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Current Treatment Approaches for the Management of Guillain Barre Syndrome: A Narrative Review of Physiotherapy Approaches

Guillain Barre Sendromunun Yönetimi İçin Güncel Tedavi Yaklaşımları: Fizyoterapi Yaklaşımlarının Derlemesi

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ABSTRACT

Objectives: In this review we explore the current physiotherapy treatment approaches for Guillain-Barre Syndrome (GBS), an immune-mediated peripheral nervous system disorder. Examining GBS epidemiology reveals its rarity, diverse clinical variants, and increased incidence with age. The pathogenesis involves subtypes like acute inflammatory demyelinating polyradiculoneuropathy (AIDP) and axonal variants, with infections, particularly C. jejuni, playing a role. The diagnostic methods include nerve conduction velocity tests and cerebrospinal fluid examination. GBS is characterized by progressive complications, ranging from muscular weakness to cardiovascular issues. The crucial role of physiotherapy in GBS assessment and treatment is emphasized, covering various evaluations and rehabilitation strategies.
Materials and Methods: Multidisciplinary rehabilitation, exercise training, pulmonary rehabilitation, electrical stimulation, robotic rehabilitation, virtual reality, and alternative therapies are discussed.
Results and Conclusions: This article stresses the need for high-quality trials, especially in the context of the observed connection between COVID-19 and GBS. It underscores the importance of physiotherapy in GBS treatment, prompting further research and consideration of alternative methods like telerehabilitation.
Keywords: Guillain-Barre Syndrome, Physiotherapy, Multidisciplinary Rehabilitation

ÖZET

Amaç: Bu derlemede, bağışıklık sistemi aracılı periferik sinir sistemi bozukluğu olan Guillain-Barre Sendromu'nun (GBS) güncel fizyoterapi tedavi yaklaşımlarını incelemekteyiz. GBS epidemiyolojisi incelendiğinde, nadir görüldüğü, çeşitli klinik özellikleri ve yaşla birlikte artan insidansı görülür. Patogenez, akut inflamatuar demiyelinizan poliradikulonöropati ve aksonal özellikler gibi alt türleri içerir ve özellikle C. jejuni hastalıklarının rol oynadığı bilinmektedir. Tanı yöntemleri arasında sinir aktarım hızı testleri ve beyin omurilik sıvısı incelemesi yer alır. GBS, kas zayıflığından kardiyovasküler sorunlara kadar ilerleyici komplikasyonlarla karakterizedir. GBS değerlendirmesinde ve tedavisinde fizyoterapinin kritik rolü vurgulanmakta olup, çeşitli değerlendirmeleri ve rehabilitasyon stratejilerini içermektedir.
Materyal ve Metod: Çok disiplinli rehabilitasyon, egzersiz eğitimi, pulmoner rehabilitasyon, elektriksel uyarım, robotik rehabilitasyon, sanal gerçeklik ve alternatif terapiler tartışılmaktadır.
Bulgular ve Sonuç: Bu makale, özellikle COVID-19 ve GBS arasındaki gözlemlenen bağlantı bağlamında yüksek kaliteli denemelerin gerekliliğine vurgu yapmaktadır. GBS tedavisinde fizyoterapinin önemini vurgulayarak, ileri araştırmaları teşvik etmekte ve telerehabilitasyon gibi alternatif yöntemlerin düşünülmesini teşvik etmektedir.
Anahtar kelimeler: Guillain-Barre Sendromu, Fizyoterapi, Multidisipliner Rehabilitasyon.

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Introduction

Guillain-Barre syndrome (GBS) is one the most common immune mediated disorders of the peripheral nervous system of both acute and the subacute onset. The most seen symptoms are generalised weakness paraesthesia of the limbs along with areflexias (1). Patients with GBS typically present with weakness and sensory signs in the legs that progress to the arms and cranial muscles, although the clinical presentation of the disease is heterogeneous, and several distinct clinical variants exist. The term GBS is often considered to be synonymous with acute inflammatory demyelinating polyradiculoneuropathy (AIDP), but with the increasing recognition of variants over the past few decades, the number of diseases that fall under the rubric GBS have grown to include axonal variants and more restricted variants, such as Miller Fisher syndrome (MFS) (2).

