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Neuropathies - Guillain-Barré syndrome: rehabilitation

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DESCRIPTION OF THE EVIDENCE COLLECTION METHODOLOGY

Articles in the MedLine (PubMed) database and other research sources were reviewed, with no age limit.

The search strategy used was based on structured questions in the P.I.C.O. format (from the initials: Patient, Intervention, Control and Outcome). The descriptors used were: Exercise, Physical OR Physical Exercise OR Physical Exercises OR prevention and control OR preventive therapy OR preventive measures OR prophylaxis OR preventions OR control OR Guillain-Barre Syndrome OR Syndrome, Guillain-Barre OR Guillaine-Barre Syndrome OR GuillaineBarre Syndrome OR Syndrome, GuillainBarre OR Polyneuropathy, Acute Inflammatory OR Acute Autoimmune Neuropathy OR Acute Autoimmune Neuropathies OR Plasmaphereses OR Plasmapheresis OR Plasma Exchange OR Immunoglobulins/therapeutic use OR Immunoglobulins/ administration and dosage OR Exercise Therapy OR Physical Therapy OR Physical Therapies OR Exercise therapies OR Resistant Training OR Strength Training OR rehabilitation OR Splints OR Splint OR Orthopedic Fixation Devices OR Orthotic Devices OR device orthotic OR devices orthotic OR Orthoses OR Orthosis OR Upper Extremity OR Upper Extremities OR Upper Limb OR Upper limbs OR Membrum Superius OR Extremities, Upper OR Limb, Upper OR Limbs, Upper OR hand deformities OR Hand Deformities, acquired OR Rehabilitation OR Lower Extremity OR Extremities, Lower OR Lower Extremities OR Lower Limb OR Limb, Lower OR Lower Limbs OR Membrum Inferius OR Walking OR Ambulation OR dependent ambulation OR Ambulation, Dependent OR gait OR gaits OR Functional Electrical Stimulation OR Electrical Stimulation, Functional OR Fes OR Electric Stimulation Therapy OR Stimulation Therapy, Electric OR Therapeutic Electrical Stimulation OR Electrical Stimulation, Therapeutic OR Stimulation, Therapeutic Electrical OR Therapy, Electric Stimulation OR Therapeutic Electric Stimulation OR Electric Stimulation, Therapeutic OR Stimulation, Therapeutic Electric OR Electrical Stimulation Therapy OR Stimulation Therapy, Electrical OR Therapy, Electrical Stimulation OR Self-help devices OR Self-help device OR Device, Self-Help device OR Assistive Technology OR Assistive Technologies OR Technologies, Assistive OR Technology, Assistive OR Assistive Devices OR Assistive Device OR Device, Assistive OR Devices, Assistive OR daily activities OR daily activity OR activity of daily living OR activities of daily living OR activities of self care OR activity of self care OR usual activities OR usual activity OR usual activity of daily living OR usual activities of daily living OR Patient Positioning OR Patient Positionings OR Positioning, Patient OR Positionings, Patient OR pressure ulcer OR pressure ulcer/prevention & control OR Guillain-Barre OR Guillain-Barre Syndrome/therapy* OR Guillain-Barre Syndrome/rehabilitation* OR Nursing care OR Pressure Ulcer OR Pressure Ulcers OR Pressure Sore OR Pressure Sores OR Decubitus ulcer OR Bed sore OR Bedsore OR Weaning Mechanical Ventilation OR Extubation OR Mechanical Ventilation Predictors OR Weaning Mechanical Ventilator Predictors OR Extubation Predictors.

QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS:

A: Experimental or observational studies of highest quality.
B: Experimental or observational studies of lower quality.
C: Case studies (uncontrolled studies).
D: Opinion with no critical evaluation, based on consensus; physiological studies, or animal models.

OBJECTIVE:

To provide information about the treatment and reabilitation of patients with dystonias.

PROCEDURES:

Therapeutic rehabilitation interventions for the main clinical manifestations that compromise the quality of life, function, and daily life activities of patients with dystonia.

CONFLICT OF INTEREST:

The authors have no conflicts of interest to declare.

INTRODUCTION

Guillain-Barré syndrome (GBS) is one of the most frequent subtypes of acute peripheral polyneuropathy[1] **(A)**. It affects 2 people per 100,000 annually, at random. There is evidence of a higher incidence of the disease among males and people aged 50-74 years, however it can affect individuals of any sex, age, or race[2] **(C)**. From 4% to 15% of

patients with GBS die during treatment and approximately 20% are left with disability[1] **(A)**.

