Effectiveness of physiotherapy interventions for foot drop in individuals with guillian-barre syndrome- A systematic review

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Abstract

Purpose: Worldwide, the incidence of Guillian-Barre Syndrome (GBS) is 1.1 to 1.8 per 100,000 annually. At three years, about 30% of patients with GBS have residual weakness resulting in activity and participation restriction. In those with persistent weakness, foot drop is a common sequel. Individuals with GBS are often treated with a multidisciplinary approach but isolated strategies for foot drop are usually neglected. The need for the review arises from the lacunae in the literature regarding PT interventions for foot drop in GBS.

Relevance: Recovery from foot drop is considered essential for functioning and independence. A systematic review of available literature could provide necessary evidence for therapists' to make informed decisions on therapeutic strategies that could aid in recovery from foot drop.

Material and Methods: PubMed, PEDro, CENTRAL and Google Scholar were searched on 24th October 2017 using a comprehensive search strategy, using 63 word variations for GBS, Foot drop, and therapies. The search results were screened by two reviewers using predetermined inclusion criteria. Intervention studies (RCT, Quasi RCT, Non RCT, single group designs) and case reports of patients with acute variants of GBS (AMAN & AMSAN) were included in the review.

Analysis: The review attempted to perform a qualitative synthesis of the included studies.

Results: The search yielded 36 articles out of which 3 papers (total of 38 participants) met the inclusion criteria and were included in the review. All studies used ankle foot orthosis (AFO) as the main line of management for foot drop. None reported the effect of exercise or electrical therapy interventions for foot drop.

Conclusion: AFO remains the management of choice for foot drop in individuals with GBS.

Implications: These findings state the dire need for future research in exercise and electrical therapies for recovery from foot drop in GBS.

Keywords: Guillian-Barre Syndrome, Foot Drop, Physiotherapy Interventions.

Introduction

Guillian Barre Syndrome (GBS) is a heterogeneous grouping of immune-mediated processes generally characterized by motor, sensory and autonomic dysfunction.[1] In its classic form, it is an acute inflammatory demyelinating polyneuropathy characterized by progressive symmetric ascending muscle weakness, paralysis and hyporeflexia with or without sensory or autonomic symptoms.[2] The overall incidence of GBS worldwide is 1.1 to 1.8 per 100,000 annually.[3] Exact triggering factor is unknown; however, it often occurs after a minor infection such as a lung or gastrointestinal infection. GBS damages the peripheral nervous system, resulting in tingling, muscle weakness and paralysis. The symptoms of GBS can worsen quickly; it can take only a few hours to reach the most severe symptoms, but weakness that increases over several days is also common. The recovery pattern is usually from proximal to distal with the foot muscles recovering last. Function can usually be restored; but there are exceptions.[4]

A systematic review on influence of exercise interventions on GBS in 2016 stated that various types of exercise programs improve physical outcomes such as functional mobility, cardiopulmonary function, isokinetic muscle strength, work rate and reduce fatigue, although the low quality of evidence of most studies decreases their external validity.[5] According to this review, cycling training seems the most warranted type of program although strengthening exercises and physiotherapy interventions can also target physical outcomes. For optimal recovery, the review suggested a two-phase rehabilitation process: the first in the early stages of recovery to diminish the disability burden, and the second in the later stages of the disease to support reconditioning. Over-exercising in individuals with GBS could lead to immediate and irreversible relapse, optimal treatment methods should quantitatively maximize therapy while minimizing the chance of fatigue. Evidence also suggests that over fatiguing the respiratory muscles during the initial period of motor unit recovery may induce respiratory failure. As individuals with GBS show marked clinical heterogeneity, it may be necessary to use standardized tools to assess severity at baseline. Therefore, there is a need for a standardized, valid, reliable, and sensitive rehabilitation outcome measures to establish and determine effectiveness and facilitate comparisons. Indeed, studies have yet to establish the optimal modalities for treating individuals with GBS and a multidisciplinary team may be required to improve future outcomes.[5]

In GBS, foot drop is often bilateral as the underlying illnesses affect both sides of the body and are relatively symmetric.[6] Foot drop may be seen within the first few days of the illness and may persist for months if the GBS is severe and protracted. Foot drop may or may not respond to treatments with IVIG, plasma exchange, cortical steroids, or other immune suppressants.[7]

