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GUILLAIN-BARRÉ SYNDROME, DIAGNOSIS AND MANAGEMENT: SIMPLE LITERATURE REVIEW

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Abstract:

Background: *GBS described as a condition associated with symmetrical weakness of the limbs, and hyporeflexia or areflexia, which reaches a maximum severity within 4 weeks. GBS is associated with sensory symptoms such as paraesthesia and numbness usually starts distally and symmetrically and sometimes it reach to death as a result of respiratory muscle paralysis.*

Objective: *Treating patients with Guillain-Barré Syndrome is difficult and needs different management approaches. In this paper we aim to discuss the pathophysiologies that stand behinds Guillain-Barré Syndrome development, diagnosis, and the management approach.*

Methods: *A comprehensive search was done using biomedical databases; Medline, and PubMed, for studies concerned with assessment of Guillain-Barré Syndrome. Keywords used in our search through the databases were as; "Guillain-Barré Syndrome Pathophysiology", "Guillain-Barré Syndrome Classification", and "Guillain-Barré Syndrome Management".*

Conclusion: *GBS is a post-infectious disorder. The typical symptoms are pain, numbness, paresthesia, or weakness in the limbs. The main features are rapidly progressive bilateral and relatively symmetric weakness of the limbs. Intravenous immunoglobulin (IVIg) therapy and plasma exchange (PE) play a leading role in GBS treatment. Severe fatigue is a common problem and considered as one of the most important symptoms leading to problems in school or work but exercise was found to be linked to improved GBS physical outcomes. Advanced age, severe disease, increased comorbidity, pulmonary and cardiac complications, mechanical ventilation, and systemic infection were found to be predictors of an increased risk of death.*

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INTRODUCTION:

Guillain-Barré Syndrome (GBS) is an acute peripheral neuropathy leading to a flaccid paralysis that is thought to be due to an autoimmune reaction triggered by a preceding infection, mainly respiratory or gastrointestinal. Possible links between GBS and vaccination have also been debated (1).

In 1916, the French neurologists Guillain, Barré, and Strohl described two soldiers who developed acute paralysis with areflexia who spontaneously recovered. They noted increased protein concentration with a normal cell count in the CSF. The combination of these clinical and laboratory features became known as the GBS (2). In recent decades, it has become clear though that GBS contains a spectrum of acute idiopathic, usually monophasic, and peripheral neuropathies (3).

GBS is also known as Landry-Guillain-Barré-Strohl syndrome and acute inflammatory demyelinating polyneuropathy (AIDP) (4). Global annual incidence is reported to be 0.6–2.4 cases per 100,000 per year. Men are more commonly affected by approximately 1.5 times than women (5). Acute inflammatory demyelinating polyradiculoneuropathy (AIDP) is the most commonly occurring subtype in North America and Europe accounting for about 90% of all cases. However, in other parts of the world (Asia, Central and South America) axonal variants of GBS i.e. acute motor axonopathy (AMAN) and acute motor sensory axonopathy (AMSAN) are found to represent 30% to 47% of cases (6).

GBS can be catastrophic on patient's life and cause a significant loss of patient ability to function normally and sometimes it reach to death as a result of respiratory muscle paralysis. In our review we aim to summarize the current data related to diagnosis, outcomes and management of GBS in order to provide the patients a better management.

METHODOLOGY:

Sample

We performed comprehensive search using biomedical databases; Medline, and Pubmed, for studies concerned with assessment of stress ulcer prophylaxis published in English language between 2013 and 2018. Keywords used in our search through the databases were as; "Guillain-Barré Syndrome", "Guillain-Barré Syndrome Diagnosis", "Guillain-Barré Syndrome Evaluation & Management" "Guillain-Barré Syndrome Pathogenesis". More relevant articles were recruited from references lists scanning of each included study.

Analysis

No software was used, the data were extracted based on specific form that contain (Title of the study, name of the author, Objective, Summary, Results, and Outcomes).

DISCUSSION:

As mentioned previously, GBS is a post-infectious disorder. Two-thirds of patients report symptoms of a respiratory or gastrointestinal tract infection before the onset of GBS. Campylobacter jejuni is a common responsible for triggering GBS. Other pathogens that cause antecedent infections related to GBS are cytomegalovirus, Epstein–Barr virus, Mycoplasma pneumonia, Haemophilus influenzae, and influenza A virus (7).

