group of peripheral neuropathies. There are several types of GBS, but unless otherwise stated, GBS refers to the most common form, AIDP. GBS is rare and has an incidence of 1 or 2 people per 100,000. It is frequently severe and usually exhibits as an ascending noted by weakness in the legs that spreads to the upper limbs and the face along with complete loss of deep tendon reflexes

## INTRODUCTION

With prompt treatment by plasmapheresis or intravenous immunoglobulins and supportive care, the majority of patients will regain full functional capacity. However, death may occur if severe pulmonary complications and autonomic nervous system problems are present. Guillain-Barré is one of the leading causes of non-trauma-induced paralysis in the world.

Guillain-Barre syndrome is a post infectious polyradiculoneuropathy. It is equally prevalent in both the adult and the paediatric populations. Usually Guillain-Barré occurs a few days or weeks after the patient has had symptoms of a respiratory or gastrointestinal viral infection. Occasionally, surgery or vaccinations will trigger the syndrome. The disorder can develop over the course of hours or days, or it may take up to 3 to 4 weeks. No one yet knows why Guillain-Barré strikes some people and not others or what sets the disease in motion. What scientists do know is that the body's immune system begins to attack the body itself, causing what is known as an autoimmune disease. Guillain-Barré is called a syndrome rather than a disease because it is not clear that a specific disease-causing agent is involved. Reflexes such as knee jerks are usually lost. Because the signals traveling along the nerve are slower, a nerve conduction velocity (NCV) test can give doctor clues to aid the diagnosis. The cerebrospinal fluid that bathes the spinal cord and brain contains more protein than usual, so a physician may decide to perform a spinal tap (David, Evans, et al, 2006).

### Classification of Guillain–Barré syndrome

Six different subtypes of Guillain–Barré syndrome (GBS) exist:

- ❖ **Acute inflammatory demyelinating polyneuropathy (AIDP)** is the most common form of GBS, and the term is often used synonymously with GBS. It is caused by an auto-immune response directed against Schwann cell membranes.
- ❖ **Miller Fisher syndrome (MFS)** is a rare variant of GBS and manifests as a descending paralysis, proceeding in the reverse order of the more common form of GBS. It usually affects the eye muscles first and presents with the triad of ophthalmoplegia, ataxia, and areflexia. Anti-GQ1b antibodies are present in 90% of cases.
- ❖ **Acute motor axonal neuropathy (AMAN)**, aka Chinese Paralytic Syndrome, attacks motor nodes of Ranvier and is prevalent in China and Mexico. It is likely due to an auto-immune response directed against the axoplasm of peripheral nerves. The disease may be seasonal and recovery can be rapid. Anti-GD1a antibodies are present. Anti-GD3 antibodies are found more frequently in AMAN.
- ❖ **Acute motor sensory axonal neuropathy (AMSAN)** is similar to AMAN but also affects sensory nerves with severe axonal damage. Like AMAN, it is likely due to an auto-immune response directed against the axoplasm of peripheral nerves. Recovery is slow and often incomplete.
- ❖ **Acute panautonomic neuropathy** is the rarest variant of GBS, sometimes accompanied by encephalopathy. It is associated with a high mortality rate, due to cardiovascular involvement, and associated dysrhythmias. Impaired sweating, lack of tear formation, photophobia, dryness of nasal and oral mucosa, itching and peeling of skin, nausea, dysphagia, constipation unrelieved by laxatives or alternating with diarrhea occur frequently in this patient group. Initial non-specific symptoms of lethargy, fatigue, headache, and decreased initiative are followed by autonomic symptoms including orthostatic light-headedness, blurring of vision, abdominal pain, diarrhea, dryness of eyes, and disturbed micturition. The most common symptoms at onset are related to orthostatic intolerance, as well as gastrointestinal and sudomotor dysfunction. Parasympathetic impairment (abdominal pain, vomiting, obstipation, ileus, urinary retention, dilated unreactive pupils, and loss of accommodation) may also be observed.