Acute acquired GBS inflammation leads to demyelination of the peripheral nerves, then to motor weakness and sensory changes. Its cause has not yet been identified, however there has been observed in some patients a relationship with acute illness caused by bacteria or virus. Among the most common infectious agents which precede GBS are found cytomegalovirus, Campylobacter Jejuni, and the Epstein-Barr vírus, among others[2] **(C)**. Although uncommon, some hepatotrophic viruses (hepatitis A, B, C) have been recognized as potential agents for the development of GBS[3] **(D)**. In such cases GBS usually occurs 1 to 3 weeks after the infectious event. The clinical course is characterized by progressive, symmetrical ascending motor loss (from lower to upper extremities) and hyporeflexia or areflexia, with compromising of the cranial nerve[2] (**C**). The progression of motor weakness occurs quickly. The acute phase begins with the first symptoms and lasts until the stabilization of demyelination, which can take days or even weeks. After this period begins the recovery phase, which can last for about two years and coincides with the regeneration and remyelination of axons[4] **(C)**. There are two main types of GBS: acute inflammatory demyelinating polyneuropathy (AIDP), which affects the myelin sheath, and acute motor axonal neuropathy (AMAN), known to be purely motor[1] **(A)**.

Therapies commonly used to treat GBS in their acute phase are plasmapheresis (PE) and intravenous immunoglobulin (IVIg). PE consists of performing dialysis in which the patient's blood is processed by a machine that separates and removes antibodies from the patient and replaces them with a fluid containing 5% albumin. In IVIg treatment, the method considered safer and more widely used, an array of antibodies with normal serology is applied intravenously in patients with GBS[4] **(C)**.

Common symptoms in the acute phase of GBS are: muscle weakness, paralysis, numbness, tingling, pain that starts in the legs and reaches the entire body, and diminished reflexes. The weakness in the trunk and the upper limbs can reach the muscles required for respiration and necessitate mechanical ventilation in about 25% of cases. Involvement of the autonomic system is frequent and may cause urine retention, tachycardia, hypertension, orthostatic hypotension and cardiac arrhythmia[1] **(A)**. Other complications associated with the acute phase of Guillain-Barré syndrome are insomnia, formation of pressure sores, difficulty communicating, nutritional deficiency, immobility, and venous thrombosis[2] **(C)**.

Studies show that treatment of GBS should be performed by a multidisciplinary team, providing symptom management and prevention of complications during the acute phase of the disease[1] **(A)**. Physical rehabilitation is required in 40% of GBS cases; action by the interdisciplinary team is essential to minimize consequences and promote the independence and autonomy of patients[5] **(D)**.

1. Which strategy is most effective in the treatment of acute-phase Guillain-Barré syndrome, treatment with plasmapheresis (PE) or administration of intravenous immunoglobulin (IVIG)?

When plasmapheresis (PE) is used in 5 sessions of plasma exchange of 50 ml/kg in an adult population with Guillain-Barré syndrome (GBS) without pre-existing disease, results are similar to intravenous immunoglobulin therapy (IVIg) with 0.4 g/kg of human immunoglobulin for 5 days. There are no statistical differences in the results of the two therapies, either in the improvement in degree of disability during a 4 week period and the pattern of functional recovery, or the time to recovery of independent walking (average days to return to walking without support was 49 days for patients who underwent PE and 51 days for patients who were treated with IVIg). The time required to discontinue mechanical ventilation in patients who need this type of resource is also similar (average of 29 days for individuals treated with PE compared with 26 days for those undergoing IVIg). The number of deaths during both therapies is comparable, about 1.7% among those who underwent PE and 2.3% for patients treated with IVIg (with Relative Risk Reduction (RRR) -35%, Absolute Risk Reduction (ARR) -0.006, and Confidence Interval (CI) 95%).

Complications that can be observed with the use of PE are: hypotension, sepsis, pneumonia, malaise, abnormal clotting, hypocalcemia. During the application of IVIg, náusea, vomiting, meningism, deteriorating renal function, myocardial infarction and possible painful erythema in the region of the infusion may occur. The combination of PE followed by IVIg (5 sessions of plasma exchange, 50 ml/kg, followed by 5 daily applications of 0.4 g/kg of Sandoglobulin starting soon after the last day of PE), also shows results similar to those cited above[6] **(A)**.

