Intensive care unit acquired weakness

Christopher Taylor

Abstract

Intensive care unit acquired weakness (ICUAW) is an acute clinical weakness that occurs in approximately 50% of ICU patients and is directly attributable to their critical care stay where other causes of weakness have been excluded. The condition is characterized by diffuse limb and respiratory muscle weakness with a relative sparing of the cranial/facial muscles and the autonomic nervous system. Patients with ICUAW are classified into three conditions: critical illness polyneuropathy (CIP), critical illness myopathy (CIM) or critical illness neuromyopathy (CINM) based on clinical criteria and further defined by electrophysiological studies and muscle biopsies. ICUAW is often a manifestation of immobility or a systemic inflammatory response syndrome especially in long-term ventilated patients who have had systemic sepsis/multiorgan failure or exposure to high-dose corticosteroids, neuromuscular blockers or hyperglycaemia. It is associated with prolonged weaning from mechanical ventilation, increased mortality/length of ICU stay and long term disability.

Keywords Critical illness; critical illness myopathy; critical illness neuropathy; electrophysiology; intensive care unit acquired weakness; muscle weakness

Royal College of Anaesthetists CPD Matrix: 2C00

Learning objectives

After reading this article, you should be able to:

- define intensive care unit acquired weakness and its subcategorization
- list the differential diagnosis of critically ill patients with generalized weakness
- understand the risk factors for developing intensive care unit acquired weakness
- outline the principles of management of patients with intensive care unit acquired weakness

Introduction

The first subtype of intensive care unit acquired weakness (ICUAW) – Critical illness Polyneuropathy (CIP) – was first described by Dr Charles F. Bolton in a series of five patients in 1984.[1] As ICU survival rates have continued to improve over the last 30 years, the diagnosis of ICUAW has been increasingly described in critically ill patients and is now a significant factor affecting the quality of life of patients following their ICU stay.

Definition and classification

ICUAW is defined as clinically identifiable weakness acquired in a critical care patient that is directly attributable to their critical care stay where other causes of weakness have been excluded. Patients with ICUAW are classified into critical illness polyneuropathy (CIP), critical illness myopathy (CIM) or critical illness neuromyopathy (CINM). CIM is further classified based on histological appearances into cachectic myopathy, thick filament myopathy and necrotizing myopathy.

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Incidence

ICUAW is a relatively common entity; while the exact incidence is unknown, it is estimated that between 30% and 57% of patients staying in the ICU longer than 7 days will be diagnosed with this condition.

Aetiology and predisposing factors

The cause of ICUAW is almost always multifactorial. Studies have identified certain cohorts of ICU patients as being particularly at risk. These include those patients that have had: prolonged immobility and mechanical ventilation (>7 days), multi organ failure and severe sepsis or those exposed to high doses of corticosteroids (>10 g over 1–2 weeks), hyperglycaemia and neuromuscular blocking agents over 3–5 days especially in the management of acute obstructive pulmonary disease or post-organ transplant.[2] According to the literature, the risk factors can be classified according to 'probable' or 'possible'; these are given in Table 1.

Immobilization

A certain degree of immobility is unavoidable in a sedated patient receiving mechanical ventilation. The inevitable muscle wasting can very quickly lead to muscle weakness especially with regard to the diaphragm where a short period of inactivity has been shown to lead to atrophy and severe dysfunction.

Neuromuscular blocking drugs

The use of these agents are obviously linked with long-term ventilation and they exacerbate muscle immobilization; their accumulation may also have a direct toxic effect on skeletal muscle, or increase its susceptibility to corticosteroid-mediated muscle weakness. Neuromuscular blockers should be used only when necessary and if a continuous infusion is deemed necessary, agents whose metabolism is independent of renal and hepatic function should be selected in order to reduce the chance of accumulation.

Corticosteroids

The role of corticosteroids in ICUAW is complex. Animal studies have shown structural changes in skeletal muscle similar to that seen in critically ill patients. Clinical studies, however, reveal conflicting results.

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Risk factors for ICUAW

Probable	Possible
Severe sepsis/septic shock	Age
Multiorgan failure	Female gender
Prolonged mechanical ventilation/ prolonged bed rest	Severity of illness on admission
	Admission APACHE II score
Increasing duration of SIRS	Hypoalbuminaemia
Increasing duration of multiorgan failure	Hyperosmolality
	Parenteral nutrition
Hyperglycaemia	Renal replacement therapy
	Vasopressors
	Corticosteroids
	Neuromuscular blocking agents
	Aminoglycosides

Table 1

Hyperglycaemia

Hyperglycaemia is an independent risk factor for ICUAW, and therefore strict glucose control has been advocated in order to reduce the occurrence of ICUAW in critically ill patients.

