Respiratory Complications of Rapidly Progressive Neuromuscular Syndromes: Guillain-Barré Syndrome and Myasthenia Gravis

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ABSTRACT

Neuromuscular respiratory failure is a common complication of both the Guillain-Barré syndrome and myasthenia gravis. Several key pathophysiological mechanisms contribute to the spiral of respiratory insufficiency in these diseases, including inspiratory, expiratory, and bulbar muscle weakness. It is important to identify patients with impending respiratory failure early to avoid emergency intubations. Several clinical features and bedside pulmonary function tests (PFTs) are useful in guiding decisions about intubation. Weaning is initiated when respiratory muscles have recovered sufficiently, and again, PFT criteria are helpful. Intravenous immunoglobulin and plasmapheresis are the cornerstones of specific therapy for both illnesses when complicated by respiratory failure. Mortality and morbidity are dramatically increased by respiratory failure and are mainly due to associated medical complications. Optimal outcomes depend on avoidance of these and prompt implementation of immunomodulatory therapy.

KEYWORDS: Neuromuscular weakness, respiratory failure, plasmapheresis, IVIG, ICU

Objectives: Upon completion of this article the reader should be able to: (1) understand the prevalence of neuromuscular respiratory failure and the pathophysiological factors leading to respiratory complications; (2) identify patients at risk for impending respiratory failure; and (3) use bedside PFTs to guide decisions about intubation. The reader should also understand mechanical ventilation and weaning strategies in these patients, specific immunotherapy to shorten the duration of ventilation, and prediction of outcome based on various clinical and laboratory features.

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Guillain-Barré syndrome (GBS) and myasthenia gravis (MG) are the leading causes of acute neuromuscular respiratory failure. In these patients, management of respiratory complications is complex, differing in several aspects from management of other causes of respiratory failure. Morbidity and mortality rise sharply once these patients require mechanical ventilation, presenting a major challenge to the treating neurointensivist. Medical complications associated with respiratory failure remain the most modifiable causes of death and poor functional outcomes in these diseases, rendering optimization of intensive care unit (ICU) management of paramount importance.

EPIDEMIOLOGY

MG has an annual incidence of 0.2 to 0.5 per 100,000 and a prevalence of 5 to 15 per 100,000. Women are more often affected, the female to male ratio being 3:2, and tend to be younger, becoming ill in the second to third decades.[1,2] Men are affected at an older age, in the fifth to seventh decades. Myasthenic crises occur at some time in 15 to 20% of MG patients.[3] Age and gender do not appear to be risk factors for myasthenic crisis. In a population-based study from Leipzig, Germany, the annual risk of myasthenic crisis was estimated to be 2.5% and about one in 10 million for the entire population.[4]

GBS is more common than MG as a cause of neuromuscular respiratory failure. It is the most common cause of acute neuromuscular paralysis in Western countries with an annual incidence of 1 to 4 persons per 100,000.[5] Respiratory failure is very common, occurring in about 30% of these patients.[6] In approximately two-thirds of patients, the illness begins 2 to 4 weeks after a nonspecific, viral respiratory or gastrointestinal illness. Less often it follows specific acute infections like mycoplasma, campylobacter, cytomegalovirus (CMV), Epstein-Barr virus (EBV), or herpesvirus (HSV). It can also occur after immunizations or postoperatively. Some cases occur in the presence of an underlying illness such as systemic lupus erythematosus (SLE), Hodgkin's disease, sarcoidosis, or recently acquired human immunodeficiency virus (HIV). Cases of GBS associated with pregnancy usually occur in the third trimester or postpartum.[7]

PATHOPHYSIOLOGY

At least four factors in various combinations contribute to a downward spiral leading to respiratory failure in patients with progressive neuromuscular weakness: upper airway compromise, inspiratory muscle weakness, expiratory muscle weakness, and secondary pulmonary complications. Facial, oropharyngeal, and laryngeal muscle weakness interfere with swallowing, impairing clearance of upper airway secretions and leading to failure to protect the tracheobronchial tree from repeated aspiration. Also, partial mechanical airway obstruction can result from weakness of the tongue and retropharyngeal muscles. Expiratory muscle weakness severely compromises the ability to clear the airways of secretions and contributes to microatelectasis.