Epidemiology

The global incidence of GBS is rare at a rate of 2.07 cases among every 100 000 persons each year and keeps increasing. The older a person is the higher their chances are of getting the syndrome (1). However, there are small peaks during childhood and between the ages of 40 and 50 years old. After the age of 80 the cases incidence increases by a 6.26 cases per 100 000 person every year (3). There are a variety of different variants that are seen with their incidences. The incidences are like this: Acute inflammatory demyelinating polyneuropathy (AIDP) at the rate of 72.1%, motor axonal neuropathy (AMAN) at the rate of 16.3%, acute motor sensory axonal neuropathy (AMSAN) at the rate of 4.7%, and Miller Fisher syndrome at the rate of 4.7% (4). Patients with a history of respiratory problems and infections have an incidence rate of 41.9% and 20.9% have had an incidence of gastrointestinal infection. In 76.7% of the patient's protein is seen in the cerebrospinal fluid. A demyelination is seen in on electromyography findings at the rate of 73.7% and axonal degeneration is seen at the rate of 26.3% (4). The number of patients who end up needing ventilatory support were at the rate of 20.9%. A 9.3% mortality rate is seen after six months. The worst prognosis is seen in patients over 80 years old, delay in admitting patients in the hospital, any previous infections in the gastrointestinal tracts, and the AMAN variant (4). 60% of the patients present with a previous illness like respiratory illness but 27% of them don't present with any previous illnesses at all (5,6). Some of the reasons behind why people get affected by these diseases are viruses and respiratory infections. There are new studies that show new cases of GBS after the onset of Coronavirus disease 2019 (COVID-19) (7). One of the cases showed signs of the rare AMSAN variant (8). A multidisciplinary therapeutic approach is needed to prevent severe respiratory complications that could require the support of a ventilator. Almost one third of the patients end up in the critical care unit during the acute phase (9,10). The syndrome could have a variety of other autonomic dysfunctions that include: arrythmias, hypotension, hypertension, and gastrointestinal issues (11,12). Recent research is connecting the onset of COVID-19 with an acute onset of GBS.

Pathogenesis

To understand the disease better we need to understand the mechanisms behind some of the subtypes and why they happen. The AIDP subtype for example, resembles an experimental autoimmune neuritis. This is caused by T cells that are directed against peptides from myelin proteins P2, P0, and PMP22. T-cell-mediated immunity in AIDP is a process that we still need more research to understand however there is some evidence of antibodies involvement. Recent evidence shows the axonal subtypes of GBS like AMAN and AMSAN are caused by antibodies

to gangliosides on the axolemma which targets the macrophages to successfully invade the axon at the node of Ranvier. An infection called C. jejuni has been seen in about a quarter of the patients before the onset of GBS. People who had this infection and other axonal forms of the disease usually have these subtypes. The C. jejuni bacterial wall has lipo-oligosaccharide that contains ganglioside like structures. The injection of these in rabbits showed an induction of neuropathy that is like acute motor axonal neuropathy (13,14,15). In acute motor axonal neuropathy it was seen that antibodies to GM1, GM1B, GD1a, and GalNac-GD1a are implicated with one exception of the GalNacGD1a in acute motor and sensory neuropathy (16).

Diagnosis

A diagnosis is made by doing a nerve conduction velocity test and the examination of cerebrovascular fluid. Both tests could show normal results at the early stages of the syndrome (10,11,12). This disease is highly progressive and could progress very fast that it could cause severe disability within just a couple of days of the onset and 50% to 80% of patients reach the peak of it within the first two to three weeks. Recovery usually starts after two four weeks. 20% of patients stay disabled even after receiving treatment (17,18). This syndrome even after treatment and full recovery still leaves patients with a level of disability that could range from mild to severe. This leads us to why the role of physiotherapy is very important. Studies are still being conducted on this group of patients and we hope that this this article will help make the role of a physiotherapist more clear and open opportunities for more research to be conducted on the matter especially post-pandemic.