The application of IVIg at a dosage of 0.5 g/kg in 4 daily doses when compared with PE therapy (200 to 250 ml/kg in 5 sessions distributed in a 7-10 day interval using the techniques of centrifugation or cell membrane separation) also shows similar results in motor function recovery 1 month from the beginning of treatment. The average time to improvement of a degree of motor function using a specific disability grade scale shows little difference in favor of the use of the PE (16.5 days to 14.0 days when using IVIg); patients treated with PE have on average 1 point more than those undergoing IVIg. Regarding complications related to both therapies it is possible to observe: hypotension, cardiac arrhythmia, pneumonia, deep vein thrombosis/pulmonary embolism, sepsis, local phlebitis and infections of the urinary tract. There is a tendency for a lower incidence of these complications in favor of IVIg ($p = 0.07$)[7] **(B)**.

When comparing PE (200 to 250 ml/kg in 5 sessions conducted between 7 to 14 days with replacement fluid containing 5% albumin and no IgG, using two management techniques: centrifugation, and ultrafiltration) and the application of IVIg (5 daily sessions of 0.4 ml/kg), there are favorable results using IVIg: improved levels of functional capacity during the first 4 weeks following initiation of treatment, about 53% of those treated with IVIg compared to 34% of patients who underwent PE, with $p = 0.024$. The average number of days required to restore independent walking is also favorable for IVIg therapy, 55 days *versus* 69 days for PE, with $p = 0.07$. The complications observed most in both groups are: pneumonia, atelectasis, thrombosis and hemodynamic changes. There are a greater number of such events in patients treated with PE, similarly, a greater proportion of subjects required mechanical ventilation in this population (48% PE *versus* 27% of patients treated with IVIg, $p < 0.05$)[8] **(A)**.

With GBS patients for whom PE is contraindicated (due to uncontrolled sepsis, severe changes in homeostasis, hemodynamic instability), the use of IVIg at a dose of 0.4 g/kg for 12 hours daily for a 6 day period is shown to be more effective than the same dose of IVIg administered for 3 days. PE has the lowest average number of days to recover walking function (84 days to walking with assistance, compared

to 131 days for patients treated with IVIg for 3 days, and 97 *versus* 152 days on average to achieve independent walking, respectively $p = 0.39$). This positive tendency in the application of IVIg for six days also occurs when evaluating the functional improvement in a 4 week period using a specific scale for measuring function in Guillain-Barré syndrome (44% *versus* 22%, $p = 0.27$)[9] **(A)**.

Recommendation

Efficacy is similar with the application of plasmapheresis therapy (PE) in 5 daily sessions of plasma exchange of 50 ml/kg, and intravenous immunoglobulin (IVIg) therapy at a dose of 0.4 g/kg human immunoglobulin for 5 days, in adult patients with Guillain-Barré syndrome (GBS) without pre-existing illness or conditions contraindicating the procedures. This relates to functional improvement in 4 weeks, the time to recovery of independent walking, mortality rate, and the duration of mechanical ventilation in patients who require this resource. The combination of PE and IVIg (5 sessions of plasma exchange, 50 ml/kg, followed by 5 daily applications of 0.4 g/kg of Sandoglobulin starting soon after the last day of PE) brings no greater benefits than treatment with PE or IVIg alone[6] **(A)**.

The results remain similar between plasmapheresis and IVIg when using the following dosages: 200-250 ml/kg in 5 sessions distributed over a 7 to 10 day interval, using the techniques of separation or centrifugation of the cell membrane and 4 doses of 0.5 g/kg for 4 consecutive days, respectively. However, IVIg has shown to be slightly safer compared to PE with regard to complications during treatment[7] **(B)**.

However, IVIg therapy (administration of 0.4 ml/kg in 5 daily sessions) is more effective than treatment with PE (200 to 250 ml/kg in 5 sessions conducted between 7 to 14 days, with fluid containing 5% albumin and no IgG, prepared using ultrafiltration and centrifugation techniques), with respect to functional recovery during a 4-week period, and the safety of treatment due to fewer complications and less need for mechanical ventilation[8] **(A)**.

