ACUTE NEUROMUSCULAR RESPIRATORY FAILURE

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Neuromuscular emergencies in the ICU are characterized by the development of respiratory failure. It is useful to conceptualize cases of severe neuromuscular weakness with neuromuscular respiratory failure into primary and secondary causes. Presentations of primary acute or acute on chronic neuromuscular respiratory failure can be seen in patients with previous diagnosis of a neuromuscular disease or without such previous diagnosis. Severe weakness in the ICU can also occur secondary to the consequences of systemic illness (e.g. sepsis, multiorgan failure), its complications (e.g. hypophosphatemia), and its treatments (steroids, paralytic agents) on nerves and muscles, a condition known as critical illness polymyoneuropathy or ICU-acquired weakness. This syllabus and presentation will mostly focus on the primary causes of neuromuscular respiratory failure.

Basic Principles for the Management of Neuromuscular Respiratory Failure

The diagnosis of primary neuromuscular respiratory failure should be suspected in any patient presenting with mixed (hypoxic-hypercapneic) or predominantly hypercapneic respiratory failure and signs of muscle weakness (bulbar or appendicular). When neuromuscular respiratory failure is considered, the next step is to confirm the anatomical localization of the weakness (to the peripheral nervous system first, and more specifically to nerves, neuromuscular junction, or muscles if possible) and to try to establish the primary diagnosis. Precipitants should be removed or treated when identified (for instance, infections or medications in myasthenics). All this should be accomplished while ensuring the safety of the airway and adequacy of ventilation and oxygenation.

Bulbar muscle weakness can lead to airway obstruction by oral and respiratory secretions due to inefficiency of protective mechanisms, most notably cough. Aspiration can rapidly accelerate the clinical decline. Respiratory muscle weakness first produces microatelectases in the lung bases; the consequent shunting is responsible for the mild hypoxia observed early in the course of the disease. As weakness becomes more severe due to worsening muscular fatigue, tidal volumes get progressive smaller and hypercapnia supervenes. Rapid and profound hypoxia develops shortly thereafter as the compensatory action of accessory breathing muscles becomes overwhelmed.

Patients present with dyspnea, tachypnea, restlessness, diaphoresis, tachycardia, staccato speech (inability to complete sentences), recruitment of accessory muscles, and paradoxical breathing pattern. Paradoxical breathing is characterized by the abnormal inward movement of the abdomen with each inspiration and it is a reliable sign of diaphragmatic weakness and impending need for ventilatory assistance. Valuable additional information can be obtained for arterial blood gases, bedside spirometry measuring forced vital capacity, maximal inspiratory pressure (also known as negative inspiratory force) and maximal expiratory pressure, and the chest X-ray.

Patients at risk of neuromuscular respiratory failure must always be closely monitored in the ICU. The decision of when to initiate ventilatory support and what type of support to provide should be tailored based on the primary diagnosis.

Causes of Primary Neuromuscular Respiratory Failure

The causes of primary neuromuscular respiratory failure are numerous, though many are quite infrequent. The two most common as Guillain-Barré syndrome (GBS) and myasthenia gravis (MG) and consequently they will be treated separately in the presentation. Myopathies, other forms of polyradiculoneuropathies, and motor neuron disease (a disorder of the central nervous system which often presents as neuromuscular failure) are also relatively common. Despite extensive work up, no specific cause can be found in nearly one in five patients with neuromuscular respiratory failure in the ICU. Inability to reach a primary diagnosis portends a poor functional outcome in our experience.

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Guillain-Barré syndrome

GBS is most frequently caused by a demyelinating inflammatory process (acute inflammatory demyelinating polyradiculoneuropathy), but axonal forms can also occur and they are more severe. Initial presentations may vary, but eventually all severe cases exhibit the characteristic ascending paralysis with bulbar weakness. Diagnosis can be confirmed by the presence of albumino-cytological dissociation in the cerebrospinal fluid and the findings on nerve conduction studies. Approximately one third of patients with GBS require ventilatory support. Rapid progression of symptoms, early presence of bulbar weakness, and more severe weakness in the limbs predict the need for mechanical ventilation. Bedside spirometry measures can also be helpful to predict the need for intubation and mechanical ventilation. The rule of 20/-30/40 is practical and easy to remember: endotracheal intubation and mechanical ventilation should be considered when the patient has a forced vital capacity below 20 mL/kg, a maximal inspiratory pressure worse than -30 cmH_2O, and a maximal expiratory pressure below 40 cmH_2O.

GBS can be a treacherous disease because of the possibility of very fast decline and the associated dysautonomia, which can cause hemodynamic instability and serious cardiac arrhythmias in the setting of an emergency intubation. Thus, elective intubation is highly recommended in patients who are rapidly worsening and have early signs of respiratory insufficiency. Non-invasive ventilation is not a safe option in patients with GBS.