Complications

Complications that can be seen in GBS can be listed as follows: loss of deep tendon reflexes, paraesthesia, muscular weakness, respiratory muscles involvement, syndrome of inappropriate antidiuretic hormone hypersecretion, cranial nerve paralysis, autonomic dysfunction, and cardiovascular abnormalities. With cranial nerve paralysis, loss of eye movements, difficulty in swallowing and especially bilateral facial paralysis can be observed. Rhythm abnormalities, consisting of tachycardia and bradyarrhythmia, are the most common cardiovascular disorders among GBS patients (19). Rapidly progressive weakness is the main clinical feature of GBS. Maximum weakness is reached within 4 weeks, but most patients have already reached their maximum weakness within 2 weeks (20). Respiratory muscle involvement is fatal for GBS patients. Approximately 25% of GBS patients were associated with dyspnoea in the acute phase and required mechanical ventilation (21). Ropper and Shahani described muscle-induced low back and proximal leg pain in 55% of their patients early in the disease and at any time during the first month in 72% of them (22). Myocardial involvements ranging from myocarditis to neurogenic stunned myocardium, heart failure, acute coronary syndrome, and electrocardiographic changes have also been documented in GBS patients (23). After GBS, disabling sequelae such as quality of life, fatigue, pain, and muscle weakness may develop (24). In addition, although rare, sleep disorders and kidney diseases may occur (25). The infectious agent in COVID-19 has a high similarity with the human-angiotensin-converting enzyme 2 (ACE2) receptor. This receptor could also be found in neurons and glial cells, therefore explain why many neurological manifestations were reported. Some of these manifestations are anosmia, peripheral neuropathy, and brain disorders. It is thought that in patients that have recovered, SARS-Cov-2 is able to stay in the central nervous system for a long period of time which makes it able to trigger or reactivate neurological complications (26). Post COVID syndrome is characterised by symptoms like residual inflammation, orange damage, and the impact it could have on pre-existing health conditions or the not specified effects of

hospitalisation or ventilation (27). The most reported neurological problems are anosmia, ageusia, and headaches. Many case series have shown several patients who develop GBS, develop cerebrovascular accidents, de novo status epilepticus, and encephalopathy (28). GBS was also associated with severe acute respiratory syndrome coronavirus (29). It was also associated with cranial nerve involvement and dysautonomia. In this case report the man was able to walk again after 5 weeks of physiotherapy (30). Other case reports reported the onset of acute GBS after taking the mRNA vector-based corona vaccine (31,32). One of the case reports showed a change in the motor units electrophysiology while being infected with COVID-19 (33). The reason why being infected with COVID-19 virus is associated with acute onset of Guillain Barre syndrome could be because of the strong response of the immunity system that could trigger an infectious process by activating pro-inflammatory cytokine cascades (34).

Physiotherapy Assessments

In GBS patients, GBS Disability Scale is used to provide information about the status of the disease. Range of motion is evaluated with a goniometer, muscle shortness is evaluated with shortness-length tests, and deep tendon reflexes such as biceps, triceps, achilleas, and patella are evaluated. Muscle strength is tested with a Manual Muscle Test or a Hand Dynamometer. In sensory evaluation, Semmes-Weinstein Monofilament Test can be used for superficial sensation and distal proprioception test can be used for proprioception (35,36). Pulmonary Function Test is performed for respiratory evaluation. Fatigue is determined by Fatigue Severity Scale, pain by McGill-Melzack Pain Questionnaire, Visual Analogue Scale and Neuropathic Pain Questionnaire, ambulation level is determined by Functional Ambulation Classification. A 6-Minute Walk Test can be used for dyspnoea and endurance. In addition, Visual Analogue Scale, Oxygen Consumption Diagram and Modified Borg Scale can be used for dyspnoea (37). Functional Independence Measure, Neuromuscular Functional Assessment Index, Jepsen-Taylor Hand Function Test and Minnesota Rate of Manipulation and Manual Dexterity Tests can be used for extremity functions and disability. In addition, Katz Personal and Extended Activities of Daily Living Indexes, the Barthel Index, the Frenchay Activity Index can be applied to evaluate disability and activities of daily living (38,39,40). Quality of Life is evaluated with scales such as 36-item Short Form (SF-36), Sickness Impact Profile, Nottingham Health Profile, and 12-item Short Form (41).

