NEUROMUSCULAR DISORDERS IN THE ICU

Nicholas J. Silvestri, MD
University at Buffalo Jacobs School of Medicine & Biomedical Sciences

Introduction: Rapidly progressive weakness and respiratory failure are common causes for admission to the ICU. Generalized weakness or failure to wean from mechanical ventilation once sedation is lifted is a common reason for neurological consultation in the ICU. It is important to rule out central nervous system disorders first in these patients which may be signaled by profound alteration in consciousness, or upper motor neuron signs on examination. In these instances, it is worth considering such diagnoses as vascular disorders (e.g. watershed infarcts), hypoxic-ischemic encephalopathy, and infectious disorders (e.g. encephalitis). Once central nervous system disorders are effectively ruled-out, then next step is to determine whether generalized weakness and failure to wean from mechanical ventilation are due to a pre-existing neuromuscular disorder or to a disorder which developed while in the ICU.

Respiratory Failure Caused By Neuromuscular Disorders: Weakness of muscles of respiration (diaphragm, intercostals, accessory muscles) leads to impaired ventilation. Orthopnea is a common finding as diaphragm placed at a mechanical disadvantage when supine. Respiratory failure in neuromuscular disorders manifests as a restrictive pattern which also occurs in various pleural, alveolar, and interstitial pulmonary disorders, or orthopaedic disorders such as kyphoscoliosis. Hypercapnic respiratory failure eventually results from progressive weakness. This is a late finding and signifies impending respiratory collapse. Hypoxemia ultimately develops due to atelectasis and impaired gas exchange within underinflated lungs. Predictors of respiratory failure include: rapid progression of weakness, neck flexor weakness, inability to converse in complete sentences, use of accessory muscles of respiration, tachypnea, or NIF < -30cc, FVC < 15cc/kg or declining trend in these parameters. Numerous neuromuscular disorders can lead to respiratory failure, several of which are discussed below.

Neuromuscular Disorders Leading to ICU Admission

1. Guillain-Barre syndrome: Most common cause of acute paralysis in Western countries. Incidence: 0.6 to 1.9/100,000 of population. Risk factors include age between 30-50 years, White race, and male gender. An antecedent illness is identified in 2/3rds of patients in the preceding weeks. Respiratory failure occurs in 1/3 of patients and is associated with rapid progression and greater severity of weakness, and a higher mortality. The EGRIS score can reliably predict who will likely develop respiratory failure at the time of admission. Dysautonomia is another frequent complication and was first described by Osler in 1892. It is seen in roughly 2/3rds of cases and is more common in patients with respiratory failure, severe paresis, and the axonal variant (AMAN). Cardiovascular involvement may lead to bood pressure lability, orthostatic hypotension, and cardiac arrhythmias due to vagal nerve involvement, which may require insertion of temporary pacemaker. Other signs of dysautonomia may include anhidrosis, gastroparesis and constipation, and urinary retention. Treatment of Guillain-Barre syndrome is either IVIg or plasmapheresis hasten time to recovery if started within 2 weeks of symptom onset. Time needed to improve after treatment is variable (6-27 days in several studies).

2. Myasthenic crisis: Myasthenic crisis is strictly defined as respiratory failure due to myasthenia gravis, though impending respiratory failure also qualifies. Crisis may also be caused by bulbar weakness severe enough to endanger protection of airway. It is estimated that crisis occurs in 15-20% patients with myasthenia gravis (MG), and is more common to occur within 3 years of initial diagnosis. Crisis can be the initial manifestation of disease in 15% of cases. Patients with MuSK antibody-positive disease are at higher risk due to higher incidence and severity of bulbar dysfunction. Cause is identifiable about 70% of the time and includes infection (40% in one series), illness, surgery, trauma, stress, medications. In addition, 10% of patients placed on high dose corticosteroids will initially worsen, usually within 7-10 days of starting medication which can at times proceed to crisis. Aggressive weaning of corticosteroids may also precipitate crisis. Treatment includes protection of airway with endotracheal intubation and ventilation or non-invasive positive pressure ventilation. It is prudent to hold acetylcholinesterase medications while

intubated to minimize secretions and to keep patients NPO to prevent aspiration. Treatment is also directed treatment toward inciting event if identifiable (e.g. infection) and either a course of plasmapheresis or IVIg. Median duration of mechanical ventilation in crisis is 14 days. Older age (>50) predicts more prolonged course. Mortality in myasthenic crisis is about 5% and usually due to complications.