- ❖ **Bickerstaff's brainstem encephalitis (BBE)** is a further variant of Guillain–Barré syndrome. It is characterized by acute onset of ophthalmoplegia, ataxia, disturbance of consciousness, hyperreflexia or Babinski's sign. The course of the disease can be monophasic or remitting-relapsing. Large, irregular hyper intense lesions located mainly in the brainstem, especially in the pons, midbrain and medulla are described in the literature. BBE despite severe initial presentation usually has a good prognosis. Magnetic resonance imaging (MRI) plays a critical role in the diagnosis of BBE.

A considerable number of BBE patients have associated axonal Guillain–Barré syndrome, indicative that the two disorders are closely related and form a continuous spectrum (Goldman, AS, et al, 2005).

### **Sign and Symptoms of Guillain–Barré Syndrome**

The first symptoms of GBS are usually numbness or tingling (paresthesia) in the toes and fingers, with progressive weakness in the arms and legs over the next few days. Some patients experience paresthesia only in their toes and legs; others only experience symptoms on one side of the body. The symptoms may stay in this phase, causing only mild difficulty in walking, requiring crutches or a walking stick. However, sometimes the illness progresses, leading to complete paralysis of the arms and legs. About one quarter of the time, the paralysis continues up the chest and freezes the breathing muscles, leaving the patient dependent on a ventilator. If the swallowing muscles are also affected, a feeding tube may be needed (Griffin, JW, et al, 1995).

The disorder is characterized by symmetrical weakness which usually affects the lower limbs first, and rapidly progresses in an ascending fashion. Patients generally notice weakness in their legs, manifesting as "rubbery legs" or legs that tend to buckle, with or without dysesthesias (numbness or tingling).

As the weakness progresses upward, usually over periods of hours to days, the arms and facial muscles also become affected. Frequently, the lower cranial nerves may be affected, leading to bulbar weakness, oropharyngeal dysphagia (drooling, or difficulty swallowing or maintaining an open airway) and respiratory difficulties. Most patients require hospitalization and about 30% require ventilatory assistance. Facial weakness is also commonly a feature, but eye movement abnormalities are not commonly seen in ascending GBS, but are a prominent feature in the Miller-Fisher variant. Sensory loss, if present, usually takes the form of loss of proprioception (position sense) and areflexia (complete loss of deep tendon reflexes), an important feature of GBS. Loss of pain and temperature sensation is usually mild.

In fact, pain is a common symptom in GBS, presenting as deep aching pain, usually in the weakened muscles, which patients compare to the pain from over exercising. These pains are self-limited and should be treated with standard analgesics. Bladder dysfunction may occur in severe cases but should be transient. If severe, spinal disorder should be suspected. Fever should not be present, and if it is, another cause should be suspected. In severe cases of GBS, loss of autonomic function is common, manifesting as wide fluctuations in blood pressure, orthostatic hypotension, and cardiac arrhythmias. Acute paralysis in Guillain–Barré syndrome may be related to sodium channel blocking factor in the cerebrospinal fluid (CSF). Significant issues involving intravenous salt and water administration may occur unpredictably in this patient group, resulting in SIADH. SIADH is one of the causes of hyponatremia and can be accompanied with various conditions such as malignancies, infections and nervous system diseases. Symptoms of Guillain- Barre syndrome such as general weakness, decreased consciousness, and seizure are similar to those of hyponatremia. The symptoms of Guillain–Barré syndrome are also similar to those for progressive inflammatory neuropathy (Ho, TW, et al, 1995).

## **Etiology and Causes of Guillain–Barré Syndrome**

All forms of Guillain–Barré syndrome are due to an immune response to foreign antigens (such as infectious agents) that are mistargeted at host nerve tissues instead. The targets of such immune attack are thought to be gangliosides, compounds naturally present in large quantities in human nerve tissues. The most common antecedent infection is the bacteria *Campylobacter*. However, 60% of cases do not have a known cause; one study suggests that some cases are triggered by the influenza virus, or by an immune reaction to the influenza virus. The end result of such autoimmune attack on the peripheral nerves is damage to the myelin, the fatty insulating layer of the nerve, and a nerve conduction block, leading to a muscle paralysis that may be accompanied by sensory or autonomic disturbances.

However, in mild cases, nerve axon (the long slender conducting portion of a nerve) function remains intact and recovery can be rapid if remyelination occurs. In severe cases, axonal damage occurs, and recovery depends on the regeneration of this important tissue. Recent studies on the disorder have demonstrated that approximately 80% of the patients have myelinloss, whereas, in the remaining 20%, the pathologic hallmark of the disorder is indeed axon loss.