Physiotherapy and Rehabilitation Approaches

Until the association between the two of those syndromes is confirmed the area of rehabilitation is being researched to provide these patients with the best rehabilitation and help them have a speedy recovery. A study that included 85 patients tested the efficacy of a rehabilitation program on a variety of neurological disorders post COVID-19. Eighteen of the patients were diagnosed with GBS (AIDP=13, AMSAN=5). The protocol for neuromuscular rehabilitation was as follows: Head was up by 10° per hour, then a progressive daily tilt table lifting as tolerated was given, venous compression stockings were used, range of motion exercises, in-bed mobilisation along with bridge and trunk exercises. Patients who developed sufficient trunk stability for using wheelchair were taught, bedside sitting, standing and balance coordination, walking in the parallel bar and the hall, step climbing, strengthening exercises and progressive resistance training were given. Functional electrical stimulation cycling was given for muscles weakness of the upper and lower extremities. Before the rehabilitation program, 55.3% patients were bedridden, 22.4% were in a wheelchair and 20% could move/walk with O2 support. Post rehabilitation the ratios changed to 2.4%, 4.7%, and 8.2%. Also, during rehab 83.5% patients

required O2 support but then it decreased to 8.2% post rehab. Barthel Index also showed great improvements from 44.82 ± 27.31 to 88.47 ± 17.56 (42). This shows the importance of how a multidisciplinary patient-based rehabilitation programs could be very effective in severe and critical COVID-19 cases.

Multidisciplinary rehabilitation

A multidisciplinary team rehabilitation approach is recommended for patients with GBS. Multidisciplinary rehabilitation may include physical therapy rehabilitation, exercise programs, occupational therapy, speech therapy, social rehabilitation, and psychotherapy. In a systematic review of rehabilitation interventions for patients with GBS, only five original studies could be identified evaluating the effectiveness of multidisciplinary rehabilitation (43). In this study patients diagnosed with GBS included 79 adults, 40 of whom were belonged to the intervention group, and 39 in the control group. The intervention program included 3-12 weeks of physical therapy for strengthening, function, endurance, specific rehabilitation program and gait training improve. Exercise program was not applied to the control group, but 30 minutes 2 days a week of low intensity maintenance training program was applied. Activity, participation, and perceived impact of their problems were assessed one year after the intervention as an outcome measure. There was a statistically significant improvement in the high-intensity rehabilitation group (44).

Exercise Training

Resistance exercise program is applied to strengthen the muscles and increase daily activities functioning, and reduce related fatigue in persons with GBS. The resistance exercise program can be applied for 70 minutes, 3 days a week for 12 weeks. 5-minute warm-up and 5-minute cool-down periods should be included in the exercise program. In the resistance exercise program, the upper extremity and lower extremity can be strengthened in 3 sets by using elastic bands (TheraBand). With different exercises and different TheraBand's, the exercise load is increased by increasing the resistance of the TheraBand's (45). The intensity, frequency and duration of exercise varies between studies, but exercise program that was applied was for 12 weeks,30-60 minutes and %70-%90 maximal heart rate (46). In patients with GBS, the effect of proximal muscle strengthening exercise program is clinically strong in distal muscle facilitation and improves functional mobility (47). Rehabilitation program during the acute phase should include individual Peripheral neuro facilitation program because PNF patterns are effective for improving stability and strength during ambulation (48).

a. Pulmonary rehabilitation

Rehabilitation management in GBS patients emphasizes the immobilization and management of commonly occurring pneumonia and respiratory failure (49). Exercise programs include respiratory muscle exercises. Chest therapy is a treatment aimed at improving the function of the respiratory system. It is done to expand the chest cavity with comfortable and controlled breathing to remove the secretions in the lungs that restrict the respiratory capacity. It can be used not only during ventilator use, but also during the recovery period to prevent pneumonia. Therapies include postural drainage, chest percussion, breathing exercises (deep breathing), coughing, chest vibration, and chest mobility exercises (50).