Inspiratory muscle weakness from diaphragmatic and intercostal muscle involvement results in inadequate lung expansion, promoting microatelectasis in the lung periphery, disrupting ventilation-perfusion matching, and contributing to hypoxemia. Respiratory rate and work of breathing increase and these, in combination with the already weakened respiratory muscles, overburden the respiratory apparatus and lead to muscle fatigue and respiratory failure. This decompensation can happen without warning and often occurs at night during sleep when the diaphragm assumes most of the work of breathing. In addition, pulmonary complications such as lobar collapse or pneumonia can rapidly worsen the situation.[8]

CLINICAL PRESENTATION

Myasthenic Crisis

The time to first occurrence of myasthenic crisis is typically between 8 months and 3 years after the diagnosis of MG.[3,4] Most often the precipitating factor is infection, most commonly pneumonitis, bronchitis, or upper respiratory tract infection.[3] Other common precipitating factors are aspiration pneumonia, changes in medications, including withdrawal of steroids or anticholinesterase inhibitors, or initiation of steroids, antibiotics (most often aminogylcosides), or other medications that can precipitate myasthenic crisis (Table 1). Myasthenic crises can also occur with parturition or postoperatively; in one series, about 20% of patients had myasthenic crises postthymectomy.[4] In about 30% of cases, no precipitating factor can be identified.

Patients in myasthenic crisis present with increasing generalized weakness, dyspnea on exertion, dysphagia, or dysphonia. Increasing dyspnea on exertion is a clue to to a worsening situation and dyspnea at rest is a sensitive marker of impending respiratory failure. Bed-bound patients with impending crisis may get tachypnic while being bathed. Difficulty swallowing and inability to handle upper airway secretions are also premonitory symptoms for respiratory complications. The progression to respiratory failure is often insidious and without obvious signs of respiratory insufficiency. Clinicians should be careful to watch for subtle signs of impending respiratory failure and not wait until oxygen saturation drops. By this time, emergency intubation may be required, a situation that is much more problematic than elective intubation.

Table 1 Drugs That Can Exacerbate Weakness in Myasthenia Gravis

Antibiotics
Aminoglycosides (gentamycin, streptomycin, others)
Peptide antibiotics (polymyxin B, Colistin)
Tetracyclines (tetracycline, doxycycline, others)
Erythromycin
Clindamycin
Ciprofloxacin
Ampicillin
Antiarrhythmics
Quinidine
Procainamide
Lidocaine
Neuromuscular junction blockers (vecuronium, pancuronium, others)
Quinine
Steroids
Thyroid hormones (thyroxine, levothyroxine, etc.)
Beta-blockers (propranolol, timolol, others)
Phenytoin

Data from Mayer[43] with permission.

Guillain Barré Syndrome

The presenting respiratory symptoms of GBS are similar to those of myasthenic crisis and include shortness of breath, inability to handle oral and upper airway secretions, difficulty swallowing, and worsening voice quality. These symptoms often follow ascending extremity weakness but can appear with minimal limb involvement or, uncommonly, as the sole presenting feature of the illness. The pace of progression to respiratory failure from onset can be dramatic, leading to quadriparesis and the need for intubation over 24 to 48 hours. Alternatively, progression can be subacute, progressing gradually over 3 to 4 weeks.