Pathogenesis of GBS can be summarized with that infections, such as Campylobacter jejuni, can trigger humoral immune and autoimmune responses. This may result in nerve dysfunction and the symptoms of GBS.

The detailed pathogenesis starts with when Lipo-oligosaccharides on the Campylobacter jejuni outer membrane elicit the production of antibodies that cross-react with gangliosides, such as GM1 and GD1a on peripheral nerves.

The antigens targeted in AMAN are located at or near the node of Ranvier. The anti-GM1 and anti-GD1a antibodies bind to the nodal axolemma, leading to complement activation followed by membrane attack complex (MAC) formation and disappearance of voltage-gated sodium channels. This damage can lead to detachment of paranodal myelin, and nerve conduction failure. Macrophages then invade from the nodes into the periaxonal space, hunting for the injured axons (8,9).

The antigens targeted in AIDP are, presumably, located on the myelin sheath. The antibodies can activate complement, which leads to formation of the MAC on the outer surface of Schwann cells, initiation of vesicular degeneration, and invasion of myelin by macrophages (10).

GBS has been reported as an adverse event following immunization (AEFI) (11). Temporal associations between GBS and more recent influenza vaccines, diphtheria–tetanus–pertussis vaccines and measles–mumps–rubella (MMR) vaccines have been reported, but epidemiologic studies have not found consistent associations (12). (Karina A. Top et al.) (11) found that GBS occurring within 30 days after immunization was a rare cause of hospitalization among Canadian children, representing

approximately 10% of GBS admissions at the Canadian Immunization Monitoring Program Active (IMPACT) centers and occurring at a rate of approximately 2 per 100,000 hospital admissions. In addition, one prospective study of children with GBS identified infectious etiologies in 75% (6 of 8) of cases vaccinated within 6 weeks of onset and 46% (40 of 87) of non-vaccine-associated cases. (Arias et al.)(13) in their meta-analysis found a small but significant increase in the risk of developing GBS associated with influenza vaccines—seasonal or pandemic. However, there is no strong evidence confirm the relationship. (Karina A. Top et al.) study provided reassuring evidence that post-immunization GBS is rare in children. The high frequency of symptoms of recent infection suggests that a temporal association between vaccination and GBS onset is most likely coincidental rather than causal (11,12,13).

Symptomatology and Classification:

In typical cases, first symptoms are pain, numbness, paresthesia, or weakness in the limbs. The main features of GBS are rapidly progressive bilateral and relatively symmetric weakness of the limbs, reaching a maximum within four weeks and reduced or absent tendon reflexes in the weak limbs. Respiratory muscles are commonly affected and 25% of patients need artificial ventilation. Cranial nerves, including the facial, bulbar and oculomotor nerves are often affected in typical cases. Autonomic dysfunction such as cardiac arrhythmia (tachycardia or bradyarrhythmia with asystole), arterial hypertension or hypotension, abnormal sweating, and gastrointestinal dysmotility occurs in up to two-thirds of patients. Urinary retention and constipation are unusual at the onset of the disease but commonly develop at the worst stage of the disease (14).

Various subtypes of GBS have been reported that differ in their clinical, and electrophysiological features (Table 1).

GBS subtypes	Main clinical features	Nerve Conduction Study findings
Acute inflammatory demyelinating polyneuropathy (AIDP)	Sensorimotor GBS, often combined with cranial nerve deficits and frequent autonomic dysfunction	Demyelinating polyneuropathy
Acute motor axonal neuropathy (AMAN)	Pure motor GBS; cranial nerves rarely affected	Axonal polyneuropathy, sensory action potential normal
Acute motor sensory axonal neuropathy (AMSAN)	Resembles severe AMAN, but sensory fibers are affected, leading to sensory deficits	Axonal polyneuropathy, sensory action potential reduced or absent
Pharyngeal–cervical brachial variant	Prominent weakness of oropharyngeal, facial, neck and shoulder muscles	Normal in most patients, sometimes abnormalities in arms, mostly axonal pattern
Miller Fisher Syndrome	Ataxia, ophthalmoplegia, areflexia	Normal in most patients; discrete changes in sensory conduction or H.reflex may be present