Postural drainage aims to maintain airway patency and prevent respiratory complications. It is accomplished by positioning the chest to promote secretion drainage and to facilitate proper air entry into the lung lobes. With hygiene and nebulization, periodic aspiration, percussion, vibration, and mobilization of secretions can be performed. The chest mobility exercise is an exercise that uses active movements of the extremities in combination with deep breathing. This

is done to increase shoulder and chest wall mobility while facilitating breathing. In some cases, patients with trunk muscle stiffness are unable to optimally expand the chest cavity during breathing. Chest therapy exercises that will stretch these muscles with deep breathing increase airflow and result in improved ventilation. These are necessary to strengthen expiration control. One way to do this is to bring the hip forward and trunk flexion during expiration. This action effectively expands the abdominal viscera and pushes the diaphragm, making expiration easier (51).

Strengthening the respiratory muscles has been proven to increase the isometric pressure produced by the inspiratory muscles (Pi Max). With these physiological principles, patients should be given threshold inspiratory muscle training non-resistance training (52). Involvement of accessory respiratory muscles, tachypnoea, and dyspnoea, and weakening of expiratory muscle strength reduce the cough reflex, reducing its ability to clear bronchial and tracheal secretions, thereby increasing the risk of aspiration (pneumonia). bulbar weakness may impair the patient's ability to maintain the airway. Decreased muscle tone of the tongue and oropharynx predisposes to airway obstruction, especially at night, when the muscle tone of the vocal cords decreases. Meanwhile, due to the weakness of the oropharyngeal muscles, the tongue and facial muscles may prevent the protective reflex and cause aspiration. The progression and pattern of damage to nerve signal transmission also compromise respiratory function. Immediate intubation is required after respiratory muscle weakness reaches a critical point where hypercapnia develops rapidly followed by hypoxia. Sudden hypercapnia may also cause upper airway obstruction due to aspiration, mucus occlusion, or bulbar muscle weakness.

Mechanical ventilation should be initiated after the patient is intubated. The most used ventilation mode in patients with GBS is synchronized intermittent mandatory ventilation (SIMV). Pressure support ventilation is often combined with SIMV to reduce respiratory effort and minimize ventilator synchronization during spontaneous breathing. At the beginning of mechanical ventilation, some patients feel more comfortable with the Assist-control mode. It is important for GBS patients, especially those who need urgent intubation, to rest in the first 24-48-hours. To achieve this goal, breathing should be minimized by providing full mechanical ventilation support. Ventilation arrangements should include adequate support pressure, Positive End-Expiratory Pressure (PEEP) to prevent further atelectasis, lung expansion. Tidal volume of 8-12 ml/kg is common in patients with neuromuscular respiratory failure (53). Regaining optimal respiratory function is a priority in GBS. Despite advances in respiratory management and immunotherapy, death from GBS is as high as 20% in ventilated patients. Mechanical ventilation is usually required by one-third of patients (54). If respiratory function is improving, it may be preferable to wait 1 more week to try to wean from the ventilator. Vital capacity <60% of predicted or below 20 ml/kg indicates imminent respiratory arrest at maximum inspiratory pressure <30 cm H2O or maximum expiratory pressure <40 cm H2O (55).
The single breath count is a simple clinical point-of-care parameter for monitoring lung function. Respiratory failure in the acute phase has been found to be associated with long-term functional impairment. The main treatment goal in the acute phase is airway clearance support. Then, prevention of pulmonary infections and maintenance of peripheral circulation with various physical techniques, e.g., chest percussion therapy, breathing exercises, restrictive inspiratory exercise and respiratory support for airway and lung clearance. Second, the recovery phase is when patients can maintain their own airways and ventilation. By reducing the dose, breathing exercises and inspiratory muscle training are performed. Third, the long-term rehabilitation phase focuses on airway maintenance and ventilation capacity, with correct instruction-based breathing techniques and effective coughing exercises (56).