ASSESSMENT OF RESPIRATORY COMPROMISE

A careful physical exam to look for the earliest signs of respiratory compromise in patients with GBS and myasthenic crisis is important. The development of rapid shallow breathing with tachycardia is a danger sign of incipient respiratory muscle compromise. Many patients also have staccato speech and need to pause between words. Accessory muscle use that can be detected visually or more sensitively by palpation and paradoxical inward motion of the abdomen during inspiration are signs that suggest diaphragmatic weakness. Also, progressive weakness of trapezius and neck muscles usually parallels deterioration of diaphragmatic function. Ventilatory reserve can be further assessed by using a simple bedside maneuver called the single breath count. The patient is asked to count as many numbers as possible after taking a single deep inspiration. A count of 50 is normal and one of < 15 signifies severely decreased ventilatory capacity.

Increasing frequency of cough, particularly after swallowing, is an important warning sign of bulbar dysfunciton. Dysphagia and the ability to protect the upper airway can be assessed at the bedside by asking the patient to swallow 3 oz. of water.[9] Coughing after swallowing indicates aspiration secondary to significant bulbar weakness, in which case oral feedings should be withheld. These clinical symptoms and signs are combined with bedside pulmonary function tests (PFTs) to guide decisions about the need for intubation.

PULMONARY FUNCTION TESTS AND CRITERIA FOR INTUBATION

Patients with GBS and worsening myasthenia should be monitored with serial bedside PFTs, pulse oximetry, and arterial blood gases (ABGs). Bedside PFTs are more sensitive for detection of incipient respiratory failure than ABGs because the latter become abnormal relatively late during the cycle of respiratory decompensation. To avoid respiratory crises, it is important to perform intubation before significant ABG abnormalities develop. Admission to an intensive or respiratory care unit and serial measurements of VC (two to four times daily) are recommended for all myasthenic and GBS patients with dyspnea and reduced vital capacity who do not require immediate intubation.

The PFT measures used to guide the decision about intubation are vital capacity (VC), maximal inspiratory pressure (MIP), and maximal expiratory pressure (MEP). When VC (normally 60–70 mL/kg) falls to 30 mg/kg or less in patients with GBS or myasthenic crises, cough becomes weakened, oropharyngeal secretions accumulate, and atelectasis and hypoxemia ensue. A VC of 15 mL/kg (~1 liter) is generally considered the level at which intubation is required (Table 2). MIP, normally < -70 cm H_2O, measures the strength of the diaphragm and other muscles of inspiration, and generally reflects the ability to maintain normal lung expansion and avoid atelectasis. MEP, normally > 100 cm H_2O, measures the strength of the expiratory muscles and correlates with strength of cough and the ability to clear secretions from the airway. An MIP of > -30 cm H_2O and an MEP of < 40 cm H_2O are additional criteria for intubation. Other factors that must be considered in the decision to intubate include baseline VC, the rate of respiratory deterioration, ABG values, and the patient's overall level of comfort.

In general, early intubation is recommended because the prompt institution of positive pressure ventilation may prevent increasing degrees of atelectasis and other complications, and permit earlier extubation. In a

Table 2 Pulmonary Function Tests in Patients with Myasthenic Crisis

	Normal	Criteria for Intubation	Criteria for Weaning	Criteria for Extubation
Vital capacity	> 60 mL/kg	≤ 15 mL/kg	≥ 10 mL/kg	~25 mL/kg
Negative inspiratory force	> 70 cm H_2O	< 20 cm H_2O	≥ 20 cm H_2O	~40 cm H_2O
Positive expiratory force	> 100 cm H_2O	< 40 cm H_2O	≥ 40 cm H_2O	~50 cm H_2O

Data from Mayer[43], with permission.

recent retrospective study of GBS patients, progression to mechanical ventilation was predicted by rapid progression of disease, bulbar dysfunction, bilateral facial weakness, VC < 20 mL/kg, MIP > −30cm H_2O, and MEP < 40 cm H_2O or reduction by 30% in the absolute values of VC, MIP, or MEP.[9] Therefore patients with these features should be monitored in an ICU, and any further decline should prompt serious consideration for elective intubation.

