Supportive Care for Patients With Guillain-Barré Syndrome

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A multidisciplinary consensus group searched MEDLINE from 1966 to May 2003, extracted relevant references, and prepared recommendations on supportive care for Guillain-Barré syndrome. In the absence of randomized controlled trials, we agreed on recommendations by consensus based on observational studies and expert opinion. In the acute phase in bed-bound adult patients, the group recommended the use of heparin and graduated pressure stockings to prevent deep vein thrombosis, monitoring for blood pressure, pulse, autonomic disturbances, and respiratory failure, and the timely institution of artificial ventilation and tracheostomy. Pain management is difficult, but carbamazepine or gabapentin may help. The cautious use of narcotic analgesics may be needed. Disabled patients should be treated by a multidisciplinary rehabilitation team and should receive an assistive exercise program. Persistent fatigue following Guillain-Barré syndrome is common and may be helped by an exercise program. Because of a very small and possibly only theoretical increase in the risk of recurrence following immunization, the need for immunization should be reviewed on an individual basis. More research is needed to identify optimal methods for all aspects of supportive care.

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A recent practice parameter recommended either intravenous immunoglobulin or plasma exchange, but not corticosteroids, as appropriate treatments for adults and probably children with severe Guillain-Barré syndrome (GBS) within 2 weeks from onset.1 Most patients in the trials of these treatments have had the demyelinating form of the disease, and the benefits of treatment in uncommon subgroups, such as those with axonal disease, cannot be distinguished. Despite immunotherapy, 4% to 15% of patients with GBS die from this syndrome2-6 and nearly 20% have a persistent disability.7 Death from GBS occurs mostly in mechanically ventilated patients. Supportive care remains the mainstay of treatment, but the evidence for the methods of supportive care is inadequate and consensus guidelines for treatment have not been published.

EVIDENCE REVIEW

The consensus group of 6 neurologists with a special interest in GBS, 1 physical medicine specialist, 1 evidence-based medicine specialist, and 1 patient advocate met and decided which questions to review.

We searched MEDLINE from 1966 onward (last search in May 2003) for articles including the term polyradiculoneuritis, limited by human and cross-referenced with the terms therapy, pain, nutrition, diet, pulmonary ventilation, tracheostomy, artificial respiration, autonomic nervous system, dysautonomia, arrhythmia, neurogenic bladder,

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urinary incontinence, urination disorders, constipation, physical therapy, occupational therapy, palliative care, supportive care, thrombophlebitis, immunization, and recurrence. We also searched the Cochrane Library register of randomized trials (issue 3, 2003) with Guillain-Barré syndrome as the search term. Two members of the group prepared draft statements and recommendations that were circulated through the entire group repeatedly until consensus was achieved. Our recommendations are, therefore, consensus statements based on observational studies of GBS, inferences from randomized controlled trials in other conditions, and expert opinion.

**PROPHYLAXIS FOR DEEP VEIN THROMBOSIS**

Immobilization owing to GBS is a risk factor for the development of deep vein thrombosis (DVT). Time to developing DVT or pulmonary embolus varies from 4 to 67 days after onset. Children have a very low incidence of DVT. There is a lack of clinical studies that address methods of prophylaxis against thrombosis in GBS, duration of prophylaxis, or monitoring of patients at risk for thrombosis. Observational studies in orthopedic or general surgery patients suggest a benefit from subcutaneous heparin (5000 U, 12-hourly) in preventing DVT. In acutely ill medical patients, prophylactic treatment with subcutaneous enoxaparin (40 mg daily) reduced the incidence of DVT from 15% in the placebo group to approximately 5% in the treated patients. In a recent meta-analysis, support stockings reduced the risk by almost 70% in patients at moderate risk for development of postoperative thromboembolism.

**RECOMMENDATION**

Subcutaneous unfractionated or fractionated heparin and support stockings are recommended for nonambulant adult patients until they become able to walk independently.

**CARDIAC AND HEMODYNAMIC MONITORING**

Serious and potentially fatal disturbances of autonomic function, including arrhythmias and extreme hypertension or hypotension, occur in approximately 20% of patients with GBS. Severe bradycardia may be preceded by wide swings, exceeding 85 mm Hg, of systolic blood pressure from day to day. Bradycardia may be so severe as to cause asystole, which may require a cardiac pacemaker. Endotracheal suction or pharmaceutical agents may provoke these changes. Other significant autonomic disturbances in GBS are adynamic ileus, hypotension, and deficiencies in bronchial mucosal function. Most, but not all, dysautonomic complications occur among patients with advanced generalized weakness and respiratory failure. In 1 prospective study, a reduction in beat-to-beat variation in heart rate predicted subsequent dysautonomia.

**RECOMMENDATION**

Monitoring of pulse and blood pressure is recommended in patients who are becoming severely affected by GBS until they have discontinued the ventilatory support and have had their tracheostomy removed or until they have begun to recover without needing either intervention. The evidence concerning the method and setting of monitoring is insufficient to make specific recommendations.