A review on rehabilitation interventions for foot drop in neuromuscular diseases concluded that exercise regimens of varying intensity and frequency have provided some evidence of benefit and should be evaluated in more detail for clinical application.[7] The review recommended investigating the use of orthotics on function and physiological cost, cost effectiveness of such interventions using outcome measures which assess function such as measures of activities of daily living. This would allow clinicians to assess the influence of interventions on everyday life and not purely concentrate on factors such as strength and range of motion. The review highlighted the importance to link changes in strength and range of motion with actual functionality.[7] This assumes importance because about 20% of patients with neuromuscular diseaseshave disability for more than a year, especially in foot muscles, needing aids to walk.[8]

Individuals with GBS are often treated with a multidisciplinary approach but isolated strategies for foot drop are usually neglected. Pathophysiology of GBS and its recovery process suggests that recovery in distal musculature may be different from recovery in proximal musculature.[9] Physiotherapy guidelines for patients with GBS have been generic and have a greater focus on proximal muscle groups. The need for the review arises from the lack of PT intervention guidelines for management of foot drop in patients with GBS. Recovery from foot drop is considered essential for functioning and independence. A systematic review of available literature could provide necessary evidence (or the lack of it) for therapists to take informed decisions on therapeutic strategies that could aid in recovery from foot drop.

Material and Methods

Database: Open access database Viz. PubMed, PeDro, CENTRAL and Google Scholar were searched on 24th October 2017 using a comprehensive set of search terms.

Search Terms: A comprehensive set of search termswere developed following a scoping literature review and consensus process among the authors. At a broader level, the PICO format was adopted for developing the search strategy and in an attempt to maximize the search results, the terms were limited to Population and Intervention. The list of terms used are summarised in Table 1. The terms for GBS, Foot Drop and Interventions were combined using the Boolean Operator 'AND'. The search was limited to articles published in English language.

Article Selection and Data Extraction: The search results were independently screened for inclusion in the review by the authors PB and NB and any conflicts were resolved by discussion with SKV. The articles were included for qualitative analysis if a) they used the following designs: RCTs, Quasi RCTs, Case reports, Clinical trials, Pilot studiesand b) reported about interventions that generically or specifically targeted foot drop in patients with both AMAN & AMSAN variants of GBS. Studies involving Miller Fischer variant, Bickerstaff brainstem encephalitis, Pharyngeal cervical brachial motor variant, sub-acute inflammatory demyelinating polyneuropathy and CIDP were excluded.

Results

The search strategy yielded a total of 38 articles: PubMed (17), CENTRAL (17), Google Scholar (3) and additional sources (1). Total of 36 studies were identified after duplicate removal out of which 28 were excluded based on the exclusion criteria. Eight full texts were screened of which five were excluded due to studies reporting on different population and intervention. Three articles were included in the qualitative synthesis for this review. The search details and article selection process are described in Fig. 1.

Out of the three studies included in the review, one study titled 'Guillain-Barre Syndrome – rehabilitation outcome, residual deficits and requirement of lower limb orthosis for locomotion at 1 year follow-up' was carried out by Gupta et.al in 2010.[10] This prospective longitudinal follow-up study was conducted in the neurological rehabilitation unit of the university hospital on patients with GBS, who were admitted between September 2005 and July 2009. All patients were received in the screening block/emergency of the hospital and were investigated (blood, lumber puncture cerebro-spinal fluid examination and nerve conduction studies). Once the diagnosis of GBS or its variant was confirmed (with ENMG), they were treated initially in neurology unit or intensive care unit as required. Rehabilitation consultation were provided during their stay in neurology unit (bed side). After receiving treatment (plasmapheresis/ IVIg) and once the patients were medically stable off ventilator, 69 patients were taken over to neuro-rehabilitation unit for inpatient rehabilitation in sub-acute/post-acute phase during the study period. Patients, who were weaned off ventilator, medically stable and in a position to participate in the rehabilitation program, were transferred to the rehabilitation unit irrespective of severity of motor weakness and paralysis, age, gender and type of GBS. Thirty-five of these 69 patients who reported for minimum 1 year in the follow-up were included in this study. Patients showing significant neurological and functional recovery in post-acute phase with independence in ambulation and performing other activities of daily living were discharge from neurology unit with home-based programme from rehabilitation team. They concluded in their study that patients with GBS continue to show significant functional recovery for long period. Despite being functionally independent, they have to use lower limb Orthosis with or without assistive devices for mobility and locomotion. They also have

residual deficits even after one year with requirement of orthosis in large number of patients.