For patients who have contraindications to PE due to uncontrolled sepsis, severe alterations of homeostasis, or hemodynamic instability, therapy with IVIg (0.4 g/kg over 12 hours, daily, for 6 days) is effective and has better results both for functional recovery in 4 weeks and for independent walking than the same protocol lowered to 3 days of application. The occurrence of adverse reactions are similar in the two forms of treatment[9] **(A)**.

2. Which techniques for stimulating active movement and strengthening are indicated for improved function and decreasing long-term disability in patients with Guillain-Barré syndrome?

Results from low and high intensity physical rehabilitation programs were compared. Patients were adults with Guillain-Barré syndrome (GBS) considered chronic, with more than three years since onset of acute symptom diagnosis, and who had not participated in rehabilitative activity within the previous 24 months. The high intensity program was developed on an individualized basis following clinical assessment, consisting of one-hour sessions up to 3 times per week. The sessions were conducted over 12 weeks, organized in 30-minute blocks of occupational therapy, physiotherapy, psychology and speech-language pathology. Physiotherapy worked on strengthening, endurance and gait training, and occupational therapy sought to improve performance in ADL, driving and work. For the low-intensity programs, home-based consults were developed, with maintenance exercises (walking and stretching) and education for self-care in 30-minute sessions twice a week. To analyze the results obtained with this intervention the following scales were used: FIM (Functional Independence Measure), World Health Organization Quality of Life (WHOQoL-BREF), Depression, Anxiety, and Stress Scale (DASS), and the PIPP tool (Perceived Impact of Problem Profile (PIPP)[10] **(A)**.

After 12 weeks of treatment, 68.6% of patients who received the high intensity rehabilitation program showed functional improvement, *versus* 32.4% in the low intensity group. A larger number of subjects reported deterioration of function in the group that underwent the low intensity program (41.2%, *versus* 2.9% of the patients who received the intensive rehabilitation treatment, $p < 0.001$). Of the patients in the latter group, 80% improved 3 points on the FIM scale compared to 8% of the individuals in the low intensity program. In the areas of self-care and mobility, the high intensity treatment group showed improvement of 54.8% and 41.9% respectively, (*versus* 5.3% and 2.6% in the low intensity group). This positive difference for individuals in the more intense program of rehabilitation was also perceived, although to a milder degree, in the skills of walking and bowel control[10] **(A)**.

There was no significant change in the scores derived from the application of the DASS, WHO-QoL and PIPP in both groups, except for the subscale of relationships in the PIPP[10] **(A)**.

Recommendation

In adult patients with chronic Guillain-Barré syndrome (GBS) with more than 3 years elapsed since onset of acute phase symptoms, and with no participation in rehabilitative activity within the previous 24 months, the development of a multidisciplinary rehabilitation program promotes improved motor function and performance of Activities of Daily Living, increases scores of Functional Independence Measure (FIM), and prevents the deterioration of functional capacity. This program consists of sessions of occupational therapy (performance improvement in the ADL, driving and work), physiotherapy (strengthening, muscle endurance and gait training), psychology and speech-language pathology. These sessions should be scheduled 2 to 3 times per week in blocks of 2 sessions per day, 30 minutes per session for 12 weeks[10] **(A)**.

3. Does the use of orthoses for positioning wrist and fingers in patients with Guillain-Barré syndrome prevent deformity and contribute to improved function?

Orthoses, by definition, are devices used in the upper limbs (UL) and lower limbs (LL) that exert external forces to that segment. They may have the goal of stabilizing and/or promoting rest for anatomical structures, maintaining bone alignment, preventing deformities and contractures, preventing unwanted movement, increasing range of motion, promoting stretching in muscle and the soft tissues of the musculoskeletal system, replacing the function of lost or damaged muscle, relieving pain, restoring function and/or assisting in the management of healing {or trauma, or injury}. Thus orthotics can help treat orthopedic, neurological, and rheumatological patients, among others. In practice, orthoses available to the public may

be prefabricated of high temperature thermoformable materials, or tailor-made, usually from thermoplastic molded at low temperatures[11] **(D)**.

There is no specific type of orthesis to be used, but their end purpose is the same in acute phase Guillain-Barré syndrome: to promote neutral joint positioning as a preventive and/or corrective measure to muscle contractures for the ankle and foot or the wrist and fingers. This approach seeks to reduce the consequences of loss of muscle strength inherent in Guillain-Barré syndrome and promote the adequate maintenance of structures to optimize patient rehabilitation[12] **(D)**.