Diagnosis

In practice, the criteria published in 1990 still provide a good basis for clinicians worldwide to make a diagnosis of GBS (15). First, there are two required features for diagnosis: Progressive weakness of more than one limb and areflexia (or decreased tendon reflexes). Also, there are features that strongly support diagnosis, such as, Progression of symptoms over days to 4 weeks, Relative symmetry of symptoms, Mild sensory symptoms or signs, Cranial nerve involvement especially bilateral weakness of facial muscles, Autonomic dysfunction (tachycardia and other arrhythmias, postural hypotension, hypertension, vasomotor symptoms), Pain (often present), High concentration of protein in CSF (after the first week of symptoms), and Typical electro-diagnostic features. In addition, Marked persistent asymmetry of weakness, Persistent bladder or bowel dysfunction, Bladder or bowel dysfunction at onset, Increased number of mononuclear cells in CSF (>50 leucocytes/mm3), polymorphonuclear leukocytes in CSF and Sharp sensory level, are features that should raise doubt about the diagnosis. This criteria is adapted from Asbury and Cornblath, 1990 (15).

CSF examination may be useful in cases of clinical uncertainty about the diagnosis, especially to exclude other causes associated with CSF pleocytosis, such as, infectious polyradiculitis and acute poliomyelitis (2). Elevated CSF protein levels are found in approximately 50% of patients in the first 3 days after onset of weakness, which increases to 80% after the first week. If the protein level in the CSF is normal, repeat lumbar punctures are not usually recommended because albuminocytological dissociation is not necessary to diagnose GBS (16). Diagnosis of GBS can sometimes be difficult in the early phase of the disease, especially when reflexes are still present or the weakness is not distributed. Therefore, nerve conduction studies (NCS) can help to support the clinical diagnosis of GBS. In current clinical practice, the value of subtyping by nerve electrophysiology is uncertain. Nerve physiology might have prognostic relevance. However, there are no definite agreed-upon diagnostic electrophysiological criteria for the diagnosis of GBS at present. All current electrophysiological criteria focus on the discrimination between axonal and demyelinating subtypes of GBS (16,17).

Management:

Immunomodulating treatments, mainly in the form of intravenous immunoglobulin (IVIg) therapy and plasma exchange (PE), hasten recovery from GBS and improve outcomes. These treatments play a leading role in GBS treatment. Nevertheless, 20% of GBS patients continue to have severe disease, and 5% die of their disease. Both IVIg and PE are considered the traditional treatment and they have been the first-line therapy for GBS patients (18). IVIg, whose major component is IgG molecule, is derived from healthy donated blood. The immunoglobulin could neutralize pathogenic antibodies and limit the activation of complement system. It is better to use IVIg within 2 weeks after onset of weakness and the dosage is 0.4 g/kg/day for 5 days. IVIg is very efficient, and safe but it is very costly (18,19). PE, which means taking out plasma from one vein and then returning into another vein with a plasma substitute, was the first therapy that was more effective than supportive treatments for GBS. IVIg or PE indication of treatment is in severely affected patients. Patients are unable to walk unaided, and have high GBS disability, especially when <2 weeks from onset of weakness (20).

There was an evidence that corticosteroids as a strong anti-inflammatory agent could inhibit the progress of GBS and promote recovery (19). (Hughes et al.)(21) in their review concluded that steroids had been useless in GBS after assessing 8 studies included a total of 653 participants.

Interferons (IFNs) are a family of inhibitory glycoproteins. As a cellular immunomodulator, IFN-α may inhibit antigen presentation and tumor necrosis factor (TNF)-α secretion in GBS patients, decrease T cell proliferation, reduce adhesions, increase anti-inflammatory cytokine production and modulate macrophage properties. However, the effects of IFN-α in GBS patients remain controversial. Some evidence have suggested that IFN-α combined with PE and IVIg has a therapeutic benefit in GBS. On the other hand, some reviews have reported that the quality of evidence for the use of IFN-α in GBS was too low to make any definitive conclusion and in one of the studies, no such improvement was observed (18,22,23).