Second study titled 'Feasibility of robotic assisted locomotor training in children with central gait impairment' carried out in 2007 by A Meyer-Heim in Germany.[11]This study was the first paediatric trial aimed to determine the feasibility of robotic-assisted treadmill training in children with central gait impairment (n=26; 11 females, 15 males; mean age 10y1mo [SD 4y]; range 5y2mo–19y5mo). Diagnoses of the study group included cerebral palsy (n=19; Gross Motor Function Classification System Levels I–IV), traumatic brain injury (n=1), Guillain-Barré syndrome (n=2), incomplete paraplegia (n=2), and haemorrhagic shock (n=1), and encephalopathy (n=1). Sixteen children were in-patients and 10 were outpatients. Twenty-four of the 26 patients completed the training which consisted of a mean of 19 sessions (SD 2.2; range 13–21) in the in-patient group and 12 sessions (SD 1.0; range 10–13) in the outpatient group. Gait speed and 6-Minute Walking Test increased significantly ($p<0.01$). Functional Ambulation Categories and Standing dimension (in-patient group $p<0.01$; outpatient group $p<0.05$) of the Gross Motor Function Measure improved significantly. Driven Gait Orthosis (DGO) training was successfully integrated into the rehabilitation programme and findings suggest an improvement of locomotor performance. The DGO is a promising tool for use with children with central gait impairment and may shorten the rehabilitation process.

Third study titled, "Modelling of human walking to optimise the function of ankle-foot orthosis in Guillan-Barré patients with drop foot" by Jamshidi N done in 2009 dealt with the dynamic modelling of human walking.[12] The main focus of this research was to optimise the function of the orthosis in patients with neuropathic feet, based on the kinematics data from different categories of neuropathic patients. The patient's body on the sagittal plane was modelled for calculating the torques generated in joints. The kinematics data required for mathematical modelling of the patients were obtained from the films of patients captured by high speed camera, and then the films were analysed through motion analysis software. An inverse dynamic model was used for estimating the spring coefficient. In their dynamic model, the role of muscles was substituted by adding a spring-damper between the shank and ankle that could compensate for their weakness by designing ankle-foot orthosis based on the kinematics data obtained from the patients. The torque generated in the ankle was varied by changing the spring constant. Therefore, it was possible to decrease the torque generated in muscles which could lead to the design of more comfortable and efficient orthosis. They concluded that the function of the ankle-foot orthosis on the abnormal gait has been quantitatively improved through a correction of the torque.

Table 1: List of Search Terms used in PubMed

GBS	Foot Drop	Interventions
Guillain-Barre Syndrome (mesh), Guillian Barre syndrome (all fields), Guillain-Barre Syndrome (all fields), Guillain-Barré Syndrome (all fields), AIDP (all fields), Acute Inflammatory Polyneuropathy (tw), Inflammatory Demyelinating Polyradiculoneuropathy, Landry-Guillain-Barre Syndrome (tw), Acute Inflammatory Demyelinating Polyneuropathy (tw), Acute Inflammatory Demyelinating Polyradiculoneuropathy (tw), Acute Inflammatory Polyradiculoneuropathy (tw), AMAN (all fields), Acute motor axonal neuropathy (all fields), AMSAN (all fields) Acute motor and sensory axonal neuropathy (all fields).	Peroneal Neuropathies (Mesh), Gait Disorders, Neurologic (Mesh), Peroneal Neuropathies (all fields), Gait Disorders, Neurologic (All Fields), Peroneal Nerve Disease (All Fields), Foot Drop (All Fields), Peroneal Neuropathies (All Fields), Peroneal Nerve Injury (All Fields), Peroneal Nerve Paralysis (All Fields), Common Peroneal Neuropathy (All Fields), Common Peroneal Neuropathies (All Fields), Gait (tw), Drop Foot (tw), Drop Foot Gait (tw), Foot Gait, Drop (tw),	Rehabilitation (mesh), Physical therapy modalities (mesh), Exercise (mesh), Splints (mesh), Exercise Therapy (mesh), Electric Stimulation Therapy (mesh), Exercise Therapy (all fields), Electrotherapy (tw), Habilitation (tw), Electric Stimulation Therapy (all fields), Therapeutic Electrical Stimulation (tw), Rehabilitation (all fields), Physical therapy modalities (all fields), Physical Therapy Techniques (tw), Neurological Physiotherapy (tw), Physiotherapy interventions (all fields), Physical exercises (all fields), Taping (all fields), Kinesiotaping (all fields), Splinting (all fields), Splints (all fields), AFO (all fields), Foot Drop Splint (all fields), Drop Foot Splint (all fields), Ankle Foot orthosis, (all fields), Faradic stimulation (all fields), NMES (all fields), Neuromuscular electrical stimulation (all fields), Exercise (all fields), Physical Exercise (tw), Acute Exercises (tw), Exercise (tw), Isometric (tw) Exercise Training (tw).

