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Review Article

An Overview on *Guillain Barre Syndrome*

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A B S T R A C T

Guillain Barre Syndrome is a peripheral neuropathy that causes acute neuromuscular failure. Guillain, Barré and Strohl used Quinckes method to determine the protein level and cell count in the cerebro spinal fluid of their patients. In 1956, Charles Miller Fisher reported three patient case histories in the New England Journal of Medicine. Guillain-Barré syndrome is rare, incidence worldwide is estimated to be 0.6-4/100,000 person/year and men are about 1.5 times more affected than women. Awareness of these complications, their detection and management may help limit the morbidity of GBS.

Keywords: cerebro spinal fluid, peripheral neuropathy, Guillain Barre Syndrome

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INTRODUCTION

Guillain-Barré syndrome is a disorder in which the immune system attacks gangliosides on the peripheral nervous system1 .Guillain-Barré Syndrome (GBS) is a term used to describe acute autoimmune peripheral neuropathy with specific characteristic of ascending symmetrical flaccid paralysis of limbs accompanied with hyporeflexia or areflexia. Many consider GBS as a post-infectious inflammatory disorder, since it is commonly preceded by a viral or bacterial infection[2-4]. Due to near eradication of Poliomyelitis, GBS is now considered the most common universal cause of acute flaccid paralysis [5.]

HISTORY

1916 Guillain, Barré and Strohl In 1916, Europe was on the brink of destruction, the Battle of the Somme had killed or wounded over one million men, yet Guillain, Barré and Strohl three army physicians at the neurological military centre of the French Sixth Army were discussing the cerebrospinal fluid (CSF) constituents and tendon reflexes of two paralysed soldiers6. In 1891, Walter Essex Wynter had published the first use of lumbar CSF sampling with a cutdown technique, and in the same year, Quincke reported the first use of the lumbar puncture 7. In 1916, Guillain, Barré and Strohl used Quinckes method to determine the protein level and cell count in the CSF of their patients. The three neurologists observed high CSF protein levels in the absence of any rise in levels of inflammatory cells their socalled dissociation albuminocytologique. This finding was distinct from the high white cell counts seen in the CSF of patients with other prevalent causes of acute flaccid paralysis, such as syphilis or polio. At the time, the finding firmly established that the condition was a clinical and pathological entity distinct from other infective causes of flaccid paralysis Gullian barre syndrome was born.

Current understanding of GBS allows for the finding of normal CSF protein levels, especially early in the disease, because we know that the CSF protein level might not be elevated until the second week, and for CSF white cell counts up to 50 cells/µl. Moreover, we also now consider a wide clinical spectrum to result from the same underlying acute immune_mediated peripheral nerve and nerve root inflammation. Nevertheless, the original CSF findings remain the CSF hallmark and a diagnostically important and supportive test result [8.]Charles Miller Fischer In 1956,

Charles Miller Fisher reported three patient case histories in the New England Journal of Medicine [9], little could he have known of the long_lasting impact these reports would have on our understanding of GBS.

EPIDEMOLOGY

Guillain-Barré syndrome is rare, incidence worldwide is estimated to be 0.6-4/100,000 person/year 10. The reported incidence for GBS is 1-2/100,000 population and increases linearly with age, and men are about 1.5 times more affected than women 11. Epidemiological studies in various countries have established an association between Campylobacter jejuni infection and the development of GBS. Campylobacter jejuni infection is identified as the single most common preceding illness in GBS patients and it is estimated that almost 25 - 40% of GBS patients world-wide have C. jejuni infection. In Europe and North America about 95% of cases are acute inflammatory demyelinating polyradiculoneuropathy and the other5% are acute axonal motor disorder and acute sensory and motor axonal neuropathy 12. The frequency of these axonal neuropathies varies throughout the world, and in Asia and South America they make up about 30% of the syndrome13.The annual incidence of Guillain-Barré syndrome is around 1-3/100 000 population according to epidemiological studies from Europe, USA, and Australia1[4-21]. It can occur in any age group. The age specific curve seems to show a bimodal distribution, with peaks in young adults and the elderly[14, 16, 19, 22]. Some studies show an increase in incidence with age, especially in the older age group 4-6, 8- 10Males appear to be aVected more commonly[16,17,19,21].The risk for Guillain-Barré syndrome is lower during pregnancy and increases after delivery[22].