It is also important to anticipate manifestations of dysutonomia in patients with GBS during intubation. Exaggerated hypotensive responses to drugs used for intubation such as propofol, benzodiazepines, barbiturates and etomidate and cardiac arrhythmias, especially vagally mediated, are common during airway manipulation. Succinylcholine should be avoided because it can cause lethal hyperkalemia.

VENTILATOR MANAGEMENT

In general, noninvasive ventilation is inappropriate in GBS or myasthenic crisis patients unless upper airway function is relatively well preserved. The initial goals of mechanical ventilation in patients with neuromuscular respiratory failure are to provide rest and promote lung expansion. Adequate pressures and volumes are used to reverse and limit progressive alveolar collapse and atelectasis. Typical tidal volumes are 8 to 10 mL/kg combined with low rates of 9 to 10 breaths per minute to maintain a normal minute ventilation of 6 to 10 liters and a pCO_2 level around 40 mmHg. Positive end-expiratory pressure (PEEP) levels are maintained around 5 to 15 cm H_2O as long as plateau airway pressure is below 35 cm H_2O. Patients with longstanding weakness and chronic CO_2 retention as evidenced by increased HCO_3-levels should not be overventilated. This causes alkalosis and renal bicarbonate wasting that can make weaning difficult because of reduced buffering capacity.

WEANING

No controlled study has identified the optimal approach to weaning in patients with neuromuscular respiratory failure. Current guidelines suggest that weaning be attempted when sufficient respiratory muscle recovery occurs as indicated by (a) signs of improvement in overall muscle strength; (b) VC > 10 mL/kg; (c) MIP < −20 cm H_2O; (d) FiO_2 requirement < 40% and PEEP ≥ 5 cm H_2O; and (e) no fever, infection, or other medical complications.[10] Weaning should begin with daily trials (2–12 hours) of PEEP and pressure support to levels of 5 to 15 cm H_20 (Table 3). Pressure support is provided to reduce the overall work of breathing and to attain spontaneous tidal volumes of 300 to 500 mL with a comfortable breathing pattern. Agitation or distress associated with an increased respiratory rate and decreasing tidal volume are signs of fatigue that call for cessation of the weaning trial and return of the patient to resting settings. The number of hours that the patient tolerates the weaning trial, a reflection of endurance, should be considered the main outcome of the weaning trial. ABGs may be useful at the end of a weaning trial, when the patient becomes tired or uncomfortable, to determine whether hypercarbia is present.

Table 3 Weaning Trial Protocol

1. Begin the weaning trial early in the day by switching the ventilator mode from SIMV to CPAP with pressure support. After 2 to 5 minutes, adjust pressure support so that respiratory rate is < 30 and tidal volume is > 4 mL/kg.
2. Every 2 to 4 hours, if the patient remains comfortable, the level of pressure support may be decreased by 1 to 2 cm H_2O.
3. In general, the weaning trial should be continued up to 12 hours or until signs of respiratory fatigue occur. *An increasing respiratory rate combined with falling tidal volumes is the most reliable indicator of respiratory fatigue.* Associated signs may include agitation, restlessness, and tachycardia. At this point, an arterial blood gas may be desirable.
4. When the weaning trial is over, return to SIMV mode overnight.
5. If the patient is comfortable on CPAP with pressure support ≤ 5 cm H_2O, maintain these settings overnight as tolerated. If successful, consider extubation the following morning.

SIMV, synchronized intermittent mandatory ventilation; CPAP, continuous positive airway pressure. Data from Mayer[43] with permission.

If the patient can tolerate weaning trials for at least a few hours, the level of pressure support can be gradually reduced by 1 to 3 cm H_2O each day, allowing for the gradual assumption of more of the breathing load. In many instances, the weaning process is facilitated by giving low doses of intravenous sedation (fentanyl or lorazepam) to patients who are anxious, agitated, uncomfortable, or fighting the ventilator.