Search Strategy

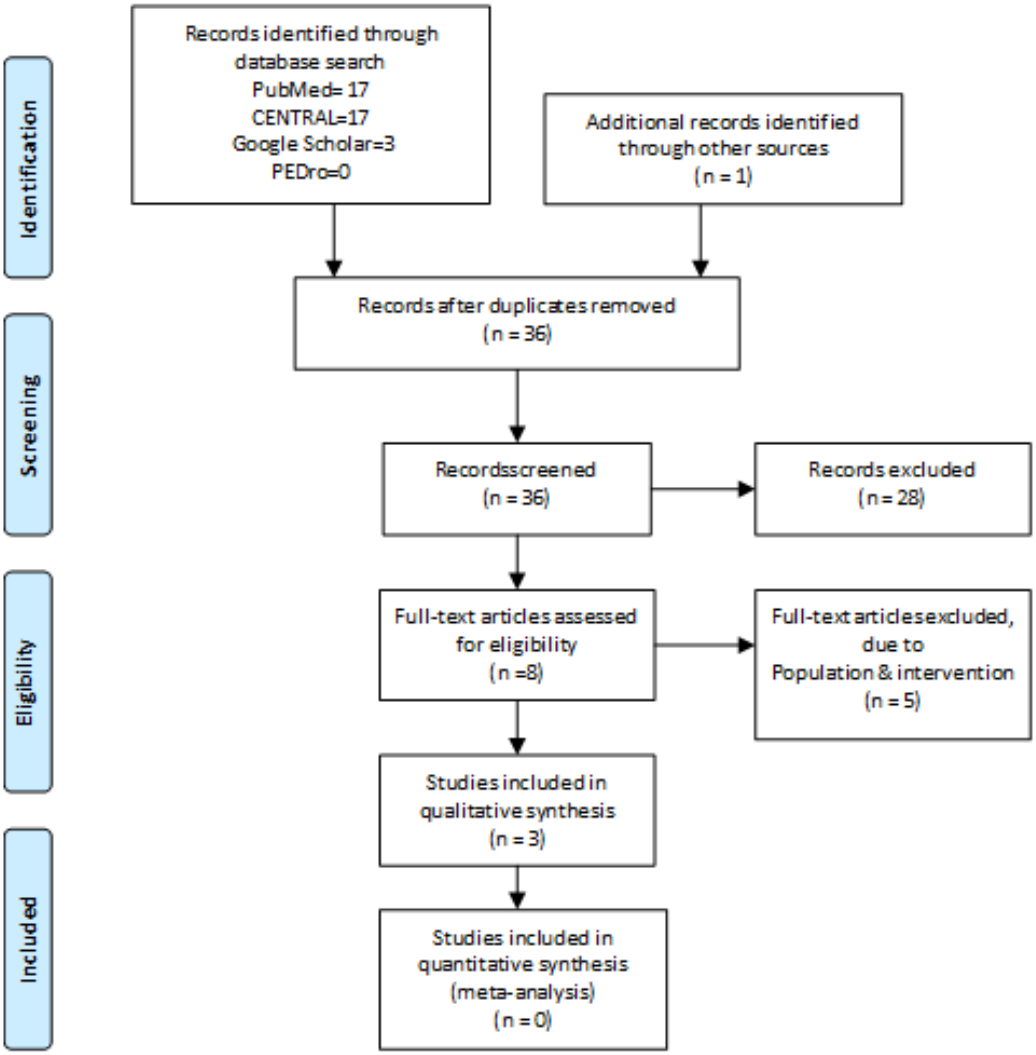

Fig. 1: PRISMA Flow Diagram of the Search Results

Discussion

This review mainly attempts at understanding the effectiveness of various physiotherapy interventions for foot drop in individuals with GBS. The results of this review show the dearth in literature regarding interventions that specifically target foot drop in patients with GBS. Despite the availability of literature on evidences for physiotherapy in different stages of GBS such as acute, sub-acute and chronic phases, very limited evidence exists especially for foot drop. The current review attempted to explore the scope of literature focusing on the interventions for foot drop in patients with GBS. We attempted to include only intervention studies that targeted foot drop in patients with GBS, but within the limitation of the small number of database selected, we would not identify any study focusing specifically on foot drop. The study by Gupta el al was included because the patients underwent rehabilitation intervention at the hospital and the study provided information on the course of the recovery at one year follow-up including information on foot drop. The remaining two were feasibility and modelling studies that addressed foot drop using orthotic devices. The lack of interventions or rather the need for targeting foot drop needs to be seen from the perspective of the pathophysiology of the health condition.

