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Neuromuscular blocking drugs in the intensive care unit: Introductory remarks

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In 1983, a letter [1] appeared in the columns of the Lancet from Professor Ledingham and Dr Watt in Glasgow which reported an unexpectedly high mortality rate and low cortisol levels in multiple trauma patients requiring mechanical ventilation who had received etomidate by infusion for long-term sedation. The letter was at first received with incredulity; how could a drug used to care for the comfort of critically ill patients do any harm? Detailed examination subsequently supported this association by using the injury severity score to exclude an increase in severity of illness as the cause for the increase in mortality [2], while others demonstrated the potent inhibitory effect of etomidate on the biosynthesis of both cortisol and aldosterone [3]. This effect had gone undetected despite the testing of etomidate in the operating theatre in numerous clinical trials at a time of particular interest in stress reponses to surgery and anaesthesia.

The etomidate story carries a number of morals relevant to this symposium. First, there is no such thing as an innocuous drug. Second, drugs tested in relatively fit populations, or in patients with stable single organ-system failures such as cirrhosis or chronic renal failure, may display very different pharmacokinetic and dynamic characteristics when applied to critically ill patients with multiple organ failure in an intensive care unit. Third, it may be very difficult to differentiate the effects of the drug from those of the disease in such patients, and stratification for severity of illness should be an integral part of studies of drug safety.

Neuromuscular blocking drugs have had a major impact on the conduct of anaesthesia and surgery, but their role in intensive care is less well defined than in the operating theatre. Their use in intensive care units in the United Kingdom, once frequent [4], has tended to decline over the years [5], and one suspects that the same phenomenon may have occurred in other countries as advances in ventilator technology have allowed assisted modes of mechanical ventilation. The original view of curare as an arrow poison may also have inhibited the casual use of relaxants by non-anaesthetic medical staff. Despite this, there is no consensus about the type of drug which should be used, what the aims of neuromuscular blockade should be, which patients should receive them, how their use should be monitored, and whether there are hazards associated with their use in critically ill patients. Late in 1992, the FDA held an enquiry [6] into neuromuscular blocking drugs, particularly the steroid-based relaxants, in intensive care, because of a perceived association between the use of these agents and the development of prolonged muscle weakness in critically ill patients [7].

This supplement to Intensive Care Medicine is the publication of a symposium that addressed a number of these issues. We had no remit, and did not attempt, to produce a consensus about the use of neuromuscular blocking drugs in intensive care, but have drawn together contributions from experienced individuals from which the reader may make informed decisions. It is clear that both nerve and muscle function may be deranged in patients with multiple organ failure; and if muscle relaxants must be used, it makes sense to employ agents with the most predictable kinetics and fewest adverse effects and to monitor their effect on neuromuscular transmission. Muscle relaxants should never be used as a substitute for adequate analgesia and sedation, or for investigating the reason for the failure of analgesic sedation to provide adequate conditions for organ-system support. Individual intensive care units should establish clear policies for the use of relaxants, and we hope that this symposium may contribute to the development of an international consensus about the place of these drugs in the supportive care of patients with critical illness.

References

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