**RESPIRATORY MONITORING AND AIRWAY PROTECTION**

Neuromuscular respiratory function becomes compromised in 17% to 30% of patients with GBS. In some patients, bulbar dysfunction causes difficulty with clearing secretions, compromising gas exchange and increasing the risk of aspiration. Clinical features that indicate fatigue of respiratory muscles are tachypnea, sweating, tachycardia, asynchronous movements of the chest and abdomen, and episodic use of accessory muscles of respiration. In 1 case series, rapid disease progression, presence of bilateral facial palsy, and autonomic dysfunction increased the likelihood of intubation. A study of 722 patients, of whom 313 required ventilation, identified 6 predictors of the need for ventilation in a multivariate analysis: time from onset to admission being less than 7 days, inability to cough, inability to stand, inability to flex the arms or head, and liver enzyme level increases. In 196 of the patients with available vital capacity measurements, predictors were time from onset to admission being less than 7 days, inability to lift the head, and vital capacity of less than 60% of that which was predicted. In many patients, a vital capacity (measured volume with forceful exhalation after maximal inhalation) below 20 mL/kg, a PImax (maximum inspiratory pressure generated after maximal sucking in through a mouth piece while occluding the nose) of less than 30 cm H2O or a PEmax (maximum expiratory pressure generated on maximal blowing out) of less than 40 cm H2O warns of imminent respiratory arrest. Rapid decline in vital capacity (eg, 50% from baseline) may further indicate impending respiratory failure, but this finding needs confirmation. Patients with pulmonary infiltrates or atelectasis generally require intubation and mechanical ventilation. Hypoxemia is also an indicator of neuromuscular respiratory failure. Hypercarbia appears later. Thus, respiratory failure in GBS is common and life threatening. Emerging diaphragmatic failure can be detected by serial clinical observation or respiratory function tests. Patients who require ventilation are at high risk of suffering major complications including pneumonia, sepsis, gastrointestinal tract bleeding, pulmonary embolus, and others. In a series of 114 patients, 60% admitted to an intensive care unit had major complications in 1 of these categories.

**RECOMMENDATION**

Respiratory function should be monitored in patients with GBS, but there is insufficient evidence to recommend specific methods. Weaning from the ventilator should be guided by improvement in strength and serial pulmonary function tests.
TIMING AND METHOD OF TRACHEOSTOMY

The mean duration of ventilation in various treatment trials has ranged between 15 and 43 days, suggesting that a proportion of patients can be spared from receiving a tracheostomy. Early tracheostomy increases patient comfort and airway safety and may help weaning. On the other hand, surgical tracheostomy results in permanent disfigurement and has sometimes been associated with life-threatening hemorrhage, infection, accidental dislodgement of the tube, fatal procedure-related necrotizing mediastinitis, chyle fistula due to a thoracic duct perforation, and a cosmetically unacceptable, hypertrophic keloid tracheostomy scar. More recently, percutaneous dilatational tracheostomy has been introduced, but this technique has not been compared with traditional tracheostomy in GBS. In a randomized trial in patients selected for elective tracheostomy, percutaneous dilatational tracheostomy was superior. The procedure involves a small skin incision and then insertion of a cannula into the trachea, followed by dilators of gradually increasing size until the desired tracheostomy tube can be accommodated. Percutaneous tracheostomy may reduce the risk of accidental extubation owing to the fact that it fits more snugly around the stoma. A better cosmetic outcome may result from a smaller skin incision.

A newly introduced pulmonary function ratio has been used to predict the need for tracheostomy. Daily vital capacity and maximal inspiratory and expiratory pressures were summed to create an integrated pulmonary function score. A pulmonary function ratio was calculated, which represents the pulmonary function score at day 12 after intubation divided by the pulmonary function score at the day of intubation. This study found that at day 12 with a pulmonary function ratio of less than 1, it is highly unlikely that patients will be weaned from the ventilator within 3 weeks and tracheostomy should be performed. The sensitivity of a pulmonary function ratio of less than 1 for predicting that the duration of ventilation would be more than 3 weeks was 70%, and the specificity and positive predictive value were 100%.

RECOMMENDATION

The decision to place a tracheostomy may be postponed for 2 weeks. If after 2 weeks the pulmonary function tests do not show any significant improvement from baseline, tracheostomy should be performed. If the pulmonary function test tends to improve above baseline, tracheostomy could be deferred for an additional week, allowing the patient to attempt to be weaned from the ventilator. Percutaneous tracheostomy may be preferred in centers with adequate experience in using the technique.

