The use of neuromuscular blockers to facilitate mechanical ventilation in severe asthma

Ensuring adequate oxygenation and ventilation in patients with severe asthma can be challenging. Although no randomized trials have been performed, neuromuscular blockade is a useful adjunct in the care of severe life-threatening asthma with respiratory failure. Neuromuscular blockers can prevent respiratory dysynchrony, help lower peak pressures and allow longer expiratory times to reduce dynamic hyperinflation and its attendant risk of barotraumas and pneumothorax. Patients with severe life-threatening asthma and respiratory failure are often young, male and can be difficult to sedate.

Neuromuscular blockers have been associated with prolonged muscle weakness following prolonged infusions (increased incidence >24 hours; Leatherman et al, 1996). Critical illness itself can cause acute muscle weakness, in a spectrum of polyneuromyopathy, with neuropathy or myopathy predominating depending on the individual case. Along with neuromuscular blocking agents other treatments for severe asthmatics can lead to muscle weakness, such as beta-2 agonists, corticosteroids, theophylline, magnesium and aminoglycosides.

This case highlights the problems particular to the ventilatory management of severe life-threatening asthma. A 38-year-old man presented to the authors' accident and emergency department with signs of acute life-threatening asthma. He was centrally cyanosed, gasping with a silent chest and so he required immediate tracheal intubation and mechanical ventilation.

Despite maximal medical therapy including infusions of salbutamol, aminophylline, magnesium and hydrocortisone, he proved very difficult to sedate and ventilate with persistent wheeze and high airway pressures (plateau pressures greater than 30 cmH_2O). Neuromuscular paralysis was administered with a vecuronium infusion, for a total of 4 days. On day 3 he had a small rise of creatinine kinase to 2334 u/litre but by day 13 this had risen sharply to 510 000 u/litre. Vecuronium was stopped and he received large volume fluid resuscitation and urinary alkalisation but despite this developed acute oliguric renal failure and required renal support. His recovery was slow and complicated by severe muscle weakness. Nerve conduction studies suggested a critical illness neuropathy. The authors were unable to get accurate electromyography results because of the patient's peripheral oedema but a muscle biopsy showed extensive necrotizing myopathy. Histologically this is usually seen as large numbers of regenerative fibres and utrophin staining.

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Discussion

Muscle weakness following mechanical ventilation for severe asthma was first described in a case of a severe myopathy (Macfarlane and Resenthal, 1977), and rates of up to 30% have been reported (Behbehani et al, 1999). Corticosteroids are known to cause myopathy, and together with an aminosteroid neuromuscular blocking agent (such as vecuronium) there may be a 'two-hit' hypothesis (Schweickert and Hall, 2007).

The causes of weakness in the intensive care unit setting are multifactorial: critical illness can cause generalized muscle weakness and a lot of the anti-asthmatic drugs can also contribute, as can pyrexia and metabolic disturbances.

The authors felt that this rhabdomyolysis was principally caused by vecuronium infusion causing a necrotizing myopathy. Rhabdomyolysis has been described in status asthmaticus (Chugh et al, 1978). Factors such as repeated coughing, increased use of accessory muscles and diaphragm are all analogous to strenuous exercise, known to cause rhabdomyolysis (Chugh et al, 1978).

Leatherman et al (1996) retrospectively reviewed 107 patients with severe asthma needing mechanical ventilation. The incidence of muscle weakness was highest in patients who received a combination of neuromuscular blockers and corticosteroids. There was no evidence of weakness in patients that only received corticosteroids. Of note the risk of weakness was not reduced by the use of atracurium (a non-steroidal neuromuscular blocking agent).

If neuromuscular blocking agents are used to facilitate mechanical ventilation they should be used with caution, at the lowest possible dose. Neuromuscular monitoring (such as train of four) should be used whenever neuromuscular blocking agents are used to prevent overdose. Most recommendations for train of four monitoring suggest drug titration to one or two twitches but also clinical bedside evaluation, i.e. sufficient to maintain ventilator synchrony and prevent clinical movement. Bolus doses could be considered (as opposed to infusion) to limit total dose and to allow partial return of muscle function and therefore evaluation of the need for further doses (Behbehani et al, 1999). Daily measurement of creatinine kinase levels should be monitored, and any rise should prompt early treatment of any impending rhabdomyolysis. Other general measures should be used, including weaning the corticosteroids as quickly as possible together with prompt treatment of metabolic disturbance and pyrexia. **BJHM**

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