Although pulmonary function criteria can be useful for guiding the decision to extubate (Table 2), there are always exceptions; some patients with adequate parameters fail extubation, whereas others with inadequate parameters will wean successfully. The patient's *ability to tolerate weaning trials with minimal pressure support* ($\leq$ 5 cm H_2O) *for extended periods of time (12–24 hours)* is probably the single best predictor of successful extubation (personal observation). Fluctuating PFTs, excessive secretions, or concurrent medical problems (i.e., infection, cardiovascular instability) are relative contraindications to extubation. To allow for close monitoring afterward, extubation should always be performed early in the day.

TRACHEOSTOMY

The optimal timing for tracheostomy in patients with neuromuscular respiratory failure who require prolonged intubations has not been established.[11,12] The advantages of a tracheostomy include a decreased risk of larnygotracheal injury, which can be as high as 10% for endotracheal intubation beyond 2 to 3 weeks, decreased dead space, increased ease of weaning, improved pulmonary toilet, and, by freeing the mouth and nose of tubes, enhanced patient comfort. The risks of tracheostomy include local hemorrhage or infection and tracheal stenosis, usually in the region of the tracheal incision or tracheostomy tube cuff, although these are unusual when studied prospectively.[13] The cosmetic disfiguration of tracheostomy should also be considered. However, when a patient requires mechanical ventilation for more than 2 to 3 weeks, the potential benefits of tracheostomy start to outweigh the risks. Therefore, tracheostomy should be performed early (around 2 weeks) if the need for prolonged ventilation is anticipated. In a recent study of GBS patients, prolonged ventilation and tracheostomy were more likely to occur in the elderly and in the presence of preexisting pulmonary disease.[14] Most experts also agree that tracheostomy is reasonable even before 2 weeks in GBS patients with severe quadriplegia, no or minimal response to plasmapheresis or intravenous immunoglobulin (IVIG), and electrophysiological studies showing severe abnormalities such as inexcitable nerves or profuse fibrillation.

A study of myasthenic crisis at our center [3] found three independent predictors of the need for prolonged ventilation: (a) preintubation bicarbonate > 30 mEq/L, (b) peak VC 1 to 6 days postintubation < 25 mL/kg, and (c) age > 50 years. These risk factors were additive with the proportion of patients intubated longer than 2 weeks being 0% among those with no risk factors, 25% with one risk factor, 46% with two risk factors, and 88% with three risk factors. It is important to note that VC measurements tend to be depressed for the first 2 days after intubation, and are only useful for prognostication thereafter.

IMMUNOTHERAPY

In patients with GBS, plasmapheresis and IVIG have been shown to be equally efficacious.[15,16] Plasmapheresis is done on alternate days, typically for five sessions, to exchange about 2 to 4 L of plasma. This has been shown to halve the median time of mechanical ventilation and to walking unassisted.[17,18] Approximately one-third to one-half of patients treated with plasmapheresis are weaned off the ventilator within 2 weeks, thus avoiding tracheostomy. Striking improvements can be seen within the first few exchanges, but more often, improvement occurs during the first week after the exchanges. For maximum benefit, plasmapheresis should be started within 2 weeks of the onset of the illness. Beyond this time, cases that benefit are the ones still showing progression of weakness.

Serious complications of plasmapheresis are infrequent at experienced centers.[19] They are most often related to the need for large-bore catheter placement, which can result in pneumothorax, hematomas at the catheter insertion site, or line infection. Also, hypotension from hypovolemia, congestive heart failure, allergic reactions, hemolysis from kinking in the tubing and, rarely, air embolization can occur. Use of 5% albumin instead of fresh frozen plasma (FFP) as replacement for plasma results in a much lower incidence of anaphylactoid reactions. Contraindications to plasma exchange include hypotension, sepsis, recent myocardial infarction, marked dysautonomia, and active bleeding.