Recommendation

There is no evidence to certify the use of ortheses in upper limbs of patients with Guillain-Barré syndrome (GBS). This resource, by placing the joint in a neutral position, helps prevent deformities and/or muscle shortening in order to optimize the process of rehabilitation, since GBS patients commonly remain confined to bed for weeks and have significant symptomatic loss of muscle strength. Undoubtedly, there is a need to develop studies that provide further evidence for recommending orthoses in this population[11,12] **(D)**.

4. Do lower limb orthoses for Guillain-Barré syndrome patients aid in walking and contribute to improved function?

The use of ortheses to stabilize the foot and ankle in patients who present "foot drop" symptoms aims to improve the function of the musculoskeletal system. This is a common condition for patients with Guillain-Barré syndrome (GBS) which can be enhanced with the use of orthesis to provide dorsiflexion support, externally applied to the ankle and foot, improving gait function[13] **(D)**. The use of orthosis is aimed at maintaining foot and ankle articulation in a neutral position, ensuring the prevention and/or correction of muscle contractures and deformities[12] **(D)**.

Recommendation

There are no studies that provide scientific evidence to support the practice of indicating lower limb ortheses for patients with Guillain-Barré syndrome during rehabilitation programs. In the patient population with GBS, gait function is impaired by the presence of motor weakness in the lower limbs and the presence of "foot drop" is a common symptom. Use of ortheses applied externally to the foot and ankle in a manner that promotes dorsiflexion shows benefits like improved gait function, prevention and/or correction of contractures and deformities, as well as increased independence[12,13] (**D**).

5. Does use of assistive and adaptive technology improve functional performance in patients with Guillain-Barré syndrome?

Assistive technology is characterized by engaging resources, strategies, methodologies, and practices to promote the functional capacity and participation of people with disabilities seeking autonomy, quality of life and social inclusion. It includes both the physical technology, i.e. the object and the equipment itself, as well as the theoretical technology or knowledge that is required to evaluate, create, select and prescribe these devices. Adaptive and assistive equipment are classified in different categories: the Activities of Daily Living, Alternative Communication Systems, Environmental Control Units, Home Environment, Computers, Wheelchairs & Mobility Devices, and Vehicle Adaptations, among others[14] **(D)**.

To the extent that patients with Guillain-Barré syndrome undergo a period of motor weakness that can range from weeks to months, with hyporeflexia or areflexia, they experience disability in different areas of daily life. About 20% of this population will have some type of disability one year after disease onset, and even with those who have a good recovery of motor function during this period residual weakness and muscle fatigue is common[1] **(A)**.

Recommendation

There is no scientific evidence that the use of assistive and adaptive technologies can improve functional performance of patients with Guillain-Barré syndrome (GBS). However, recognizing that patients with GBS experience incapacity in several areas of their lives and that a percentage of subjects will be left with some type of disability, the use of adaptive and assistive technology can contribute to greater independence, autonomy and social inclusion for this patient population[14] **(D)**. We emphasize the importance of further scientific studies in this area.

6. Are stretching and passive mobilization approaches effective for the prevention of contracture and promoting functional improvement in patients with acute-phase Guillain-Barré syndrome?

Patients with Guillain Barré syndrome (GBS) in its acute phase experience a prolonged period of immobilization that can cause complications and impair patient recovery and rehabilitation. Among the symptoms that can manifest during this acute phase of the illness and hospitalization are postural hypotension, increased levels of *serum calcium*, pressure ulcers, compression of nerves, and heterotopic calcification with an increase in the level of calcium. Early mobilization of the patient allows *serum calcium* levels to decrease and prevents hypercalcemia caused by immobility[5] **(C)**.

The immobility experienced by GBS patients due to paralysis and muscle weakness also puts them at risk for developing deep vein thrombosis. Among the preventive treatments, passive mobilization has been used to reduce the incidence of deep venous thrombosis in this population. Regular physiotherapy, including passive mobilization exercises, also helps in preventing contractures and, coupled with isometric and isotonic exercises, promotes a reduction in loss of muscle strength in patients with acute-phase GBS[2] **(C)**.

There are few studies showing scientific evidence to support the practices and methods in the area of multidisciplinary rehabilitation. The studies are more oriented toward individual and institutional experiences. However, rehabilitation has shown to be as important as pharmacological medical treatment[1] **(A)**.