SIGNS & SYMPTOMS

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 [23]. Symptoms are preceded by an antecedent event in about two thirds of patients[24, 25]. Respiratory infections are the commonest, reported in about 40% of cases within one month before the onset of the disease.[24,25]. About 20% experience gastroenteritis as the antecedent cause [24, 26]. The commones manifestation is limb weakness, more proximal than distal. Facial palsy is the commonest type of cranial nerve involvement (in 53%), followed by bulbar weakness, ophthalmoplegia, and tongue weakness [27]. In about half the cases the illness is heralded by sensory symptoms [28].

ETIOLOGY

Around 75% of patients have a history of preceding infection, usually of the respiratory and gastrointestinal tract 29. A large number of infections have been linked to the onset of the syndrome, but only a few associations have been established. The infections that have been linked to gullian barr syndrome are Campylobacter jejuni, eEpstein barr virus, Cytomegalo virus, Mycoplasma, Human Immunodefficiency virus.

Drug-induced GBS is a rare entity and considered infrequent. It was first observed in a group of people who received the influenza vaccine[30].Most common drugs reported so far are allopurinol, gold therapy, d-penicillamine, streptokinase, corticosteroids, captopril, oxytocin, zimeldine, gangliosides, danazol, tumor necrosis factor-alpha antagonists, and second-generation antipsychotics such as risperidone.[31-33]. Fluoroquinolones and penicillin were more common antibiotics reported with the occurrence of GBS.Among thrombolytics, streptokinase causing GBS has been reported so far.34. Newer anticoagulants such as rivaroxaban, apixaban, and dabigatran have risen to limelight in the current era of oral anticoagulation. The onset of GBS symptoms after initiation of the drug was noted as few as 6 days to 14 months.

RISK FACTORS

SEX: Males are more likely to contract GBS.Age: risk increses with age.Campylobacter jejuni bacterial infection: A common cause of food poisoning.Influenza virus, HIV, Epstein Barr virus (EBV): These have occured in association with cases of GBS.Mycoplasma pneumonia, Surgery, Hodgkin's lymphoma.influenza vaccination or childhood vaccination: these have also been linked to GBS in rare cases.[35]

CLINICAL FEATURES

Motor dysfunction

- Symmetrical limb weakness: proximal, distal and global
- Neck muscle weakness
- Respiratory muscle weakness
- Cranial nerve palsies: III, VII, IX, XII
- Areflexia

Sensory Dysfunction

- Pain
- Numbness, Paraesthesia
- Loss of joint position sense, vibration,touch and pain distally
- Ataxia

Autonomic Dysfunction:

- Sinus tachycardia and bradycardia
- Other cardiac arrhythmias (both tachy aaand Brady)
- Hypertension and postural hypotension
- Wide fluctuations of pulse and blood pressure
- Tonic pupils
- Hypersalivation
- Anhydrosis of excessive sweating
- Urinary Sphincter disturbances
- Constipation
- Gastric dysmotility
- Abnormal vasomotor tone causing venous pooling and facial flushing

Other

- Papilloedema

PATHOGENESIS

Pathogenesis of C jejuni: The pathogenesis of C jejuni associated Guillain-Barré syndrome is explained on the basis of a mechanism called molecular mimicry. Gangliosides are important surface molecules of the nervous system. According to the concept of molecular mimicry, antibodies formed against ganglioside-like epitopes in the lipopolysaccharide moiety of C jejuni cross react with peripheral nerves causing damage. Molecular mimicry was first demonstrated between the lipopolysaccharide of O:49 serotype and GM1 ganglioside of the nervous tissue.[36]

Pathogenesis of Cytomegalo virus: The exact pathogenesis is not clear in this group, and molecular mimicry has been proposed as a possible mechanism. Anti-GM2 antibodies are found significantly more often in cytomegalovirus associated Guillain-Barrésyndrome than in control cases [37.] A recent report on the occurrence of anti-GM2 antibodies in acute cytomegalovirus infection without neuropathy raises the question of host factors in the pathogenesis.[38]