Guillain-Barré, unlike disorders such as multiple sclerosis (MS) and Lou Gehrig's disease (ALS), is a peripheral nerve disorder and does not generally cause nerve damage to the brain or spinal cord (Kuwabara, S, et al, 2004).

### **Influenza vaccine**

GBS may be a rare side-effect of influenza vaccines; a study of the Vaccine Adverse Event Reporting System (VAERS) indicates that it is reported as an adverse event potentially associated with the vaccine at a rate of an excess of 1 per million vaccines (over the normal risk). There were reports of GBS affecting an excess of 10 per million who had received swine immunizations in the 1976 U.S. outbreak of swine flu—25 of which resulted in death from severe pulmonary complications, leading the government to end that immunization campaign (Stowe, J, et al, 2009).

However, the role of the vaccine in these cases has remained unclear, partly because GBS had an unknown but very low incidence rate in the general population making it difficult to assess whether the vaccine was really increasing the risk for GBS. Later research has pointed to the absence of or only a very small increase in the GBS risk due to the 1976 swine flu vaccine. Furthermore, the GBS may not have been directly due to the vaccine but to a bacterial contamination of the vaccine (Sivadon-Tardy, V, et al, 2009).

Since 1976, no other influenza vaccines have been linked to GBS, though as a precautionary principle, caution is advised for certain individuals, particularly those with a history of GBS. On the other hand, getting infected by the flu increases the risk of developing GBS to a much higher level (approx. 10 times higher by recent estimates) and, all in all, the flu vaccination contributes protection against the risk of GBS (Haber, P, et al, 2009 and Vellozzi, C, et al, 2009).

### **Diagnosis of Guillain–Barré Syndrome**

Because its symptoms vary and its cause is unknown, GBS can be difficult to diagnose. If the symptoms occur uniformly across the body and progress rapidly, the diagnosis is easier. Observation of the patient's symptoms and an evaluation of the medical history provide the basis for diagnosis of Guillain-Barre syndrome, although no single observation is suitable to make the diagnosis.

**Tests:** Three tests can confirm a diagnosis of Guillain-Barre syndrome.

**Lumbar puncture (spinal tap):** The patient is given local anaesthetic. Once the anaesthetic has taken effect, a needle is inserted between two lower (lumbar) vertebrae and a sample of cerebrospinal fluid is drawn. An elevated level of protein without an increase in the number of white blood cells (WBCs) in the fluid is characteristic of GBS.

**Electromyogram (EMG):** This is an effective diagnostic tool because it records muscle activity and can show the loss of individual nerve impulses due to the disease's characteristic slowing of nerve responses.

**Nerve conduction velocity (NCV):** This test is performed with EMG, and together, they are often referred to as EMG/NCV studies. NCV records the speed at which signals travel along the nerves. These signals are characteristically slowed in GBS, although the findings may evolve over several weeks.

### **Management of Guillain–Barré Syndrome**

Guillain–Barré Syndrome is considered a medical emergency and most patients are admitted to the hospital soon after diagnosis. If the patient's breathing seems to be at risk, he or she is usually managed in an intensive care unit (ICU). Although GBS can improve spontaneously, there are a number of treatments that facilitate recovery. Like GBS, CIDP (Chronic Inflammatory Demyelinating Polyneuropathy) can improve spontaneously. However, recovery may be very slow and the illness can either get progressively better or worse, or can follow a relapsing/remitting course. Most patients with GBS and CIDP are treated with plasmapheresis or immunoglobulin. Corticosteroids may be used to treat CIDP but are not used to treat GBS, as it worsens rather than improves the condition (McKhann, GM, et al, 1991).

#### **Plasmapheresis**

Patients diagnosed early in the course of the disease and those who are acutely ill often respond well to blood plasma exchange (plasmapheresis). In this procedure, blood is withdrawn and passed through a series of filters that separate the different types of blood cells. The blood cells are then suspended in donor or synthetic plasma and returned to the patient's body. The patient's plasma is discarded. Plasmapheresis is thought to remove the substances that damage myelin. It can shorten the course of GBS, alleviate symptoms, and prevent paralysis.