Recommendation

There is little scientific evidence to indicate the use and certify the benefits of stretching exercises and passive mobilization in patients with Guillain-Barré syndrome during its acute phase, whether to prevent deformities or to improve motor function. However, in practice, the approach of early passive joint mobilization with isometric and isotonic exercises helps both in the prevention

of contractures and deformities, such as complications related to immobility and loss of strength, and maintenance of muscle trophism. Developing studies with greater scientific evidence is necessary[1,2,5] **(C).**

7. Is the use of carbamazepine and gabapentin indicated for the management of pain in patients with acute-phase Guillain-Barré syndrome? Is there a better result with one drug compared to the other?

Carbamazepine (3 days of treatment, 100 mg every 8 hours through the feeding tube) was compared to placebo in controlling pain in patients in the recovery phase of Guillain-Barré syndrome (GBS) under mechanical ventilation in the Intensive Care Unit. At the end of therapy, a moderate reduction in the need for analgesic use of intravenous pethidine (0.5-1 mg/kg) was obtained, with an average consumption of 1.1 ± 1.0 mg/kg/day during use of carbamazepine, *versus* 3.7 ± 0.9 mg/kg/day of individuals who received placebo, with $p < 0.001$. Scoring pain on a scale (0-10, ten being the worst pain level), there is a perceptible decrease in pain intensity over the period of use with carbamazepine, 1.7 ± 0.8, compared to the use of placebo 3.1 ± 0.9, $p < 0.001$. The score for sedation of patients on carbamazepine was also better compared to the placebo, 2.3 ± 0.9 *versus* 4.2 ± 0.9 respectively, $p < 0.001$. There were no significant side effects observed. Supportive therapies were continued during treatment with carbamazepine, such as enteral nutrition, antibiotic coverage to prevent infections, respiratory physiotherapy, motor physical therapy, protecting the digestive tract, venous thrombosis prophylaxis, sedation overnight to maintain sleep patterns[15] **(A).**

The use of gabapentin in 3 divided doses of 15 mg/kg/day for 7 days dissolved in 5 ml of water and administered through Ryle tube was able to reduce the average pain score from 7.22 ± 0.83 at baseline to 06.02 ± 0.63, $p < 0.001$, compared to placebo. Although there was also a decrease in this score when using placebo, it was not significant. The need for analgesic, evaluated from the amount consumed, also significantly decreased during application of gabapentin, dropping from 211.11 ± 21.38 (μg) on the first day to 65.55 ± 16.17 (μg) at the end of the treatment period, with $p < 0.001$. With placebo, there was no significant change in analgesic consumption, 319.44 ± 25.08 (μg) on the first day and 316.67 ± 24.25 (μg) at the end of 7 days. Patients undergoing application of gabapentin, on average, went from the level of anxious and agitated to oriented and cooperative or responding to commands on the Ramsay Scale of sedation level (1.38 ± 0.5 to 0.5 ± 2:44 at the end of treatment). However with the placebo, the subjects passed from a state of agitation to decreased consciousness, a fall of 1.44 ± 0.51 to 3.63 ± 0.5 on the Ramsay Scale. Few side effects were reported with the use of gabapentin compared to the application of placebo, suggesting a causal relationship with fentanyl, which was used in higher doses as a rescue analgesic in the placebo subjects, and was probably responsible for nausea and constipation in these patients[16] **(A).**

Comparison of the results of the use of carbamazepine in 3 daily doses of 100 mg for 1 week and gabapentin 300 mg in 3 daily doses for 7 days (dissolved in 10 mL of water delivered through Ryle tube), with a control group that used placebo showed: significant reduction in the average score on the numeric pain scale (where 10 is the maximum intensity of pain) from 8.0 to 2.0 with the use of gabapentin, and from 8.0 to 3.0 with carbamazepine, with $p < 0.05$, while the control group was reduced from 8.0 to 6.0 with no statistical significance. Regarding the average Ramsay Score for sedation level, the use of gabapentin and carbamazepine provided lower rates of sedation compared to the placebo group, with $p < 0.05$, with final averages of (2.0, 3.0, 4.0, respectively). As for average daily need for application of analgesic, use of fentanyl IV (2μg) decreased both with the use of the medications and with placebo. However, at the end of treatment a higher average daily amount of analgesic was used in patients who received placebo (350.7 ± 34.2) $p < 0.05$ compared to the groups on gabapentin, 126.0 ± 26.2 and carbamazepine 174.5 ± 30.0. The patients showed no side effects during treatment[17] **(A).**