How are nerves damaged- The syndrome is triggered by infection in three quarters of patients; a third have serological evidence of C jejuni infection and a few continue to excrete C jejuni in faeces[39] This association with preceding infection suggested that the altered immunity in the syndrome may result from the infectious organism sharing epitopes with an antigen in peripheral nerve tissue. It has now been established that C jejuni lipopolysaccharide shares epitopes with certain gangliosides in figure-1[40] .The closest association between antibodies and the neurological disease is seen with Miller Fisher syndrome, where more than 90% of patients have antibodies against the ganglioside GQ1b41, although only a small proportion of these patients have evidence of a preceding C jejuni infection. Thus, several different organisms may cross react with peripheral nerve antigens. Evidence that these antibodies are responsible for the clinical signs of Miller Fisher syndrome comes from studies in which anti-GQ1b antibody and monoclonal antibody raised against GQ1b block conduction in a mouse hemidiaphragm preparation.42. Antiganglioside antibody is present in the serum of many patients with acute motor axonal neuropathy,[43]. and this together with the pathology suggests that antibodies fix complement, which attracts macrophages and leads to axonal damage (fig 2).[44] .Many of these antibodies are of the IgG1 or IgG3 subtype, which usually need T cell help; however, no convincing T cell immunity has been established. Unusual T cells such as those with aγδ receptor have been cultured from peripheral nerve biopsy specimens[45], but their relation to the development of the neuropathy is uncertain. In addition, histological examination at autopsy of nerves from patients with acute motor and sensory axonal neuropathy supports antibody mediated damage to the axon, as does a rabbit model of acute motor axonal neuropathy. Many unanswered questions remain about the relation between antiganglioside antibody and Guillain-Barré syndrome. Acute inflammatory demyelinating polyradiculoneuropathy is the most common form of the syndrome in Europe and North America, yet relatively few affected patients have antibody to gangliosides. Experimental allergic neuritis in rats and mice seems to be predominantly a cell mediated disease, but no convincing evidence of T-cell immunity to protein antigens exists for the human disease. Complex biochemical association of lipids can influence the available antigenic determinants, however[46], and the role of combinations of protein and lipid antigens remains to be determined, as does the role of lipid immunity.

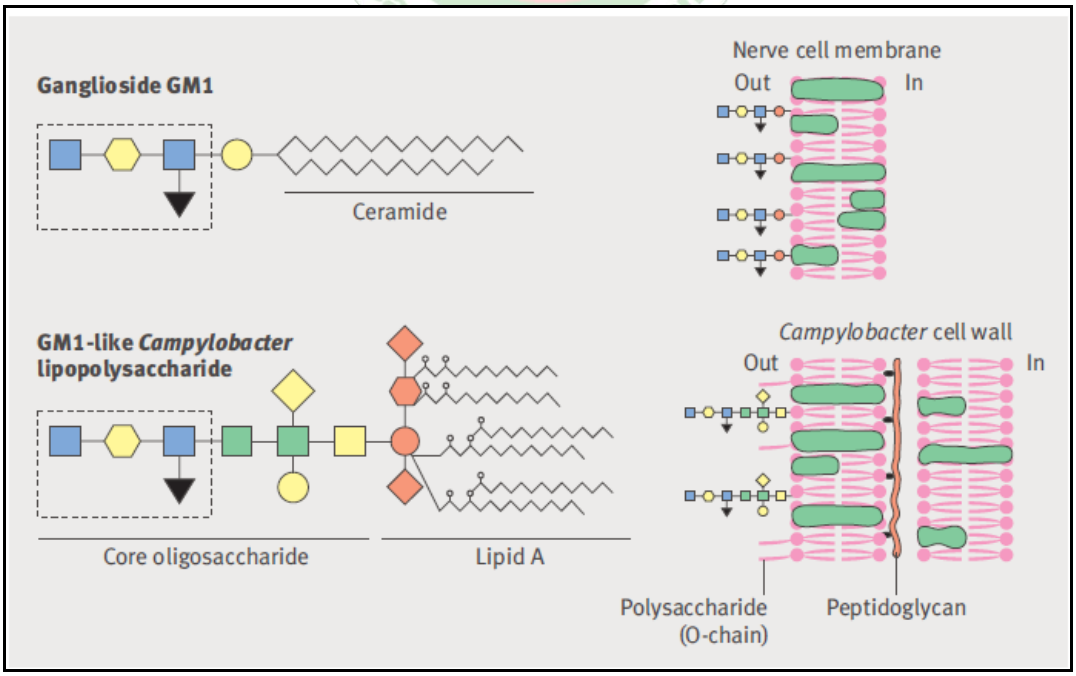

Figure 1: Structural similarities between ganglioside GM1 in nerve cell membranes and a Campylobacter jejuni lipopolysaccharide. Adapted, with permission, from a review by Ang