Cyclophosphamide (CY) is a well-known, first-line, antineoplastic agent. In patients with severe autoimmune disease, high-dose CY (200 mg/kg) can improve the quality of life (QoL) and exert potent immunosuppressive activity, even though tolerance is commonly induced. This beneficial immunosuppression was mediated by the reduction of lymphoproliferation, abrogation of regulatory T (Treg) cell functions and inhibition of interleukin (IL)-12 (24). However, therapeutic treatment only had an impact on the clinical features. In addition, prolonged CY treatment was associated with infections and neoplastic diseases (18).

Rituximab is an antibody against CD20 and causes targeted B cell depletion. The mechanisms of rituximab action mainly involve complement-mediated cytotoxicity, antibody-dependent cell-

mediated cytotoxicity and apoptosis. Thus, rituximab has immunoregulatory effects by increasing Treg cells. Rituximab has been licensed for use in rheumatoid arthritis. No clinical trial has directly examined the effects of rituximab in GBS. However, some evidence showed that rituximab may improve the patient's muscle strength and reduce Epstein–Barr virus viremia. Thus, rituximab may be used as a therapy for refractory GBS (25).

Acupuncture originated in ancient China as a part of traditional Chinese medicine, and was accepted in Western countries a long time ago. Acupuncture is the practice of inserting thin needles into specific sites on the body surface, which are called acupoints. Electro-acupuncture (EA) is a modified technique of acupuncture and uses electrical stimulation to cure diseases. Several studies showed that acupuncture/EA had a remarkable effect on GBS, especially, the convalescent phase and sequelae of GBS. Immune therapy combined with acupuncture/EA has been a tendency in treating GBS in China (18,26).

Complications:

The long-term effects of GBS may be improved by targeted interventions. Severe fatigue is a common problem and considered as one of the most important symptoms leading to problems in school or work. Fatigue is also an important complaint after GBS in adults, which may in part be attributed to residual peripheral nerve damage (27,28). (Garssen et al.) (29) demonstrated a persistent decrease in fatigue after a bicycle exercise training program in adult GBS patients. Training may also be of benefit to reduce fatigue in patients with GBS in childhood.

In a recent systematic review, exercise was found to be linked to improved GBS physical outcomes (30). One study also showed that low-aerobic exercise with walking (10 weeks) followed by cycling (15 weeks) increased exercise capacity, pulmonary functions, and grip strength to enhance functional capacity (31).

In (Roodbol et al.) (32) paper, a broad range of behavioral problems was reported suggest that targeted psychological therapy may be beneficial to promote further recovery and prevent sequelae. Also, they found that QoL was impaired in the domain of vitality. However, survivors appreciate their QoL more after a life-threatening disease, explained by a mechanism of post-traumatic growth. This may also play a role after childhood GBS. The residual long-term effects of childhood GBS, despite good clinical recovery in general, require recognition and attention during rehabilitation and follow-up. Caretakers should be aware of potential residual problems, even after good neurological recovery.

The reported predictors of poor prognosis of GBS in (Rajabally et Uncini)(33) paper are age above 40 years, preceding diarrheal illness, need of mechanical ventilation, facial and bulbar palsy, conduction block >44% at common peroneal nerve, inexcitable motor nerves, and low Central Mean Arterial Pressure amplitude (20% of lower limit of normal). Another study conducted in India found that 3-month poor outcome was related to age (>50 years), short interval between onset and admission, limb power (<grade 3), cranial nerve palsy, generalized areflexia, dysautonomia, peak disability, ventilator requirement, and inexcitable motor nerves (34).

As mentioned earlier, mortality from GBS varies between 3% and 7%. Predictors of an increased risk of death are advanced age, severe disease, increased comorbidity, pulmonary and cardiac complications, mechanical ventilation, and systemic infection. Consequently, severely affected patients in the recovery phase of GBS and after discharge from the ICU still require good observation and supportive care. The most common causes of death are respiratory insufficiency, pulmonary infection, autonomic dysfunction, and cardiac arrest (10,35,36).