More recently, IVIG was introduced as specific therapy for GBS,[15,16] given at a dose of 0.4 mg/kg per day for 5 days. Complications are uncommon and include anaphylatic shock, aseptic meningitis, thomboembolic events, and renal failure. IVIG offers distinct advantages over plasmapheresis, including ease of infusion through a peripheral catheter, the need for less technical support, and lower costs. IVIG is the preferred treatment at centers inexperienced with plasmapheresis. A higher relapse rate with IVIG than with plasmapheresis was a concern raised by earlier small case series,[6,26] but this has not been borne out in larger trials showing no difference in outcome at 48 weeks between IVIG and plasmapheresis.[15] Also, the two treatments in combination did not improve the outcome as compared with each treatment alone.[15] Ultimately, the choice between the two treatments depends on availability, local experience, provider costs, and clinician preference.

For patients with unexpected deterioration after an initial favorable response to IVIG or plasmaphereis, another 5-day course of the therapy should be considered, but no studies that establish this practice are available. Further, it is not known whether use of the alternative therapy after initial failure is beneficial.[20]

Similar to GBS, plasmapheresis and IVIG are the two treatment modalities available for myasthenic crises, but there are no controlled clinical trials comparing them. Plasmapheresis remains the mainstay of therapy in North America, based on the greater experience with this treatment,[21–23] and some reports of treatment failure with IVIG responding later to plasmapheresis.[24] The success rate of plasmapheresis has been reported to be in the order of 75%.[21,22] The protocol for plasmapheresis is the same as has been used for GBS. More recently, small case series have shown that IVIG also improves weakness in myasthenic crisis.[25–27] Thus, when patients cannot tolerate plasmapheresis because of medical comorbidities such as sepsis, severe anemia, or difficult large-bore venous access, IVIG is used as an alternative,[28] at the same dose as for GBS.

Anticholinesterase medications are discontinued in myasthenic crises requiring mechanical ventilation to avoid worsening of bronchial secretions, mucous plugging, and atelectasis. These medications are restarted on the day of extubation at one-half the baseline dose and then gradually increased. Corticosteroids, if the patient is not already receiving them, are started only for prolonged crisis (>2 weeks) at doses equivalent to prednisone at 1mg/kg/day. The response to steroids may be delayed for 10 to 14 days.

Continuous intravenous (IV) pyridostigmine is another treatment alternative for myasthenic crysis studied mainly in Europe. In one large retrospective population-based study, IV pyridostigmine (2 mg/min) alone did not shorten the duration of mechanical ventilation or improve overall outcome, compared with plasmapheresis alone or the combination of pyridostigmine plus prednisone.[4] Cardiac arrythmias were increased in patients treated with IV pyridostigmine, although the authors did not consider these related to the treatment.[29] Consequently, this treatment is currently not widely used in North America.

MEDICAL COMPLICATIONS ASSOCIATED WITH NEUROMUSCULAR RESPIRATORY FAILURE

Guillain-Barré Syndrome

Dysautonomia and its manifestations are the most frequent medical complications of GBS, occurring in about 20% of all patients and in up to 75% of those with quadriplegia.[30,31] Wide blood pressure fluctuations and cardiac arrhythmias are the most frequently seen manifestations, associated with impaired baroreceptor buffering. These are usually self-limited and best treated conservatively with Trendelenburg positioning and fluid boluses as needed. Pressors and beta-blockers should be avoided because of the risks of overcompensation and cardiac arrest, respectively. Arrhythmias such as sinus bradycardia, sinus arrest, and atrio-ventricular block are manifestations of vagal hyperactivity that can be seen in up to 35% of patients, often in association with tracheal suctioning. Complete heart block occurs occasionally, necessitating placement of a temporary pacemaker. Other dysautonomic manifestations are bladder and gastrointestinal dysfunction, neurogenic pulmonary edema, salivary and lacrimal gland dysfunction, temperature and sweating abnormalities, the syndrome of inappropriate antidiuretic hormone (SIADH) secretion and bronchial smooth muscle dysfunction.