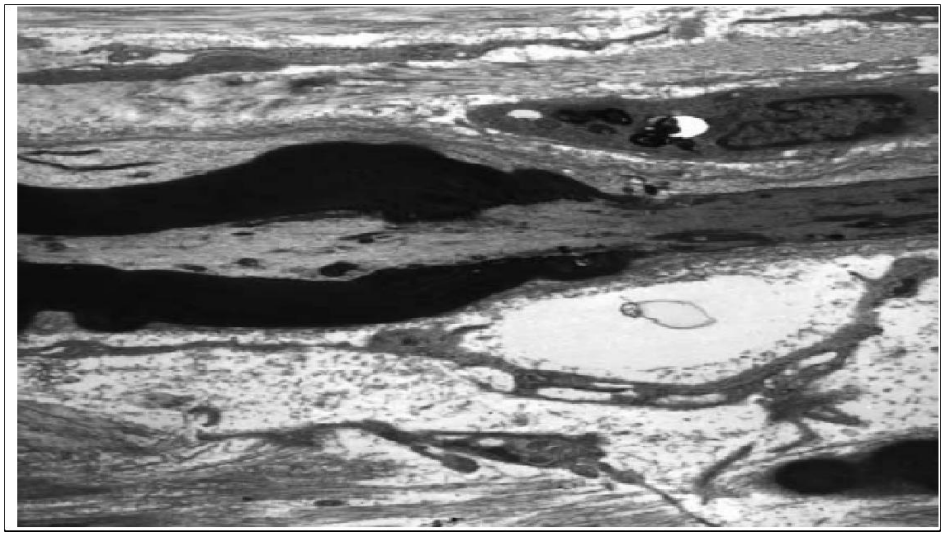

Figure 2: Electron microscopy of a nerve biopsy specimen from a patient with Guillain-Barré syndrome associated with HIV infection showing a macrophage apparently stripping myelin from a denuded axon. Reproduced, with permission, from the book byHughes[92]

COMPLICATIONS

LONG TERM COMPLICATIONS

Possible long term complications include:

Not being able to wlk unaided, loss of sensation (numbness), lack of co-ordination caused by the loss of sensation (sensory ataxia), and weakness -for example, in arms or legs, loss of balance. Problems with sense of touch (dysesthesia), which can cause a burning or tingling sensation in your skin; or abnormally sensitive skin that causes severe pain when you come into contact with objects, such as bedding or towels.

LIFE-THREATENING COMPLICATIONS

There is a small chance (about 1 in 20) of dying from Gullian Barr Syndrome. This usually occurs as a result of complications that develop during the first weeks of the condition. For example: Respiratory Distress syndrome-, Sepsis, Pneumonia, Cardiac arrest, Inflammation

DIAGNOSTIC CRITERIA

Diagnostic criteria for Guillain-Barré syndrome have been laid down, based on clinical, laboratory, and electrophysiological features[47]. Progressive motor weakness and areflexia are prime requirements for diagnosis. Cerebrospinal fl uid analysis is the only laboratory criterion. However, other laboratory tests provide corroborative evidence for diagnosis and are useful in the management.In CSF, an elevated or rising protein level on serial lumber punctures and 10 or fewer mononuclear cells/mm3 strongly support the diagnosis. CSF protein level may be normal during the first week. In one of the studies 12% of patients were found to have > 5 cells/µl in the CSF[48] .The presence of more than 50 mononuclear cells raises doubts about the diagnosis. CSF pleocytosis is well recognised in HIV associated Guillain-Barré syndrome[49]. Electrophysiological features diVer according to the clinicopathological type[50,51,52] .Magnetic resonance imaging can be useful in diagnosis, especially when the electrophysiological findings are equivocal. It is a sensitive but unfortunately non-specific test. Spinal nerve root enhancement with gadolinium on MRI is a non-specific feature seen in inflammatory conditions and caused by disruption of the blood—nerve barrier. Selective anterior root enhancement appears to be strongly suggestive of Guillain-Barré syndrome[53]. A study showed that 83% of patients had enhancement of the cauda equina nerve roots [54]. Prominent nerve root enhancement was found to correlate with pain, disability grade, and time for recovery [54].