CONCLUSION:

GBS is a post-infectious disorder. Two-thirds of patients report symptoms of a respiratory or gastrointestinal tract infection before the onset of GBS. The typical symptoms are pain, numbness, paresthesia, or weakness in the limbs. The main feature are rapidly progressive bilateral and relatively symmetric weakness of the limbs. Intravenous immunoglobulin (IVIg) therapy and plasma exchange (PE) play a leading role in GBS treatment. These Immunomodulating treatments hasten recovery from GBS and improve outcomes. Severe fatigue is a common problem and considered as one of the most important symptoms leading to problems in school or work but exercise was found to be linked to improved GBS physical outcomes. Advanced age, severe disease, increased comorbidity, pulmonary and cardiac complications, mechanical ventilation, and systemic infection were found to be predictors of an increased risk of death.

REFERENCES:

1. Haber, Penina, James Sejvar, Yann Mikaeloff, and Frank Destefano. "Vaccines and Guillain-Barré Syndrome." Drug Safety 32, no. 4 (2009): 309-23. doi:10.2165/00002018-200932040-00005.
2. Guillain G, Barre J, Strohl A. Sur un syndrome de radiculo-névrite avec hypoalbuminémie du liquide céphalorachidien sans réaction cellulaire.

Remarques sur les caractères cliniques et graphiques des réflexes tendineux. Bull Soc Med Hop Paris 1916;28:1462–70.
3. Willison, H. J. "Peripheral Neuropathies and Anti-glycolipid Antibodies." Brain 125, no. 12 (2002): 2591-625. doi:10.1093/brain/awf272.
4. Bogliun, Graziella, and Ettore Beghi. "Incidence and Clinical Features of Acute Inflammatory Polyradiculoneuropathy in Lombardy, Italy, 1996." Acta Neurologica Scandinavica 110, no. 2 (2004): 100-06. doi:10.1111/j.1600-0404.2004.00272.x.
5. Mcgrogan, Anita, Gemma C. Madle, Helen E. Seaman, and Corinne S. De Vries. "The Epidemiology of Guillain-Barré Syndrome Worldwide." Neuroepidemiology 32, no. 2 (2008): 150-63. doi:10.1159/000184748.
6. Hughes, Rac, and Dr Cornblath. "Guillain-Barré Syndrome – Authors Reply." The Lancet 367, no. 9509 (2006): 473-74. doi:10.1016/s0140-6736(06)68176-2.
7. Jacobs, B. C., P. H. Rothbarth, F.g.a. Van Der Meche, P. Herbrink, P. I.m. Schmitz, M. A. De Klerk, and P. A. Van Doorn. "The Spectrum of Antecedent Infections in Guillain-Barre Syndrome: A Case-control Study." Neurology 51, no. 4 (1998): 1110-115. doi:10.1212/wnl.51.4.1110.
8. Ang, C. W. "Structure of Campylobacter Jejuni Lipopolysaccharides Determines Antiganglioside Specificity and Clinical Features of Guillain-Barre and Miller Fisher Patients." Infection and Immunity 70, no. 3 (2002): 1202-208. doi:10.1128/iai.70.3.1202-1208.2002.
9. Kuijf, M. L., J. N. Samsom, W. Van Rijs, M. Bax, R. Huizinga, A. P. Heikema, P. A. Van Doorn, A. Van Belkum, Y. Van Kooyk, P. C. Burgers, T. M. Luider, H. P. Endtz, E. E. S. Nieuwenhuis, and B. C. Jacobs. "TLR4-Mediated Sensing of Campylobacter Jejuni by Dendritic Cells Is Determined by Sialylation." The Journal of Immunology 185, no. 1 (2010): 748-55. doi:10.4049/jimmunol.0903014.