Pathophysiology

The pathophysiological mechanisms underlying ICUAW are thought to be multifactorial, and various processes have been proposed. The dysfunctional microcirculation characteristically associated with sepsis and critical illness may lead to neuronal injury and axonal degeneration. This axonal damage may be particularly important in the development of CIN. The oxidative stress associated with systemic inflammation has also been suggested as an important mechanism responsible for ICUAW. Other proposed mechanisms include sodium channel inactivation and mitochondrial dysfunction, as well as protease-mediated muscle breakdown. None of these mechanisms are mutually exclusive and it is likely that all play their part to varying degrees.

Clinical features

The commencement of weakness usually occurs at least 1 week after the onset of the critical illness. One of the earliest signs elicited is facial grimacing in response to stimulation with no associated limb movement. It is characterized by diffuse, symmetric limb (hip girdle and shoulders) weakness with relative sparing of the cranial/facial muscles and the autonomic nervous system but importantly, respiratory muscle weakness occurs that often impedes ventilator weaning. In patients who are not intubated, the respiratory manifestations of ICUAW may include rapid shallow breathing, the use of accessory respiratory muscles and paradoxical abdominal movement on inspiration suggestive of diaphragmatic weakness. Other signs may include a hoarse or nasal voice, breathlessness when talking ('staccato speech') and an ineffective cough leading to the accumulation of bronchial secretions, atelectasis and the risk of aspiration. Muscle wasting may not be immediately apparent as it may be concealed by dependent limb oedema. Extra-ocular muscle involvement is uncommon. It is often difficult to distinguish be myopathy and neuropathy on clinical examination, one crucial difference is that in CIM peripheral nerve sensation remains intact unlike in CIP where there is distal sensory loss of pain, temperature and/or vibration sensation. Neurological examination should include an assessment of consciousness, cognition, cranial nerves, motor and sensory signs as well as deep reflexes and coordination. The assessment of limb muscle power is via the Medical Research Council (MRC) sum score (Box 1). This involves the assessment of muscle power from three movements of each limb bilaterally: shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension and ankle dorsiflexion. The maximal power obtained for each movement is graded 0–5 and a total sum score out of 60 is calculated.

Investigation and diagnosis of ICUAW

The first question to be answered is: when was the onset of weakness first identified? This can be established from a review of the clinical history. The answer is of fundamental importance because the diagnosis of ICUAW can only be made if the onset of the weakness occurs during and usually at least, 1 week after the onset of the critical illness. If weakness preceded or was implicated in the reason for the ICU admission, then one should be seeking an alternative diagnosis other than ICUAW. This alternative differential diagnosis is vast and is revealed in Table 2. An alternative diagnosis will usually include a neurology referral and multiple investigations including blood tests (electrolytes, creatine kinase, erythrocyte sedimentation rate, auto-antibodies), lumbar puncture, neurophysiological assessment (nerve conduction studies, EMG) and a magnetic resonance scan of the brain/spinal cord.

ICUAW is quite often a diagnosis of exclusion. It is a clinical diagnosis that will only need further investigation if there is diagnostic uncertainty, there is no improvement after 1–2 weeks or the weakness is very severe. The criteria for the diagnosis of ICUAW are shown in Box 2. Neurophysiology (nerve conduction studies and electromyography), nerve and muscle biopsies are helpful in diagnosing and distinguishing between the subcategories of ICUAW. The criteria for the diagnosis of subcategory of ICUAW are shown in Box 3.

Neurophysiological investigations

Neurophysiology investigations are undertaken by neurophysiologists and consist of the application of skin and fine-needle electrodes to stimulate nerve and muscle activity. They are essential in order to help to differentiate neuropathy from myopathy and form part of the criteria distinguishing CIP from CIM and CINM and can be helpful to refine prognosis. The types of tests are:

MRC sum score of muscle weakness

0 No muscle movement
1 Flicker
2 Movement, but not overcoming gravity
3 Movement, overcoming gravity
4 Movement against resistance
5 Normal power

Box 1

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