Diagnostic criteria for Gullian-Barre Syndrome [92]

Features needed for diagnosis of Gullian-Barre Syndrome in clinical practice: Progressive weakness in legs and arms (sometimes initially only in legs). Arefl exia (or decreased tendon refl exes) in weak limbs. Additional Symptoms-Progressive phase lasts days to 4 weeks (often 2 weeks). Relative symmetry. Mild sensory symptoms or signs (not present in acute motor axonal neuropathy). Cranial nerve involvement, especially bilateral weakness of facial muscles. Autonomic dysfunction. Pain (common). Features that should raise doubt about the diagnosis of Gullian_barre Syndrome CSF: increased number of m ononuclear cells or polymorphonuclear cells (>50 cells per µL). Severe pulmonary dysfunction with little or no limb weakness at onset. Severe sensory signs with little or no weakness at onset. Bladder or bowel dysfunction at onset. Fever at onset.Sharp spinal cord sensory level.Marked, persistent asymmetry of weakness. Persistent bladder or bowel dysfunction.Slow progression of weakness and without respiratory involvement (consider subacute infl ammatory demyelinating polyneuropathy or acute onset chronic in fl ammatory demyelinating polyneuropathy).

Nerve conduction studies

Can be helpful in clinical practice, but are generally not required to diagnose Guillain-Barré syndrome.

Needed to meet all Brighton criteria for Guillain-Barré syndrome.[93] Essential for classifi cation of Guillain-Barré

syndrome in acute infl ammatory demyelinating polyneuropathy or acute motor axonal neuropathy.

Acute infl ammatory demyelinating polyneuropathy: features of demyelination (decreased motor nerve conduction velocity, prolonged distal motor latency, increased F-wave latency, conduction blocks, and temporal dispersion).[94] Acute motor axonal neuropathy: no features of demyelination (one demyelinating feature in one nerve, if distal CMAP amplitude is less than 10% LLN, can be found; distal CMAP amplitude less than 80% LLN in at least two nerves.94. Transient motor nerve conduction block might be present.[95]

Classifi cation of Guillain-Barré syndrome as either acute infl ammatory demyelinating polyneuropathy or acute motor axonal neuropathy is not required for diagnosis of Guillain-Barré syndrome, whether acute inflammatory demyelinating polyneuropathy and acute motor axonal neuropathy require different treatments is unknown. The amount of conduction slowing required to define demyelination differs between classifi cation systems.CSF=cerebrospinal fluid. CMAP=compound muscle action potential. LLN=lower limit of normal.

DIFFERENTIAL DIAGNOSIS[96]

Diffrential diagnosis of rapidly progressive limb weakness (with or without respiratory failure) CNS Encephalitis, acute disseminated encephalomyelitis, transverse myelitis, brainstem or myelum compression, leptomeningeal malignancy.

Motor neurons

Poliomyelitis, West Nile virus anterior myelitis, amyotrophic lateral sclerosis, progressive spinal muscular atrophy.

Plexus

Neuralgic amyotrophia, diabetes mellitus Nerve roots Guillain-Barré syndrome, acute onset chronic infl ammatory demyelinating neuropathy, Lyme disease, cytomegalovirus-related radiculitis, HIV-related radiculitis, and leptomeningeal malignancy.

Peripheral nerves

Guillain-Barré syndrome, acute onset chronic infl ammatory demyelinating neuropathy, iatrogenic, toxic, critical illness myopathy-neuropathy, vasculitis, diphtheria, porphyria, thiamine defi ciency, porphyria, Lyme disease, metabolic or electrolyte disorders (hypokalaemia, phosphataemia or magnesaemia, hypoglycaemia).

Neuromuscular junction

Myasthenia gravis, botulism, intoxication Muscles Critical illness myopathy-neuropathy, mitochondrial disease, acute rhabdomyolysis, polymyositis, dermatomyositis.

SPECIFIC TREATMENT

Plasma Exchange

In 1978, Brettle et al first drew attention to the improved outcome in a patient with GuillainBarré syndrome following plasma exchange.subsequently the eYcacy of plasma exchange was established by large multicentre trials. [55,56.] Plasma exchange beginning within the first two weeks of the illness reduced the period of hospital stay, the duration of mechanical ventilation, and the time to reach ambulation[55].The French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome recommends two exchanges in mild cases and four in moderate or severe cases, based on their randomised trial involving over 500 patients[57] The complications of plasma exchange include hypotension, septicaemia, hypocalcaemia,and abnormal clotting[58].It could particularly be hazardous in haemodynamically unstable patients.