b. Electric stimulation

Long-term immobility and denervated muscles will have atrophy and motor dysfunction, which will result in long-term contractures, weakness, and loss of strength (53,58). Previous studies have shown that neuromuscular electrical stimulation (NMES) is effective in such critical illness and to prevent muscle wasting (59,60). NMES may not be effective in severe muscle weakness due to conduction failure, in which case direct muscle fibers stimulation (MFS) can be used (61). It is a method that performs muscle contractions without the need for participation using NMES (59,60). In one study, stimulation was initiated with the STIWELL med4 (Otto Bock, Konigsee Germany) device 2 weeks after the onset of symptoms and continued until discharge from the hospital. 20 minutes of MFS and 40 minutes of NMES were applied every weekday. Stimulation intensity was adjusted individually and during the study to the weekly maximum contraction point and as tolerated. As a result, GBS is premature. Appeared to be effective and safe at the time (61). Another well-proven study has training on the effect of NMES on muscles. In addition to traditional treatment methods in acute and subacute excesses of GBS, NMES was applied to the quadriceps muscle for one hour every weekday. This stimulation was initiated on an average of 17 (4-95) sessions and 2 weeks after he showed signs of illness and was continued throughout the hospital Rehabilitation program (participation time 27 days). During the study, each patient lost an average of 3.4 kg of muscle, indicating that they were weak. NMES is a safe treatment in addition to standard treatment and can be applied in the acute and subacute phases of GBS (62).

c. Robotic rehabilitation

Regaining the ability to walk in various neurological diseases is the most important goal of rehabilitation. To regain walking ability, it is necessary to strengthen critical muscles and increase endurance. There are various treatment methods for this, robot-assisted gait training (RAGT) is one of these treatment methods. In various studies, RAGT has shown that it is more advantageous than traditional methods, we can say that patients with severe conditions start gait training, less efforts of physiotherapists, longer and higher intensity gait training, more physiological and repeatable gait patterns, and patient performance measurement (63). In addition, RAGT has positive aerobic effects on cardiopulmonary as demonstrated in other diseases (64). In a study, the latest model RAGT device Morning Walk was used on patients over 19 years old. Patients total 24 sessions and each session lasted 30 minutes. Patients were evaluated before and after treatment. The results showed that RAGT had positive effects on gait in patients with GBS (65).

d. Virtual reality

Latest generation technologies Virtual engine Offers low-cost platforms like Nintendo Wii in rehabilitation. It contains several daily sessions for 6,12,18 months to be effective in GBS. Traditional rehabilitation programs are found boring by patients due to lack of resources and time, which affects their participation in rehabilitation. For this reason, we can make it more exciting and attractive by adding virtual reality to the rehabilitation program. Resources are very limited on this subject and only one study has applied to two GBS patients so far (66). In this study, an additional 30-minute Nintendo Wii balance Board and virtual bit environment tool were added to 30 minutes of traditional Rehabilitation. The number of rehabilitation sessions was 20. The results showed that patients improved their compliance with Rehabilitation. We recommend that the virtual reality be developed in the future to include more and more branches of the rehabilitation program (67).

e. Alternative therapy approaches

Yoga, relaxation, and meditation techniques appeared to improve sleep quality in patients with GBS (68). Yoga has also been shown to influence reducing pain and increasing functional status (69). According to studies conducted to date, there are hypotheses that acupuncture reduces pain, increases muscle strength, improves neurological functions, and improves psychological state in this disease, but there is no evidence-based evaluation. Therefore, a systematic review and meta-analysis could be planned on this subject (70). There's provided evidence that personalized home exercise is acceptable for individuals with GBS and that participation in a telerehabilitation program is associated with significant improvements in activity limitation, fatigue, quality of life, and mood.

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Conclusion

The GBS is disease that comes with a variety of complications and sometimes lifelong lasting disabilities. This is where the role of physiotherapy is very important and crucial. In this review we tried to cover the most recent articles about the role of physiotherapy in the treatment of GBS. We have found a need for high quality randomised controlled trials to be able to support many of the therapy methods. A multidisciplinary approach showed to be a very important aspect when planning an exercises program for the patients. Pulmonary rehabilitation seemed to be lacking a lot of strong evidence articles despite the importance of it specially post ventilation. Robotics, virtual reality, and electrical stimulation are found to be very effective. During the COVID-19 pandemic a connection between the onset of COVID-19 and GBS was found. Some researchers are working on finding the exact connection and others are working on creating the needed rehabilitation program. All of this emphasises on the need for alternative methods like telerehabilitation. It was seen to be effective when patients are given a specific personalised exercises program. Finally, we were able to find how important the role of physiotherapy is in the treatment of the disease, and we hope this could be the reason more research is done on the topic (71).

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