#### **Immunoglobulin**

Large doses of immunoglobulin given intravenously can help shorten the duration of symptoms. This treatment is just as effective as plasmapheresis. It often is preferred to plasmapheresis because it does not require insertion of a large venous catheter. Overall, about 70% of patients respond to plasmapheresis or immunoglobulin. There is no evidence of additional benefit from treatment with both procedures.

#### **Medications**

Muscle and joint pain can be treated with over-the-counter analgesics such as aspirin. If necessary, stronger pain medication (e.g., acetaminophen with hydrocodone) may be prescribed. Muscle spasms can be controlled with relaxants such as diazepam. There is no known cure for Guillain-Barré syndrome, but therapies can lessen the severity of the illness and accelerate the recovery in most patients. There are also a number of ways to treat the complications of the disease. As told earlier currently, plasmapheresis and high-dose immunoglobulin therapy are used. Plasmapheresis seems to reduce the severity and duration of the Guillain-Barré episode.

In high-dose immunoglobulin therapy, doctors give intravenous injections of the proteins that in small quantities, the immune system uses naturally to attack invading organism. Investigators have found that giving high doses of these immunoglobulins, derived from a pool of thousands of normal donors, to Guillain-Barré patients can lessen the immune attack on the nervous system. The most critical part of the treatment for this syndrome consists of keeping the patient's body functioning during recovery of the nervous system. This can sometimes require placing the patient on a respirator, a heart monitor, or other machines that assist body function. Supportive care with monitoring of all vital functions is the cornerstone of successful management in the acute patient. Of greatest concern is respiratory failure due to paralysis of the diaphragm. Early intubation should be considered in any patient with a vital capacity (VC) <20 ml/kg, a negative inspiratory force (NIF) <-25 cmH<sub>2</sub>O, more than 30% decrease in either VC or NIF within 24 hours, rapid progression of disorder, or autonomic instability.

Once the patient is stabilized, treatment of the underlying condition should be initiated as soon as possible. Either high-dose intravenous immunoglobulins (IVIg) at 400 mg/kg for 5 days or plasmapheresis can be administered, as they are equally effective and a combination of the two is not significantly better than either alone. Therapy is no longer effective two weeks after the first motor symptoms appear, so treatment should be instituted as soon as possible. IVIg is usually used first because of its ease of administration and safety profile, with a total of five daily infusions for a total dose of 2 g/kg body weight (400 mg/kg each day). The use of intravenous immunoglobulins is not without risk, occasionally causing hepatitis, or in rare cases, renal failure if used for longer than five days. Glucocorticoids have not been found to be effective in GBS. If plasmapheresis is chosen, a dose of 40-50 mL/kg plasma exchange (PE) can be administered four times over a week. Following the acute phase, the patient may also need rehabilitation to regain lost functions. This treatment will focus on improving ADL (activities of daily living) functions such as brushing teeth, washing, and getting dressed. Depending on the local structuring on health care, a team of different therapists and nurses will be established according to patient needs (Kuwabara, S, et al, 2004).

An occupational therapist can offer equipment (such as wheelchair and special cutlery) to help the patient achieve ADL independence. A physiotherapist would plan a progressive training program and guide the patient to correct, functional movement, avoiding harmful compensations which might have a negative effect in the long run. A speech and language therapist would be essential in the patient regaining speaking and swallowing ability if they were intubated and received a tracheostomy. The speech and language therapist would also offer advice to the medical team regarding the swallowing abilities of the patient and would help the patient regain their communication ability pre-dysarthria. There would also be a doctor, nurse and other team members involved, depending on the needs of the patient. This team contribute their knowledge to guide the patient towards his or her goals, and it is important that all goals set by the separate team members are relevant for the patient's own priorities. After rehabilitation the patient should be able to function in his or her own home and attend necessary training as needed (Yuki, N, et al, 2008).

#### **Prognosis**

Guillain-Barré syndrome can be a devastating disorder because of its sudden and unexpected onset. Most people reach the stage of greatest weakness within the first 2 weeks after symptoms appear, and by the third week of the illness 90 percent of all patients are at their weakest.