Intravenous Immunoglobulins

Intravenous immunoglobulin is used in the treatment of several immunologically mediated disorders. It is supposed to act through several mechanisms including anti-idiotypic suppression of autoantibodies. The benefits of intravenous immunoglobulin in Guillain-Barré syndrome were first reported by Kleyweg et al in 198859.The mechanism of action of intravenous immunoglobulin is uncertain and probably multifactorial, including the provision of antiidiotype antibodies, blockade of Fc receptors, and interference with complement activation. Increased catabolism of antibodies may also play a part. A large, multicentre, randomised trial compared plasma exchange, intravenous immunoglobulin, and combination treatment of plasma exchange followed by intravenous immunoglobulin, there was no significant difference in efficacy between plasma exchange and intravenous immunoglobulin. No significant advantage in combined treatment was evident[60.] Based on these results it was concluded that intravenous immunoglobulin treatment may be preferable to plasma exchange when started within two weeks in severely affected adults with no contraindications to intravenous immunoglobulin, because it was more convenient, equally effective, and of comparable overall cost [60].

A retrospective multicentre study found that intravenous immunoglobulin accelerated recovery in children with Guillain-Barré syndrome who were unable to walk [61]. Intravenous immunoglobulin currently remains the preferred choice in treating GuillainBarré syndrome. It is a reasonably safe form of treatment, though its side effects and contraindications should be borne in mind.

Corticosteroids

Steroid treatment in Guillain-Barré syndrome has yielded disappointing results. However, a pilot study suggested that combined treatment with intravenous methylprednisolone (0.5 g/d) and intravenous immunoglobulin (0.4 g/kg body weight/d) for five days was more beneficial than intravenous immunoglobulin alone [62].Mortality in Guillain-Barré syndrome dropped dramatically with the advent of intensive care and safe ventilation, and it is now about 10% [63] .Clinical studies document infections, pulmonary emboli, and cardiac rhythm disturbances as the major causes of death[64]. Mildly affected patients who remain capable of walking unaided and are stable for more than two weeks are unlikely to progress and can be managed as outpatients.

Most patients need emergency admission to hospital, where they can be carefully monitored. A multidisciplinary consensus group has recommended subcutaneous heparin and graduated stockings to prevent deep venous thrombosis and pulmonary emboli.[65].Pain management is not easy, but gabapentin and carbamazepine may help. Narcotic analgesics may occasionally be need.[65] .The timely institution of mechanical ventilation is important. Studies of patients who needed ventilation suggest that those with a vital capacity of less than 20 ml/kg are most at risk.66 .A Cochrane review has shown that plasma exchange is better than supportive treatment[67]

Supportive Care

Despite the improved prognosis with IVIg or PE treatment, patients with moderate or severe GBS still spend an average of 1 to 2 months in the hospital 68. Improved supportive care can minimize the morbidity these complications produce.

Respiratory Care

Respiratory failure is one of the most common and dreaded complications of GBS. Prior to mechanical ventilation, the mortality rate in GBS exceeded 30%, mostly from respiratory failure69.The percentage of patients with GBS ultimately requiring mechanical ventilation depends on study methodology (clinical trials versus population-based) but ranges from 25% to 44%.[70-73.]Phrenic and intercostal nerve demyelination produce restrictive lung mechanics while bulbar muscle weakness may prevent adequate airway protection and place patients at risk for aspiration.Respiratory failure can occur precipitously in patients with GBS and, if unnoticed, can be life-threatening or result in significant morbidity. The respiratory status of patients with GBS must therefore be carefully and frequently monitored. Pulse oximetry and blood gases are inadequate for early detection of failure because hypoxemia and hypercarbia are very late manifestations. Instead, regular bedside monitoring of the vital capacity, maximal inspiratory pressure (MIP or PImax), and maximal expiratory pressures (MEP or PEmax) should be used. The recovery of independent breathing can be slow in GBS, resulting in prolonged periods of mechanical ventilation. One half of intubated patients with GBS ultimately require tracheostomy74.Delaying tracheostomy >14 days after intubation has been associated with a higher incidence of ventilator-associated pneumonia[75].Some have advocated waiting 10 to 14 days prior to tracheostomy[76,77.] But individual patient characteristics must be considered.

Dysautonomia

Autonomic dysfunction occurs to some degree in 65% of patients with GBS78 .Manifestations are protean, including brady- or tachy-arrhythmias, episodic hypertension, orthostatic hypotension, abnormal hemodynamic responses to vasoactive medications, gastrointestinal dysfunction, and sweating abnormalities.Signs of autonomic over-and under-activity may coexist or alternate in the same patient.