The management of GBS patients is complex and requires attention to multiple aspects of care including monitoring for manifestations of dysautonomia (cardiovascular, ileus, bladder dysfunction), respiratory hygiene, nutrition, treatment of neuropathic pain, depression, and systemic complications (infections, venous thromboembolism). The care of these patients is therefore best accomplished in a dedicated neuroscience ICU with personnel experienced in the treatment of this disease.

Immunomodulatory therapy with plasma exchange (PLEX) or intravenous immunoglobulin (IVIG) should be initiated promptly. These treatments have been shown to improve the speed and extent of motor recovery. They are probably comparable in efficacy. IVIG might be associated with a lower rate of side effects (though most of the difference is related to the requirement of a central line for the administration of PLEX). The combination of both treatments was not beneficial in the only trial testing this approach. A second course of IVIG may be considered in some refractory cases. Corticosteroids have no proven value for the treatment of GBS.

Myasthenic crisis

MG is an autoimmune disorder affecting the post-synaptic acetylcholine receptors in the neuromuscular junction. It is clinically characterized by fluctuating weakness and fatigability with early involvement of facial and bulbar muscles. A myasthenic crisis (MC) is defined by the development of respiratory failure. The diagnosis can be confirmed by serology and electrophysiology (repetitive nerve stimulation leading to a decremental response). Patients with anti-MuSK may be at higher risk of developing episodes of MC.

Although MC shares some features with GBS, they differ in some very important ways. In MG, the muscles are fatigued because of the failing neuromuscular transmission. Yet, if promptly supported, the muscle function can improve (unlike the situation in GBS in which once the motor failure is established, it will not recover until the nerves heal). In addition, patients with MC do not have prominent dysautonomia. These two major differences make MC patients excellent candidates for early support with non-invasive ventilation using BiPAP. Early institution of non-invasive ventilation with BiPAP can actually alter the course of a myasthenic exacerbation and prevent a full-blown crisis or substantially decrease the duration of ventilatory support.

Immunomodulatory therapy with PLEX or IVIG is considered standard of care for patients with MC, although all trials evaluating these therapies have been conducted in patients with MG exacerbation rather in patients with true MC (i.e. patients in these trials did not have respiratory failure requiring ventilatory support). Thus, there is no proof that these treatments reduce the duration of mechanical ventilation requirement. Yet, their use in MC is very reasonable given the strong evidence supporting their value in improving weakness in less severely ill myasthenic patients. PLEX and IVIG have comparable efficacy, but IVIG might be associated with lower risk of complications and lower cost. As with GBS, both treatments are good options and the choice can be guided by local practice and experience.

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We recommend continuation of the corticosteroid in patients already receiving it and cautious initiation in those who were not because steroids can induce worsening weakness within days of its first initiation. This is not a major problem in intubated patients, but can be very problematic in patients supported with BiPAP. Pyridostigmine should be continued in patients on BiPAP, but can be temporarily stop in intubated patients with abundant secretions. In such cases, the medication must be restarted in anticipation of the first trial of ventilatory weaning.

Lastly, need for reintubation is a relatively common problem in patients with MC. Use of BiPAP for a few hours after extubation, and particularly during the first night, can be useful to decrease the risk of reintubation.

Critical Illness Neuromyopathy (ICU acquired weakness)

Critically ill patients in the ICU can develop severe weakness of limb and respiratory muscles from an axonal polyneuropathy (critical illness polyneuropathy) or a myopathy (critical illness myopathy), which are often combined. It may occur in over 50% of patients with severe sepsis and multiorgan failure who have been ventilated for more than 72 hours, and it is a common cause of failure to wean from mechanical ventilation.

Diagnosis is based on history and examination and it can be confirmed by electrophysiology and nerve and muscle biopsies. Patients typically exhibit generalized, symmetric flaccid weakness of all extremities along with weakness of ventilatory muscles. However, facial and ocular muscles are usually not involved. Deep tendon reflexes are depressed or absent if the nerves are involved. Sensory function is no affected. Electrophysiological studies can be useful to confirm the diagnosis and differentiate between degrees of nerve and muscle involvement. Critical illness polyneuropathy shows reduced amplitude of compound muscle and sensory nerve action potentials with normal or mildly diminished conduction velocities. Meanwhile, critical illness myopathy is characterized by myopathic motor unit potentials, often with abnormal spontaneous activity (fibrillation potentials and positive sharp waves). Prolongation of compound muscle action potentials may be the earliest sign of critical illness myopathy. Muscle biopsy in critical illness polyneuropathy may exhibit signs of acute denervation with atrophy of types 1 and 2 fibers; grouped atrophy is seen in advanced cases. Nerve biopsy in these patients shows signs of an axonal neuropathy.

Treatment is supportive. Early mobilization may help prevent this complication. Recovery is generally slow and it may incomplete. Prognosis is particularly less favorable in the elderly and in patients with predominant polyneuropathy.

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