PAIN MANAGEMENT

Retrospective observational analyses of GBS case series have documented pain as an early symptom, with an incidence ranging from 33% to 71%. One study examined incidence and intensity of pain prospectively and quantified the response to medical pain intervention. Pain was reported by 89% of the patients and was severe in half. First-line drugs that were used were acetaminophen and nonsteroidal anti-inflammatory drugs. However, 75% of the patients additionally required oral or parenteral opioids and 30% of the patients were treated with intravenous morphine infusions (range, 1-7 mg/h). Ten percent of the patients received tricyclic antidepressants and a further 10% received carbamazepine as adjuvant treatments for neuropathic pain during the later course of the illness. In a randomized, double-blind, crossover trial involving 18 participants, gabapentin (15 mg/kg daily) or placebo was given by a nasogastric tube for 7 days before switching to the alternate treatment. There was prompt substantial and significant relief of pain and reduction in the need for rescue medication. In a similar study of 12 patients, greater pain relief was obtained from carbamazepine (300 mg daily for 3 days) than from placebo. Excellent relief of intractable and severe pain by epidural infusions of morphine (1-4 mg/morphine bolus injections every 8-24 hours) has been reported in a single case study. Opioid analgesics may aggravate autonomic gut dysmotility and bladder distention.

RECOMMENDATION

Simple analgesics or nonsteroidal anti-inflammatory drugs may be tried but often do not provide adequate pain relief. Single small randomized controlled trials support the use of gabapentin or carbamazepine in the intensive care unit for the treatment of pain in the acute phase of GBS. Appropriate narcotic analgesics may be used but require careful monitoring of adverse effects in the setting of autonomic denervation. Adjuvant therapy with tricyclic antidepressant medication, tramadol, gabapentin, carbamazepine, or mexilitene may aid in the long-term management of neuropathic pain.

MANAGEMENT OF BLADDER AND BOWEL DYSFUNCTION

Constipation occurs frequently in bed-bound patients. Approximately half of the patients develop adynamic ileus in the acute phase, often but not invariably in conjunction with other features of dysautonemia. In other instances, the risk is increased by long-term immobilization, incremental doses of opiates for pain control, or preexisting causes such as prior abdominal procedures. Bladder function has only been studied infrequently in the acute phase of GBS, partly because most patients are catheterized as part of their general nursing care to maintain bodily hygiene and to avoid bladder distention. Voiding is more frequently compromised with autonomic denervation and monitoring of opioid administration are recommended. In addition to suspension of gut-feeding nasogastric and rectal tubes, erythromycin or neostigmine may be effective in treating adynamic ileus. Promotility agents are contraindicated in patients with dysauto-
nomia. Bladder catheterization is often needed as part of the intensive care of severely affected patients. A sterile, closed urinary drainage system should be used with avoidance of breaking the seal to obtain urinary samples and irrigation of the bladder.

REHABILITATION

Although most patients with GBS need rehabilitation, there are no long-term rehabilitation outcome studies or comparisons of different methods. In neuromuscular disease, overfatiguing the affected motor unit in therapy may impede recovery and cause paradoxical weakening. Attention needs to be paid to many details that cannot be summarized briefly. There is a danger of muscle shortening and joint contractures. Prolonged immobilization leads to a reduction of blood volume and increased episodes of postural hypotension. For some immobilized patients, a tilt table has been useful. Weight loss and significant sensory loss make patients susceptible to peripheral nerve compression and the development of decubitus ulcers, requiring proper bed positioning with frequent postural changes. In patients noted to have immobilization hypercalcemia, early mobilization was correlated with a therapeutic drop in the serum calcium levels. In the acute stage, patients lose weight. During recovery, they regain weight owing to reduced activity levels.

RECOMMENDATION

Treatment in the acute phase should include an individual program of gentle strengthening involving isometric, isotonic, isokinetic, and manual resistive and progressive resistive exercises. Rehabilitation should be focused on proper limb positioning, posture, orthotics, and nutrition.

MANAGEMENT OF FATIGUE

A large proportion of patients with GBS remain seriously affected in their psychosocial functioning even when their physical recovery was complete or when they were left with only mild residual signs. Severe fatigue persists in 80% of patients and is unrelated to age, duration, or severity of the initial illness. Frequency and severity of fatigue in GBS were comparable with that encountered in other immunemediated neuropathies. The cause and contributing factors are not fully known, but fatigue appears in part to be a sequel of forced inactivity and general muscle deconditioning. Both fatigue and functional abilities were measurably improved with a supervised exercise program in 2 single case studies. Pharmacological approaches are being evaluated.

RECOMMENDATION

An exercise program may be beneficial for persistent fatigue.

FUTURE IMMUNIZATIONS

Recurrence of GBS after immunization is rare. Reported recurrent symptoms within 6 weeks after immunization, but it was possible to deduce with 95% confidence that the chance of developing GBS severe enough to require hospital admission was less than 1.2%. In 2 previously reported cases, recurrence occurred following swine influenza vaccine. Recurrent attacks of chronic inflammatory demyelinating polyradiculoneuropathy have followed tetanus toxoid immunization.

RECOMMENDATION

Immunizations are not recommended during the acute phase of GBS and probably not during a period, possibly of 1 year, after the onset of the disease. After that, immunizations need not be withheld, but the need for the immunization should be reviewed on an individual basis. If GBS occurs within 6 weeks after a particular immunization, consideration should be given to avoiding that immunization in that individual in the future.

CONCLUSION

This review has highlighted the need for more research into all aspects of supportive care for GBS.

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