Severe autonomic dysfunction occurs in those with severe disease. This has 2 important implications. First, the same patients who are at risk for autonomic complications are at risk for other complications producing arrhythmia, cardiovascular collapse, and blood pressure fluctuations (sepsis, pulmonary embolism, heart failure, etc). These causes should be considered and excluded before attributing symptoms to GBS-related autonomic failure. Second, the GBS patients who are at highest risk for autonomic complications are typically already being managed in the ICU, where continuous cardiac and blood pressure monitoring are routine. Episodic bradycardia, sinus arrest, and asystole have been blamed for deaths in GBS or necessitated pacemaker placement.[79].These arrhythmias can be triggered by tracheal suction or other vagotonic stimulation, Caution should be used in tracheal suctioning, with ready access to atropine and external pacing devices. Paroxysmal hypertension also occurs but is generally short-lived and rarely requires treatment. If fluctuations are severe enough to cause end-organ damage, quickly titratable, short-acting medications are recommended to avoid hypotension. Orthostatic hypotension generally resolves by the time patients have regained the ability to walk and responds to volume expansion with intravenous hydration. If refractory, sodium chloride tablets, fludrocortisone, or midodrine could be considered.

Gastrointestinal autonomic dysfunction results in constipation, gastric immotility, and ileus. Retrospective series have identified ileus in up to 15% of patients with GBS requiring ICU care 80. Demyelinated nerves, immobility, and opiate medications are likely contributing factors. Detection with careful examination, output monitoring, and radiography should allow early institution of treatments to prevent perforation. Cessation of enteral feeding, gastric decompression, promotility agents, reduced opiate medications, and even parental nutrition may be needed.

Parental nutrition may be needed. Some degree of urinary dysfunction is found in 25% of patients and complete urinary retention in up to 9%.[81,82.] The severity of these symptoms correlate with the severity of weakness and are therefore more commonly seen in ICU patients. To minimize infection risks, intermittent catheterization is preferred over indwelling urinary catheters.

Thromboembolism

Deep-vein thrombosis and subsequent pulmonary embolism are recognized complications of immobility from GBS. The incidence of this potentially lethal outcome in GBS is unknown, but pulmonary embolism has long been recognized as a cause of death.[83,84] .Studies have not addressed specific antithrombotic prophylaxis for GBS, but it is recommended that all minimally-ambulant or nonambulant patients receive thromboembolism prophylaxis according to the American College of Chest Physician guidelines.85 .This approach will typically include either unfractionated heparin (5000 units twice daily)orlow—molecular-weight heparin (40 mg daily) Prophylaxis should be tailored to the patients comorbidities, including bleeding risk, renal function, recent spinal tap, etc86.The optimum duration of prophylaxis is unclear but should extend into the rehabilitation phase and until ambulation is regained. Even

with these measures, thromboembolism can still occur in GBS, sometimes with fataloutcome.[84]

Neurological

Neuropathic pain is common and occurs in around 50% of patients. Non-opioid analgesics (Paracetamol, NSAIDs) in combination with opioid analgesia should be instituted initially, but may provide inadequate pain relief. Adjunctive treatments such as anticonvulsants (e.g. gabapentin or carbemazepine), and tricyclic antidepressants may be effective.

Malnutrition

Patients with GBS are at high risk for inadequate nutrition throughout the course of their illness. Gastrointestinal symptoms produce dehydration and weight loss even prior to hospital admission. Progressive bulbar dysfunction or adynamic ileus can limit or eliminate oral intake.GBS is a hypermetabolic and hypercatabolic state on the same order as sepsis or trauma[87].Inadequate nutrition is associated with increased risk for fluid and electrolyte abnormalities, decubitus ulcers, as well as nosocomial infections. Therefore, nutritional support should begin as quickly as possible by appropriate means (eg, modified diet, nasogastric tube, or parenteral nutrition). To combat the hypermetabolic/hypercatabolic state, it has been recommended that patients receive ahigh-protein diet at 1.35 to 1.58 x their calculated basic energy expenditure (BEE) plus an additional 30% to 50% for weight stabilization[87].Close monitoring of hydration status, weight, vital proteins, and nitrogen balance will help guide adjustments to this initial diet.

Psychological

There is a high incidence of depression among patients with GBS. If available, it is important for the patient and their family to have access to support groups. It is also important that counseling and psychiatric help be available if needed. [88]

Anesthetic Considerations

Suxamethonium is absolutely contraindicated in patients with GBS. There have been a number of case reports of severe hyperkalaemia, life threatening arrhythmias, and cardiac arrest after its administration. [89].