Nondysautonomic problems associated with GBS include pain syndromes, hypercatabolism,[32] and pressure nerve palsies. Pain occurs in up to 50% of patients and is of different types.[33] Most common is a deep muscle ache distributed in the low back, quadriceps, buttocks, or calves that responds well to conservative measures such as warm compress, acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), or narcotics. Epidural narcotics may be necessary to obtain adequate pain relief in some patients. Neuropathic pain, the second most common type, is effectively treated with carbamazepine, gabepeutin, or narcotics.[34] A high calorie, high protein enteral diet is administered to counter the hypercatabolic state, and frequent repositioning of the patient is needed to avoid pressure injury to nerves.[35]

Myasthenia Gravis

Medical complications associated with myasthenic crises are common and constitute the most important modifiable risk factors for prolonged intubation. In a retrospective 12-year study at our institution,[3] fever was the most common complication (70%) followed by pneumonia (50%) and atelectasis (40%). All were more common in older patients. On multivariate analysis, four factors were independently associated with prolonged intubation: atelectasis, congestive heart failure, *Clostridium difficile* diarrhea, and anemia needing transfusion. *C. difficile* diarrhea and congestive heart failure accounted for the greatest prolongation of mechanical ventilation (median of 41 days). Prompt treatment of these and other medical complications is paramount in minimizing the duration of mechanical ventilation (Table 4).

PROGNOSIS

Mortality in myasthenic crisis has dramatically declined from 80% in the pre-mechanical ventilation era[36] to 40% in the early 1960s to 5% in the late 1970s, largely

Table 4 Ten Strategies to Minimize the Duration of Myasthenic Crisis

1. Perform conservative early intubation to prevent atelectasis, infiltrates, or worsening muscle weakness that might occur if intubation is delayed.
2. Discontinue anticholinesterase medications (i.e., pyridostigmine), which can aggravate secretions and mucous plugging, immediately upon intubation.
3. Initiate plasmapheresis as soon as possible. Insert a large-bore central venous catheter to avoid delayed or incomplete treatments early in the course of crisis due to inadequate venous access.
4. Avoid or discontinue medications that can exacerbate myasthenic weakness.
5. Employ a ventilator strategy using large tidal volumes (~15 ml/kg) and generous levels of positive end expiratory pressure (5–15 cm H_2O), to expand collapsed alveoli and prevent further atelectasis.
6. Perform fiberoptic bronchoscopy aggressively in patients with significant mucous plugging or lung collapse, to clear trapped secretions and promote lung reexpansion.
7. Reserve full-course antibiotics for culture-documented infections, to avoid *Clostridium difficile* infection.
8. Transfuse for significant anemia (hematocrit < 30%), which can limit endurance during the weaning process.
9. Diagnose and treat hypokalemia and hypophosphatemia, which can exacerbate muscle weakness.
10. After 2 weeks, perform tracheostomy, which facilitates weaning by reducing dead space and the extra work of breathing associated with an endotracheal tube.

Data from Mayer[43] with permission.

because of advances in intensive care management. In our review of myasthenic crisis from 1983 to 1994, three of 73 patients (4%) died during the crisis, and four patients died after extubation, for a total hospital mortality of 10%.[3] All deaths were due to severe medical comorbidity rather than the crisis itself. Despite the dramatic reduction in mortality, the median duration of intubation associated with myasthenic crisis (14 days) has changed remarkably little over the past 30 years.[3,37]

As a general rule, approximately 25% of patients in crisis will be extubated by 1 week, 50% by 2 weeks, and 75% by 1 month (Fig. 1).[3] The longest crisis on record lasted almost 2 years.[38] Prolonged intubation is closely associated with poor functional outcome after crisis. In our series, nearly 50% of patients were functionally dependent at discharge.[3] Intubation for more than 2 weeks was associated with a threefold increase in hospital stay (median 63 days versus 22 days) and a twofold increase