10. Berg, Bianca Van Den, Christa Walgaard, Judith Drenthen, Christiaan Fokke, Bart C. Jacobs, and Pieter A. Van Doorn. "Guillain–Barré Syndrome: Pathogenesis, Diagnosis, Treatment and Prognosis." Nature Reviews Neurology 10, no. 8 (2014): 469-82. doi:10.1038/nrneurol.2014.121.
11. Top, Karina A., Shalini Desai, Dorothy Moore, Barbara J. Law, Wendy Vaudry, Scott A. Halperin, and Julie A. Bettinger. "Guillain–BarrÉ Syndrome After Immunization in Canadian Children (1996–2012)." The Pediatric Infectious Disease Journal 34, no. 12 (2015): 1411-413. doi:10.1097/inf.0000000000000903.
12. Marks, J. S. "Guillain-Barre Syndrome in Recipients of A/New Jersey Influenza Vaccine." JAMA: The Journal of the American Medical Association 243, no. 24 (1980): 2490-494. doi:10.1001/jama.243.24.2490.
13. Arias, L.h. Martín, R. Sanz, M. Sáinz, C. Treceño, and A. Carvajal. "Guillain-Barré Syndrome and Influenza Vaccines: A Meta-analysis." Vaccine 33, no. 31 (2015): 3773-778. doi:10.1016/j.vaccine.2015.05.013.
14. Eldar, Adi Hersalis, and Joab Chapman. "Guillain Barré Syndrome and Other Immune Mediated Neuropathies: Diagnosis and Classification." Autoimmunity Reviews 13, no. 4-5 (2014): 525-30. doi:10.1016/j.autrev.2014.01.033.
15. Asbury, Arthur K., and David R. Cornblath. "Assessment of Current Diagnostic Criteria for Guillain-Barré Syndrome." Annals of Neurology 27, no. S1 (1990). doi:10.1002/ana.410270707.
16. Fokke, C., B. Van Den Berg, J. Drenthen, C. Walgaard, P. A. Van Doorn, and B. C. Jacobs. "Diagnosis of Guillain-Barre Syndrome and Validation of Brighton Criteria." Brain 137, no. 1 (2013): 33-43. doi:10.1093/brain/awt285.
17. Hadden, R. D. M., D. R. Cornblath, R. A. C. Hughes, J. Zielasek, H.-P. Hartung, K. V. Toyka, and A. V. Swan. "Electrophysiological Classification of Guillain-barré Syndrome: Clinical Associations and Outcome." Annals of Neurology 44, no. 5 (1998): 780-88. doi:10.1002/ana.410440512.
18. Xiao, Jinting, Alain R. Simard, Fu-Dong Shi, and Junwei Hao. "New Strategies in the Management of Guillain–Barré Syndrome." Clinical Reviews in Allergy & Immunology 47, no. 3 (2013): 274-88. doi:10.1007/s12016-013-8388-5.
19. Koningsveld, R. Van, Pim Schmitz, Fga Van Der Meché, Lh Visser, J. Meulstee, and Pa Van Doorn. "Effect of Methylprednisolone When Added to Standard Treatment with Intravenous Immunoglobulin for Guillain-Barré Syndrome: Randomised Trial." The Lancet 363, no. 9404 (2004): 192-96. doi:10.1016/s0140-6736(03)15324-x.
20. Raphaël, Jean Claude, Sylvie Chevret, Richard Ac Hughes, and Djillali Annane. "Plasma Exchange for Guillain-Barré Syndrome." Cochrane Database of Systematic Reviews, 2012. doi:10.1002/14651858.cd001798.pub2.
21. Hughes, Richard Ac, and Pieter A Van Doorn. "Corticosteroids for Guillain-Barré Syndrome." Cochrane Database of Systematic Reviews, 2012. doi:10.1002/14651858.cd001446.pub4.