Recommendation

The use of carbamazepine (100 mg every 8 hours administered by enteral feeding dissolved in 10 mL of water) and the use of the anticonvulsant gabapentin (3 divided doses of 15 mg/kg/day for 7 days administered via Ryle tube dissolved in 5 mL of water) are effective in the treatment of pain in adult patients with Guillain-Barré syndrome in ICU making use of mechanical ventilation. Both are effective in reducing the average intensity of pain and the use of analgesics, and also improve the level of sedation[15,16] **(A)**. In addition, gabapentin applied in a dosage of 300 mg 3 times daily for one week proves more effective in comparison to carbamazepine, 100 mg in 3 daily doses during the same period (each dissolved in 10 mL of water delivered through Ryle tube), not only reducing pain intensity on a numeric scale, but also the need for analgesic medication use, as well as improving sedation levels in these patients[17] **(A)**.

8. Is changing decubitus position of the Guillain-Barré syndrome patient during the acute phase effective in preventing development of pressure ulcers?

The patient with Guillain-Barré syndrome (GBS), during the acute phase of the disease experiences progressive motor weakness, mostly with an ascending and symmetrical pattern. Among the symptoms are: muscle weakness, numbness, tingling and pain. As a consequence of partial or complete paralysis and a state of poor nutrition (due to complications that affect the feeding of individuals in this situation, such as dysphagia and loss of active movement), the skin integrity of these patients becomes quite vulnerable to injury. Among the measures employed to maintain the integrity of the skin, the following are indicated: frequently changing decubitus and positioning (every 30 minutes), applying lotions on bony prominences, massage, performing movement and passive exercises, as well as maintaining the patient's skin dry and using sheets without wrinkles. Air mattresses, special beds, and pillows for heels and elbows are also useful to prevent the formation of pressure ulcers[2] **(C)**.

It is necessary to involve the interaction of different professionals on the team to prevent the formation of pressure ulcers in the acute phase of GBS. Frequent change of decubitus added to the assessment of skin condition is recommended, as well as passive motion exercises performed by therapists or by caregivers[18] **(C)**.

It is also necessary from the outset of treatment and hospitalization to encourage the patient to change his position frequently. When immobility is present, it is necessary to train family members and caregivers on how to perform these maneuvers for

postural changes of the patient. A schedule of posture changes may be placed near the bed in view of the patient and family to facilitate their execution. Special beds can also help prevent ulcers[19] **(C)**.

Recommendation

The frequent change of decubitus, every 30 minutes, is indicated as the primary method to prevent the formation of pressure ulcers in patients with Guillain-Barré[2,18] **(C)**. However, more scientific studies are needed with greater evidence to evaluate and prove the utility of position change in this population, as well as to verify the use of equipment and other resources for prevention and treatment of skin ulcers, such as special beds, the use of specific skin hydrating creams, massage, air mattresses and pillows[2,19] **(C)**.

9. What are the predictive factors for the need of mechanical ventilation and success in the weaning process in Guillain-Barré patients?

To predict and assess the need to use mechanical ventilation support for prolonged periods in patients with Guillain-Barré syndrome (GBS) with acute respiratory failure, it was observed that of 61 individuals admitted to the Intensive Care Unit (ICU) from 1996 to 2009, 65.57% of the patients required mechanical ventilation with an average duration of 24 days. Of these, 70% underwent tracheostomy, with an average of 14 days between tracheal intubation and tracheostomy procedure. Patients who underwent mechanical ventilation had higher scores on specific tests of disease severity (Simplified Acute Physiologic Score II-SAPS II) compared to those who did not need it, scoring 28.2 ± 18.6 and 14.1 ± 6.8 respectively, $p = 0.0052$. The glycemic index was significantly higher among those who required respiratory support, 8.07 on average *versus* 6.51 mmol/L, $p < 0.01$. About 60% of mechanically ventilated patients showed autonomic dysfunction compared with 14% of those non-ventilated, $p = 0.0006$. Through a multiple logistic regression model, it was found that the risk of needing mechanical ventilation increased significantly when the individual with GBS exhibited at least one sign of cardiovascular autonomic dysfunction and inability to actively raise the head when lying down (odds ratio 10.66, 95% confidence interval [CI] 2.4 to 49, $p < 0.05$, and 9.86, 95% CI 1.7 to 56, $p < 0.05$, respectively)[20] **(B)**.