40% of patients who suffer from GBS will need admission for inpatient rehabilitation. Careful attention should be paid to limb positioning and posture as limb weakness can lead to compression nerve palsies, pressure sores and contractures. Extensive input from physiotherapists and occupational therapists is essential to provide tailored strengthening exercises and supportive aids.

Patients may also suffer from persistent fatigue, which may respond to an exercise programme. [88, 90]

Table 1: Biological Approaches used for treatment of GBS in Animal studies [97]

Drugs	Biological Approach	Type of Study	Subjects	Efficient (Non-efficient)	Year and Author
Cobra venom factor (CVF)	Complement modulation	Original article	Lewis rats	Efficient	1987/Feasby [31]
Soluble complement receptor type 1 ($_s$CRI)	Complement modulation	Original article	Lewis rats	Efficient	1995/jung[32]
IFN type I (ã & ß)	Cytokine modulation	Original article	Lewis rats	Efficient	1996/Vnesendorp [76]
Anti-CD2 mAb (OX34)	T cell modulation	Original article	Lewis rats	Efficient	1996/Jung [55]
Linomide	Cytokine modulation	Original article	Lewis rats	Efficient	1997/Bal [89]
Anti L-selectin mAb (HRL3)	Cytokine modulation	Original article	Lewis rats	Efficient	1997/Archelos [56]
IFNß	Cytokine modulation	Original article	Lewis rats	Efficient	1999/Zou [78]
Rolipram	Cytokine modulation	Original article	Lewis rats	Efficient	2000/Abbas [93]
Anti-II-18 Mab	Cytokine modulation	Original article	mice	Efficient	2002/Yu [94]
TNF receptor type I (TNFR I)	Cytokine modulation	Original article	mice	Efficient	2003/Bao [82]
APT070 (Micrococept)	Complement modulation	Original article	mice	Efficient	2005/Halstead [33]
Neutralizing anti-MIF mAb	Cytokine modulation	Original article	mice	Efficient	2005/Nikoletti [96]
rEV576	Complement modulation	Original article	mice	Efficient	2008/Halstead [45]
Eculinumab	Complement modulation	Original article	mice	Efficient	2008/ Halstead [41]
Nafamostat mesilate (NM)	Complement modulation	Original article	rabbit	Efficient	2008/Phongsisay[46]
Anti-GD3 anti-idiotype mAb (BEC2)	Autoantibody modulation	Original article	Lewis rats	Efficient	2010/Usuki [49]
Erythropoietin	Cytokine modulation	Original article	Lewis rats	Efficient	2011/Manusberg [100]
Erythropoietin	Cytokine modulation	Original article	Lewis rats	Efficient	2011/Zhang [101]
Anti-C1q monoclonal antibody (M1)	Complement modulation	Original article	mice	Efficient	2016/McGonigal [50]

Table 2: Biological Approaches used for treatment of GBS in Human studies [97]

Drugs	Biological Approach	Type of Study	Subjects	Efficient (Non-efficient)	Year and Author
Anti-T cell monoclonal Ab (OK3)	T cell modulation	Original article	3 adult GBS patient	Non-Efficient	1991/Feasby [54]
IFNß	Cytokine modulation	Case report	1 adult GBS patient	Efficient	1998/Creange [77]
IFNß	Cytokine modulation	Original article	26 GBS patients & healthy control	Efficient	2001/Creange [79]
IFNß+IVIg	Cytokine modulation	Case report	1 adult GBS patients	Efficient	2001/Schaller [80]
IFNß+IVIg	Cytokine modulation	Randomized controlled clinical trial	13 GBS cases (IFNß-IVIg) & 6 health control (placebo+IVIg)	Non-Efficient	2003/Pritchard [81]
Rituximab	B cell modulation	Case report	1 adult GBS patient	Efficient	2008/Ostronoff [65]
Eculizumab	Complement modulation	Case report	1 pediatric GBS patient	Efficient	2014/Ram [42]
Alemtuzurnab	T and B modulation	Case report	1 adult GBS patient	Efficient	2014/Tzachanis [74]
Eculizumab	Complement modulation	Clinical trial	Unknown	Unfinished	2014/Start Glassgow [43]
Eculizumab	Complement modulation	Clinical trial	Unknown	Unfinished	2015/Start/Kuwabara [44]

CONCLUSION:

GBS is a autoimmune disorder.Symptoms of GBS significantly increase the risk of serious long term complications.More research is to be carried to identify appropriate molecular targets of intervention,novel diagnostics and development of effective and cost effective therapies.

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