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Postal survey on the long-term use of neuromuscular block in the intensive care

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Abstract *Objective:* To assess the long-term use of neuromuscular blocking (NMB) agents in intensive care, expecially with reference to the potential problems of the long-term use of NMB drugs in the intensive care unit (ICU).
Method: A postal survey questionnaire was sent to 409 ICUs in Great Britain.
Results: Two hundred thirty-eight completed questionnaires were returned and analysed. Most ICUs were anaesthetist-led (85.8%) with only five ICUs being staffed by full-time intensivists. Facilitation of mechanical ventilation and increased intracranial pressure were the main indications for the prolonged use of neuromuscular blockade. Atracurium and vecuronium (83%) were administered most commonly by bolus alone (13.8%), bolus followed by continuous infusion (23.9%) or continuous infusion only (60.9%). The most frequently cited criteria for the use of either vecuronium or stracurium were their pharmacokinetics and haemodynamic stability. Neuromuscular block was most commonly monitored clinically (91.7%), with only 8.3% of the responders using a peripheral nerve stimulator. All responders indicated the concomitant use of sedatives (propofol/midazolam alone or in combination in 89.4% of responders) and/or opioids (morphine, fentanyl or alfentanil in 74.8% of respondents) with muscle relaxants.

Conclusion: Most responders agreed that while neuromuscular block in the ICU population may provide advantages, it cannot be considered benign. Indeed, a great majority consider that NMB agents should be used only as a last option and for as short a period as possible.

Key words Neuromuscular blocking agents · Intensive care unit · Long-term use · Survey

Introduction

A recent US study surveyed the practice patterns of "anesthesiologist-intensivists" regarding their use of neuromuscular blocking (NMB) drugs for prolonged periods in critically ill patients [1]. The drugs were administered routinely by this sub-speciality group with concurrent sedatives and/or analgesics. The most frequent indications reported by this group for neuromuscular block were to: 1) facilitate mechanical ventilation, 2) maintain the patient in a motionless state, 3) help limit oxygen consumption, 4) treat severely agitated patients (where sedation and analgesia were inadequate), 5) aid in the treatment of patients with severe rigidity (tetanus or neuroleptic malignant syndrome) and 6) facilitate the performance of various procedures. The survey also emphasised the lack of guidelines or recommendations on the use of these drugs in this population.

The method of administering NMB agents to the patient in an Intensive Care Unit (ICU) varies between clinicians and is based on clinical experience. However, concern regarding the serious consequences that may occur during continuous neuromuscular block has also had an impact upon their use. In addition, recently published case reports and small clinical series [2–5] from several medical centres have drawn attention to a dangerous but still unrecognised complication of long-term neuromuscular block, notably that patients who receive NMB drugs continuously for more than 48 h to facilitate mechanical ventilation remain profoundly weak long after the drug has been discontinued. Several important issues need to be examined regarding the use of neuromuscular block in the critically ill. Which is the best NMB drug for use in the ICU? Should the effects of neuromuscular block be monitored and how completely should patients be paralysed? Is there a limit to the duration that NMB drugs can be safely administered?

Formerly NMB agents were frequently used in British ICUs [6] but this practice has declined in recent years [7]. With recent advances in ventilation techniques that have allowed "patient-friendly" assisted modes of ventilation, the present survey was performed to determine the preferences of British intensivists in the use of NMB drugs in the critically ill patient.

Table 1 Survey questionnaire

1. a) Type of intensive therapy unit: general/surgical/specialist surgical/medical/paediatric
   b) Is the ITU run mostly by: anaesthetists/surgeons/physicans/paediatrician/other
2. Number of beds open
3. Type of hospital: teaching/DGH/specialist
4. a) Size of hospital
   b) Average number of patients treated on your ITU per month
5. Number of patients requiring neuromuscular blockade per month
6. Average number of patient-days on neuromuscualr blockade (use your most recent month as an example)
7. What are your general indications for neuromuscular blockade?
8. a) Which muscle relaxant do your use regularly?
   b) What criteria do you use in choosing a neuromuscular blocking agent?
9. a) Mode of delivery of neuromuscular blocking agent
   b) If intermittent boluses are used, who decides whether the patient need another bolus?
   c) What technique do they use to determine redosing?
10. a) Do you routinely monitor neuromuscular blockade on ITU?
    b) If clinical monitoring is used, what parameters are followed?
11. What sedatives/narcotics do you use with neuromuscular blockade?
12. How do you assess the adequacy of sedation/analgesia?
13. a) How do you decide to discontinue neuromuscular blockade?
    b) Do you routinely use neuromuscular blockade antagonists?
    c) If yes to 13b), which agents do you use?
    d) Do you think it is important to stop neuromuscular blockade on a periodic basis for comprehensive patient evaluation? (e.g. every 24 h for a complete neurological assessment)
    e) If yes to 13c), list the time interval in hours
    f) If yes to 13d), do you allow the agents to wear off spontaneously or do you antagonise them?
14. a) Do you think there is a place for a new neuromuscular blocking agent for use in the intensive therapy unit?
    b) If yes to 14a), what properties should it have?
15. Do you have any additional comments on your experience with neuromuscular blocking agents that dictates your clinical practice?