Regarding factors that may help determine the need for prolonged mechanical ventilation, there was a lower rate of vital capacity (VC) between those who required ventilatory support for more than 15 days on admission to the ICU, 46% *versus* 63% among patients with a ventilation period < 15 days, $p < 0.01$. The plasma sodium concentration was found to be significantly decreased in patients ventilated for longer than 15 days ($p < 0.05$), and the ability to flex the foot was frequently absent in these subjects, 64.2% *versus* 33.3% of patients who required ventilation for a shorter period $p < 0.004$. This difference remained after the application of immunotherapy 82.1% compared to 41.6%, respectively, $p = 0.001$. With the end of immunotherapy treatment differences were observed in the presence of nerve conduction block also. By analyzing these data, it was determined that the combination of lack of standing flexion at admission to ICU and at the end of immunotherapy treatment, with the presence of sciatic nerve motor conduction block with a sensitivity of 56%, has a positive predictive value of 100% for the need for greater duration of mechanical ventilation, $p < 0.001$[20] **(B)**.

As to the factors that predict the success of weaning from intubation in this population, 44 patients with GBS undergoing mechanical ventilation with assisted or intermittent control were evaluated. Of these, 31.8% underwent successful extubation, in 13.6% weaning failed and 45.5% of the subjects underwent tracheotomy without weaning trials. There was no significant difference between patients who had successful extubation and the others in relation to demographic and clinical characteristics. The hospitalization time was longer among patients whose weaning failed or who underwent tracheostomy (21.5 ± 11.1 days *vs.* 12.5 ± 8.7 days in subjects with successful extubation, $p = 0.005$). In the patient group analyzed, the following factors demonstrate power in predicting and facilitating the evaluation of the optimal time for weaning from mechanical ventilation: on the day of weaning from intubation, a VC (Vital Capacity) index equal to or greater than 20 ml/kg (with 70% positive predictive value for successful extubation), the reduction of negative inspiratory force reaching approximately -50.0 cm H_2O, the improvement in CV such that it reaches the previous index measured at the time of intubation or increases 4 ml/Kg between the time of pre-intubation and extubation, and the absence of pulmonary comorbidities. Although it has not shown statistical significance, another factor that should also be considered in both intubation and in the weaning process is the presence of autonomic dysfunction[21] **(B)**.

Recommendation

The presence of at least one sign of cardiovascular autonomic dysfunction and the inability to actively raise the head when lying down are predictors of mechanical ventilation in patients with Guillain-Barré syndrome (odds ratio 10.66, 95% confidence interval [CI] 2.4 to 49, $p < 0.05$ and 9.86, 95% CI 1.7 to 56, $p < 0.05$, respectively[20] **(B)**. To predict the need for mechanical ventilation over a prolonged period, it is recommended that the combination of the absence of standing flexion on admission to ICU and at the end of immunotherapy treatment, with the presence of sciatic nerve conduction block (with sensitivity of 56%, positive predictive value of 100%, $p < 0.001$) be considered[20] **(B)**. With respect to weaning from intubation, it is important to consider a Vital Capacity (VC) index equal to or greater than 20 ml/kg at the time of the procedure, reduced negative inspiratory force reaching approximately -50.0 cm H_2O, the improvement in CV such that it reaches the index measured previous to intubation, or increases 4 ml/Kg between the time of pre-intubation and extubation and/or the absence of pulmonary co-morbidities[21] **(B)**.

10. Is the application of functional electrical stimulation (FES) in upper or lower limbs indicated to promote active movement and increase strength in patients with Guillain-Barré syndrome?

There are no articles that address the use of the application of Functional Electrical Stimulation (FES) in the population with Guillain-Barré syndrome or acute polyneuropathies, during rehabilitation and functional recovery.

Recommendation

There is no evidence to support the use of Functional Electrical Stimulation (FES) applied to higher or lower limb muscles in patients with Guillain-Barré syndrome. FES is a widely used resource in the rehabilitation of patients with neurological injuries, thus it is necessary to develop studies in this area **(D)**.

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