22. Odaka M. "CSF filtration and interferon-beta for Guillain–Barré syndrome." Nippon Rinsho, 2008. 66:1200–1204.
23. Créange, Alain, Hervé Lerat, Christian Meyrignac, Jean-Denis Degos, Romain K. Gherardi, and Pierre Cesaro. "Treatment of Guillain-Barré Syndrome with Interferon-β." The Lancet 352, no. 9125 (1998): 368-69. doi:10.1016/s0140-6736(05)60466-7.
24. Mangano, K., G. Dati, C. Quattrocchi, L. Proietti, C. Mazzarino, R. Dimarco, K. Bendtzen, B. Greco, P. Zaratin, and F. Nicoletti. "Preventive and Curative Effects of Cyclophosphamide in an Animal Model of Guillain Barrè Syndrome." Journal of Neuroimmunology 196, no. 1-2 (2008): 107-15. doi:10.1016/j.jneuroim.2008.03.008.
25. Andrade-Ortega, Lilia, Fedra Irazoque-Palazuelos, Sandra Muñóz-López, and Victor Manuel Rosales-Don Pablo. "Efficacy and Tolerability of Rituximab in Patients With Rhupus." Reumatología Clínica (English Edition) 9, no. 4 (2013): 201-05. doi:10.1016/j.reumae.2013.03.004.
26. Yan, Qing, Jing-Wen Ruan, Ying Ding, Wen-Jie Li, Yan Li, and Yuan-Shan Zeng. "Electro-acupuncture Promotes Differentiation of Mesenchymal Stem Cells, Regeneration of Nerve Fibers and Partial Functional Recovery after Spinal Cord Injury." Experimental and Toxicologic Pathology 63, no. 1-2 (2011): 151-56. doi:10.1016/j.etp.2009.11.002.
27. Merkies, Ingemar S.j., and Bernd C. Kieseier. "Fatigue, Pain, Anxiety and Depression in Guillain-Barré Syndrome and Chronic Inflammatory Demyelinating Polyradiculoneuropathy." European Neurology 75, no. 3-4 (2016): 199-206. doi:10.1159/000445347.
28. Drenthen, J., B. C. Jacobs, E. M. Maathuis, P. A. Van Doorn, G. H. Visser, and J. H. Blok. "Residual Fatigue in Guillain-Barre Syndrome Is Related to Axonal Loss." *Neurology* 81, no. 21 (2013): 1827-831. doi:10.1212/01.wnl.0000436073.21406.e6.
29. Garssen, M. P.j., J. B.j. Bussmann, P. I.m. Schmitz, A. Zandbergen, T. G. Welter, I. S.j. Merkies, H. J. Stam, and P. A. Van Doorn. "Physical Training and Fatigue, Fitness, and Quality of Life in Guillain-Barre Syndrome and CIDP." Neurology 63, no. 12 (2004): 2393-395. doi:10.1212/01.wnl.0000148589.87107.9c.
30. Arsenault, Nicholas Simatos, Pierre-Olivier Vincent, Bai He Shen Yu, Robin Bastien, and Aaron Sweeney. "Influence of Exercise on Patients with Guillain-Barré Syndrome: A Systematic Review." Physiotherapy Canada 68, no. 4 (2016): 367-76. doi:10.3138/ptc.2015-58.
31. Karper, William B. "Effects of Low-Intensity Aerobic Exercise on One Subject with Chronic-Relapsing Guillain-Barré Syndrome." Rehabilitation Nursing 16, no. 2 (1991): 96-98. doi:10.1002/j.2048-7940.1991.tb01189.x.
32. Roodbol, Joyce, Marie-Claire Y. De Wit, Femke K. Aarsen, Coriene E. Catsman-Berrevoets, and Bart C. Jacobs. "Long-term Outcome of Guillain-Barré Syndrome In children." Journal of the Peripheral Nervous System 19, no. 2 (2014): 121-26. doi:10.1111/jns5.12068.
33. Rajabally, Yusuf A., and Antonino Uncini. "Outcome and Its Predictors in Guillain–Barré Syndrome." Journal of Neurology, Neurosurgery & Psychiatry 83, no. 7 (2012): 711-18. doi:10.1136/jnnp-2011-301882.
34. Kalita, Jayantee, Usha K. Misra, Gaurav Goyal, and Moromi Das. "Guillain-Barré Syndrome: Subtypes and Predictors of Outcome from India." Journal of the Peripheral Nervous System 19, no. 1 (2014): 36-43. doi:10.1111/jns5.12050.
35. Berg, B. Van Den, C. Bunschoten, P. A. Van Doorn, and B. C. Jacobs. "Mortality in Guillain-Barre Syndrome." Neurology 80, no. 18 (2013): 1650-654. doi:10.1212/wnl.0b013e3182904fcc.
36. Lawn, N. D., and E. F. M. Wijdicks. "Fatal Guillain-Barre Syndrome." Neurology 52, no. 3 (1999): 635. doi:10.1212/wnl.52.3.635.