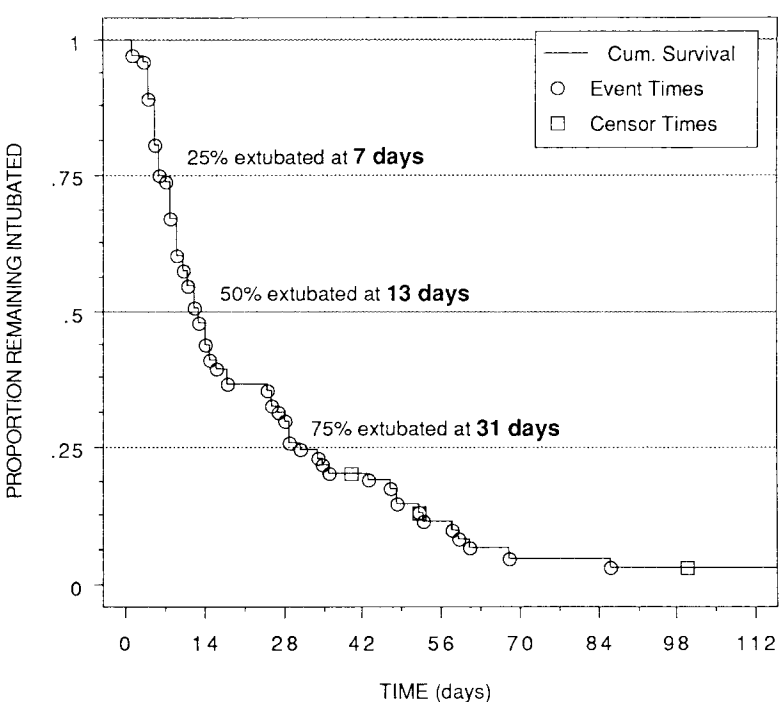

Figure 1 Kaplan-Meier survival curve depicting the proportion of patients remaining intubated (death or extubation) over time in 73 episodes of myasthenic crisis. Three censored event times (40, 52, and 100 days) refer to patients who were transferred from our institution while still intubated. A single patient with a crisis duration of 159 days is not shown. (From Thomas et al,[3] with permission.)

in functional dependence at discharge (77% vs 36%). Future efforts should focus on reducing the duration of intubation and disability at discharge.

Patients with GBS typically have near complete recovery over a period of weeks to months. About 65% recover with minor deficits that do not impair function significantly, 15% have full recovery without any detectable deficits, and 5 to 10% have permanent disabling weakness.[7] Severely reduced muscle action potentials on electromyogram (EMG) consistently predict residual muscle weakness.[39] Advanced age, need for mechanical ventilation for more than a month, and rapidly progressive severe disease are also prognostic of poor outcome.[40,41] In GBS patients who need mechanical ventilation, age and delay in transfer were found to be predictive of poor outcome on multivariate analysis.[42] Overall mortality in GBS ranges from 3 to 8%, largely from avoidable complications such as sepsis, acute respiratory distress syndrome (ARDS), pulmonary emboli, or rare cases of unexplained cardiac arrest possibly secondary to dysautonomia. Mortality in patients who need mechanical ventilation is approximately 20%.[42]

CONCLUSION

Treatment of neuromuscular respiratory failure and associated medical complications in patients with GBS and MG has advanced rapidly in the last two decades related to the development of specific immunotherapy and improvements in intensive care. Several key studies now provide evidence that serves as the basis for guidelines to manage these patients. Presently, either intravenous immunoglobulin or plasmpheresis are considered the treatments of choice, and anticipation and avoidance of medical complications are key to successful management. Nevertheless, continued research to test new therapeutic approaches is needed to bring further improvements in outcomes in these patients with largely reversible disease.

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