Neuromuscular Disorders Occurring During ICU Admission

1. Critical Illness Polyneuropathy (CIP): This is an acute sensorimotor axonal polyneuropathy. It is estimated that 30-80% of patients who are critically ill for at least one week develop this type of neuropathy. Patients experience sensory loss and generalized, though distally-predominant weakness. Phrenic nerve involvement can lead to respiratory failure. Risk factors for the development of CIP include the presence of the systemic inflammatory response syndrome (SIRS), severity of illness, longer duration of multi-organ failure, older age, female gender, and higher mean daily blood glucose concentration. It is diagnosed by clinical exam with electrodiagnostic studies playing an ancillary role. Treatment includes prevention- avoidance of risk factors (early, aggressive treatment of sepsis, treatment of hyperglycemia), supportive care (physical and occupational therapy, nutritional support), and avoidance of complications (e.g. deep venous thrombosis, decubitus ulcers, compression neuropathies). In terms of prognosis, the CRIMYNE study demonstrated that 53.6% of patients with either CIP or CIM that survived ICU stay had persistent deficits (mainly weakness) at the time of hospital discharge. One-third recovered strength within 3 months after discharge, and 67% experienced prolonged and at times severe disability (n=15). Persistent weakness and sensory deficits are common in many patients up to four years after ICU discharge. In general, upper limb and proximal lower limb strength more likely to fully recover. Patients with more severe symptoms attributable to CIP less likely to recover completely.

2. Critical Illness Myopathy (CIM): Also known as acute quadriplegic myopathy, the most common subtype is thick filament myopathy. Other subtypes include acute necrotizing myopathy and cachectic myopathy. This is a fairly rapidly progressive myopathy affecting both proximal and distal muscles equally, often making it difficult to clinically distinguish from CIP. Facial muscles, neck flexors, and the diaphragm are also variably involved and sensation is spared. Major risk factors for the development of CIM include: exposure to high-dose corticosteroids and neuromuscular blocking agents (NMBAs). Other possible inciting agents include aminoglycoside antibiotics and propofol. CIM has also been described in patients with sepsis and multi-organ failure who did not receive corticosteroids or NMBAs. Creatine kinase (CK) levels are modestly elevated in 50% of patients and usually peak during first two weeks of illness. Electromyography may disclose “myopathic” appearing motor-units. Treatment includes supportive care as in CIP and prevention including judicious use of high-dose corticosteroids and NMBAs. Prognosis is a better than in CIP, with most patients demonstrate significant functional recovery over the course of 2 to 3 months. Those patients with more severe weakness at their nadir, however, may have a more prolonged or incomplete recovery.

Suggested Readings:

1. Benditt JO, BoitanoLJ. Pulmonary issues in patients with chronic neuromuscular disease. Am J Respir Crit Care Med 2013;187,1046–1055
2. Bolton CF. Neuromuscular manifestations of critical illness. Muscle Nerve 2005;32:140-163
3. Dhar R. Neuromuscular respiratory failure. Continuum Critical Care Neurology 2009;15(3):40-67
4. Guarneri B, Bertolini G, Latronico N. Long term outcome in patients with critical illness myopathy or neuropathy: the Italian multicenter CRIMYNE study. J Neurol Neurosurg Psychiatry 2008;79:838-841
5. Jani-Ascadi A, Lisak RP. Myasthenic crisis: guidelines for prevention and treatment. J Neurol Sci 2007;261:127-133
6. Koch S, Wollersheim T, Bierbrauer J, Haas K, Morrgeli R, et al. Long-term recovery in critical illness myopathy is complete, contrary to polyneuropathy. Muscle Nerve 2014;50:431-436
7. Ropper AN. The Guillain-Barre syndrome. N Engl J Med 1992;326:1130-1136
8. Walgaard C, Lingsma HF, Ruts L, Drenthen J, von Konigsveld R, et al. Prediction of respiratory insufficiency in Guillain-Barre syndrome. Ann Neurol 2010;67-781-787