Pathophysiology in GBS:

GBS is considered to be an immune-mediated polyneuropathy where deposits of complement, immunoglobulins, and infiltration of macrophages are seen in the peripheral nerves.[13] Anti-ganglioside antibodies, inflammatory cytokines and activated T-cells are also found in the blood of individuals with GBS. Gangliosides are glycosphingolipids which differ from each other with respect to the oligosaccharide attached. Gangliosidesare found in relatively high concentrations in neural membranes.[14] Their role is possibly in multiple

signal recognition processes. Specific gangliosides are distributed typically in peripheral nerves; GM1 is concentrated in axons, and in myelin of motor nerve fibres, while GQ1b is majorly found in myelin of occulomotor nerves.[15]

The concept of molecular mimicry as a possible mechanism, via which infections may induce pathogenic immune responses, has been proposed in many autoimmune diseases.[16] The role of molecular mimicry between microbial and autologous antigens in producing a cross-reactive immune response can be established at different levels: (i) homology in biochemical structure or linear amino acid sequence, (ii) cross-reactivity of antibodies with both structures, (iii) cross-reactive antibodies could be induced by process of immunisation with the microbial antigen and (iv) induction of cross-reactive antibodies which induce dysfunction or tissue damage.[17] For a cross-reactive immune response to be initiated against autologous antigens, two primary events need to occur.[17] The first being similarity between the microbial and the autologous antigen so that immune responses can cross-react. The second requirement being sufficient dissimilarity of the microbial antigen from the autologous antigen. This is required so that the immune systems tolerance to self is broken and a very specific immune response is generated. This could occur by affinity maturation of isotype switch processes. Lipopolysaccharide (LPS) found in cell walls of *C jejuni* strains have been found to induce anti-ganglioside antibodies in some individuals. Anti-ganglioside antibodies also play a role in pathogenesis of GBS. LPS are cell wall components of most gram-negative bacteria. They usually mediate the disease progression by complement dependent action.[17]This pathogenesis of GBS can be correlated with its recovery pattern with the proximal muscles recovering first and the distal muscles recovering last.

Difference between GBS and Other Conditions

Usually in individuals presenting with muscular weakness, the mainstay of treatment is strengthening of the weakened muscles. In individuals recovering from GBS, it has been shown that overworking partially innervated muscles can cause further damage, paradoxical weakening which includes a loss of functioning motor units.[18] Thus it is clear that the strategies used for treatment of foot drop secondary to other health conditions may not be effective in treating foot drop secondary to GBS.

It is also shown that there is an increase in proximal muscle recruitment from 0 to 88% of maximum voluntary contraction, whereas in distal muscles no additional motor units were recruited at forces greater than 50% of maximal voluntary contraction. With increasing load, small, distal muscles rely more on increase in firing rate whereas their counterpart recruit additional motor units.[19] Therefore the strengthening interventions used in training proximal girdle musculature cannot be used for distal muscles.

The studies in the review highlight this fact as no therapeutic strategies are used in recovery of foot muscles; it focuses only on substitution and compensatory strategies by use of AFO. It looks like there is a need for physiotherapists to review approaches to facilitate recovery in patients with GBS. Studies elucidating the molecular mechanisms underlying the beneficial effects of exercise are emerging.[20]Future research need to explore the effects of exercise interventions with reference to the pathophysiology and recovery process of GBS rather than focusing only on compensatory strategies.

Strengths and Limitations

Within the limits of the database, to our knowledge, this is the first review that has attempted to identify studies targeting physiotherapy interventions for foot drop in patients with GBS. The study used a comprehensive set of search terms to maximize the scope of identifying articles. The review clearly shows the lacunae in literature regarding foot drop. The absence of any intervention strategies indicates the need for high quality, clinical trials to lay down guidelines for the management of foot drop. The primary limitation of the review is the lack of intervention studies specifically targeting foot drop in GBS. The review was also limited by inclusion of only open access database and studies published in English language, but this was due to feasibility.

Conclusion

Ankle foot orthosis remains the management of choice for foot drop in individuals with Guillain-Barre Syndrome. Studies targeting interventions for foot drop are needed.

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