Dealing with ICU-acquired weakness

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Acquired generalized muscle weakness is a frequent problem in the Intensive Care Unit (ICU). Most often, this condition is encountered in patients with no history of neurological disease prior to admission to the ICU. A number of terms are used to describe ICU-acquired weakness: critical illness polyneuropathy (CIP), critical illness myopathy (CIM), critical illness polyneuromyopathy (CIPNM or CRIMYNE), acute quadriplegic myopathy (AQM) and ICU-acquired weakness or paresis [1-4]. Although the term CIP is often used, muscle biopsies may also show abnormalities indicating primary involvement of muscle tissue [5,6]. Therefore, the term ICU-acquired weakness (ICU-AW) was proposed in a recent review [1]. However, the designation ICU-AW does not make a distinction between neuromuscular (or peripheral) and central nervous system causes of muscle weakness. However, for the purpose of this article we will use ‘ICU-AW’ only for neuromuscular causes of weakness.

Intensivists frequently encounter patients who, after several days or weeks of mechanical ventilation and sedation, regain consciousness with symmetrical absence of voluntary movements of the limbs. When the patient has regained consciousness but is still not, or only barely able, to move their extremities the diagnosis ‘critical illness polyneuropathy’ (CIP) is frequently made on clinical grounds. Therefore, the term ICU-acquired weakness (ICU-AW) was proposed in a recent review [1]. However, the designation ICU-AW does not make a distinction between neuromuscular (or peripheral) and central nervous system causes of muscle weakness. However, for the purpose of this article we will use ‘ICU-AW’ only for neuromuscular causes of weakness.

Another important question is whether electrophysiological tests are necessary to confirm ICU-AW or if clinical examination in the appropriate clinical setting is sufficient. Electrophysiological testing has superior sensitivity in the detection of critical illness-related neuromuscular disorders [2]. However, the clinical importance of finding electrophysiological evidence of polyneuropathy without muscle weakness in a critically ill patient is unclear. Morris and Trinder [7] have argued against the use of electrophysiology in the diagnosis of ICU-AW, because the result of a small case series failed to alter the diagnosis made on clinical grounds and failed to predict outcome and duration of respiratory support. In addition, needle EMG may not be entirely without risks in patients with sepsis and coagulation abnormalities. The same authors have proposed criteria to make a clinical (or bedside) diagnosis of ICU-AW without EMG. These criteria are: onset of flaccid, hyporeflexic weakness, after 7 days of either 1) systemic inflammatory response syndrome, 2) multi-organ dysfunction syndrome, 3) sepsis, and 4) mechanical ventilation with normal serum phosphate, potassium and magnesium concentration. We would like to add normal creatine kinase (CK) to this list to exclude inflammatory or hereditary myopathies that present with failure to wean from mechanical ventilation, and myonecrosis [8]. According to the authors, the presence of one of the following criteria excludes the clinical diagnosis of ICU-AW: 1) weakness before or causing admission, 2) cranial nerve dysfunction (grimacing on painful stimuli without movement of the limbs is quite typical), 3) lateralizing signs/hyperreflexia (we would also like to add: sensory level and other evidence of central motor neuron dysfunction such as Babinski’s sign, whereas normal reflexes do not exclude the diagnosis), 4) autonomic dysfunction, or 5) use of muscle relaxants in the previous 48 hours/abnormal train-of-four response [7]. We agree that there are no
strong arguments for carrying out an EMG in patients fulfilling the proposed criteria. However, if there is any doubt about the diagnosis, e.g. fluctuating weakness including ptosis during the day (such as may occur in myasthenia), electromyography should be strongly considered. Detailed neurological examination is a prerequisite to differentiate ICU-AW from other causes of quadriparesia or quadriplegia, such as cervical myelopathy, thereby warranting neurological consultation in many cases. Finally, a lasting and fixed neurological deficit without any evidence of recovery over the course of several weeks is atypical and a reason for further investigation.

Can we prevent ICU-AW? Several studies have identified prognostic variables that predict ICU-AW. In a study by De Jonghe et al. [9] corticosteroid administration was the strongest independent risk factor for ICU-AW (OR 14.9, 95% CI 3.2 to 69.8), followed by female sex (OR 4.66, 95% CI 1.19 to 18.3), number of days with dysfunction in ≥2 organs (OR 1.28, 95% CI 1.11 to 1.49) and duration of mechanical ventilation (OR 1.1, 95% CI 1.0 to 1.22). This study included only patients who had regained consciousness on the ventilator, were cooperative after at least 7 days of mechanical ventilation, and whose paresis score graded by the Medical Research Council score (MRC) was at most grade 4 (on a scale of 0 [no movement] to 5 [normal strength]) in all four extremities. These patients seem to most accurately represent the patients with ICU-AW we encounter in daily practice. Other studies have examined prognostic factors for ICU-AW as determined by EMG, which may not be as clinically relevant as weakness assessed at the bedside in a cooperative patient [2]. A recent systematic review confirmed an association between ICU-AW and several risk factors (glucocorticoid use, neuromuscular blocking agents, severity of illness, hyperglycaemia, and renal replacement therapy) only in some studies. However, a relation between the positive studies and methodological quality was not reported [10]. Notably, several randomized clinical trials using corticosteroids in ICU patients reported conflicting results on the association with ICU-AW [11,12,13]. Therefore, the issue of the glucocorticoids as a cause of ICU-AW seems unresolved at this time. Large randomized trials showed that the duration of mechanical ventilation can be shortened with interruption of sedation [14] and a combination of awakening and spontaneous breathing trials [15]. Unfortunately, these RCTs did not report on the incidence of ICU-AW. Intensive insulin therapy was associated with both a reduced requirement for prolonged mechanical ventilation and ICU-AW [16]. In short, it seems that some interventions that have been shown to improve the outcome of ICU patients may also decrease the incidence of ICU-AW, but no interventions have proven effective in specifically decreasing the risk of developing ICU-AW.

In conclusion, ICU-AW is a general designation for the heterogeneous entity of critical-illness-related neuromuscular disorders, mostly consisting of CIP, CIM or a combination. We would like to conclude:

- Care should be taken not to be too negative about the prognosis of neuro-ICU patients with impaired consciousness, based on the motor score if the diagnosis of ICU-AW has not been excluded.
- Clinical examination by a consulting neurologist without confirmatory electrophysiology is probably sufficient to diagnose ICU-AW in typical cases. If this is not the case, electromyography should be considered.
- Interventions that improve outcome in ICU patients may also (but not specifically) decrease incidence of ICU-AW.

References