The recovery period may be as little as a few weeks or as long as a few years. About 30 percent of those with Guillain-Barré still have a residual weakness after 3 years. About 3 percent may suffer a relapse of muscle weakness and tingling sensations many years after the initial attack.

#### **Epidemiology**

The incidence of GBS during pregnancy is 1.7 cases per 100,000 of the population. The mother will generally improve with treatment but death of the fetus is a risk. The risk of Guillain-Barré syndrome increases after delivery, particularly during the first two weeks postpartum. There is evidence of *Campylobacter jejuni* as an antecedent infection in approximately 26% of disease cases, requiring special care in the preparation and handling of food. Congenital and neonatal Guillain-Barré syndromes have also been reported.

#### **Research being done on Guillain-Barré Syndrome**

Scientists are concentrating on finding new treatments and refining existing ones. Scientists are also looking at the workings of the immune system to find which cells are responsible for beginning and carrying out the attack on the nervous system. The fact that so many cases of Guillain-Barré begin after a viral or bacterial infection suggests that certain characteristics of some viruses and bacteria may activate the immune system inappropriately. Investigators are searching for those characteristics. Neurological scientists, immunologists, virologists, and pharmacologists are all working collaboratively to learn how to prevent this disorder and to make better therapies available when it strikes.

## **Role of homeopathy**

It has been clinically observed that homeopathy helps cases of GB Syndrome. It seems to help by correcting the altered immune system. The medicines are very effective in treating the residual symptoms of Guillain-Barré syndrome. Muscle weakness and power in the limbs can be corrected. In the acute stage, in cases of danger of respiratory paralysis, allopathic medicines have an advantage, but for the residual neuro-muscular symptoms, Homeopathic medicines are highly effective and strongly recommended.

## **REFERENCES**

David, Evans., Simon, Cauchemez., Frederick G, Hayden. (2009). "Prepandemic" Immunization for Novel Influenza Viruses, "Swine Flu" Vaccine, Guillain-Barré Syndrome, and the Detection of Rare Severe Adverse Events. *The Journal of Infectious Diseases*. 200 (5):321–328.

Goldman, AS., Schmalstieg, EJ., Freeman, DH., Goldman, DA., Schmalstieg, FC (2003). "What was the cause of Franklin Delano Roosevelt's paralytic illness?" . *J Med Biogr*. 11 (4): 232–240.

Griffin, JW., Li, CY., Ho, TW. (1995). "Guillain–Barré syndrome in northern China. The spectrum of neuropathological changes in clinically defined cases". *Brain*. 118 (3): 577–595.

Haber, P., Sejvar, J., Mikaeloff, Y., Destefano, F. (2009). "Vaccines and Guillain-Barré Syndrome". *Drug Saf*. 32 (4): 309–323.

Ho, TW., Mishu, B., Li, CY. (1995). "Guillain-Barré syndrome in northern China. Relationship to *Campylobacter jejuni* infection and anti-glycolipid antibodies". *Brain*. 118 (3): 597–605.

Kuwabara, S. (2004). "Does *Campylobacter jejuni* infection elicit "demyelinating" Guillain-Barré syndrome?". *Neurology*. 63 (3): 529–533.

McKhann, GM., Cornblath, DR., Ho, T. (1991). "Clinical and electrophysiological aspects of acute paralytic disease of children and young adults in northern China. *Lancet*. 338 (8767): 593–597.

Sivadon-Tardy, V. (2009). "Guillain-Barré syndrome and influenza virus infection". *Clinical Infectious Diseases*. 48 (1): 48–56.

Stowe, J., Andrews, N., Wise, L., Miller, E. (2009). Investigation of the temporal association of Guillain-Barré syndrome with influenza vaccine and influenza-like illness using the United Kingdom General Practice Research Database. *Am J Epidemiol*. 169:382-388.

Vellozzi, C., Burwen, D., Dobardzic, A., Ball, R., Walton, K., Haber, P. (2009). "Safety of trivalent inactivated influenza vaccines in adults: background for pandemic influenza vaccine safety monitoring.". *Vaccine*. 27 (15): 2114–2120.

Yuki, N. (2008). "Campylobacter genes responsible for the development and determinant of clinical features of Guillain-Barré syndrome" (in Japanese). *Japanese Journal of Clinical Medicine*. 66 (6): 1205–1210