Materials and methods

A 26-question, multiple-choice survey (Table 1) was constructed in order to address these issues. A list of current adult and paediatric ICUs in Great Britain was obtained from the Directory of Emergency and Special care units 1994 (CMA Medical Data Ltd., Cambridge, U.K.). The total number of eligible ICUs was 409. The questionnaire, and a brief covering letter with background information on the rationale of the study, was sent to the director of each unit.

Results

Of the 409 sent 238 (58.2%) completed questionnaires were received and analysed. The majority of replies (80%) were from general ICUs (Table 2). Two-thirds of the responders were from ICUs based in district general hospitals (64.7%) while 26.9% were in University teaching hospitals and 8.5% units were in "specialist" hospitals. Specialist hospital ICUs were the largest with an average of 9.3 beds (range 5–26), while university hospital ICUs had, on average seven beds (range 4–20). District general hospital ICUs have fewer beds, on average 4.6 (range 3–14). Most ICUs were anaesthetist-led (85.8%), with only five ICUs staffed by full-time intensivists. Overall, on average five patients required NMB for a period exceeding 24 h/month (range 0–25). However, the prolonged use of NMB in paediatric ICUs was greater despite the smaller size of these units, with an average of 11 patients/month (range 6–25). NMB was used most frequently for

Table 2 Type of Intensive Care Unit (ICU) expressed as a percentage of total number of replies ($n = 238$)

Type of ICU	% or replies ($n = 238$)
General	80
Surgical	1
Neurosurgical	4
Cardiac	7
Medical	2
Paediatric	7

facilitation of mechanical ventilation (41%). Other indications included patients with head injury and increased intracranial pressure (29%) and patients with critical oxygenation (13%). Further indications were tetatnus, and severe rigidity in patients with neuroleptic malignant syndrome.

NMB agents with an intermediate duration were the most popular NMB drugs used in ICUs (83%). Pancuronium and other NMB drugs were used by 16% of responders. The most frequently cited criterion for the selection of atracurium and/or vecuronium was pharmacokinetic profile (duration of action, drug metabolism). Other cited criteria were minimal haemodynamic effects, lack of side effects, ease of use, cost and familiarity. Most units used continuous infusion as the primary mode of delivery of these NMB drugs with 60.6% using continuous infusion only, 23.9% using bolus dose followed by continuous infusion. However, 13.8% of the ICUs used bolus only. In these ICUs, the decision to give a bolus was taken by the nurses in 85% of the cases.

In the majority of units (91.7%), neuromuscular block was monitored using a variety of clinical indicators, relying upon the subjective opinion of trained nurses and doctors aided by autonomic responses to various stimuli. Routine peripheral nerve stimulator monitoring was used in only 8.3% of the units. All responders indicated the concomitant use of sedatives and/or opioids during neuromuscular block. Propofol was used as frequently as midazolam. Morphine was used by 74.8% of the responders. However, only half of the ICUs regularly used a sedation scoring system [8] to assess sedation. More than half (52.8%) of the ICU stopped NMB agents routinely after at most 24 h to assess neuromuscular function clinically. In 85.8% of ICUs, neuromuscular block was stopped when patients were clinically stable. In a small number of units (2%) the neuromuscular block was antagonised routinely.

More than two-third of the responders (68.4%) said that there was no need for a new neuromuscular blocker dedicated to long-term use in the critically ill. However, almost a third (31.6%) though that such a drug was desirable. This new muscle relaxant should have a better pharmacokinetic profile with no cumulation, should be suitable for long-term use in patients with multiorgan failure, should be devoid of side effects (no histamine release, good cardiovascular stability) and should not be expensive. Most of the responders agreed (92.6%) that while long-term neuromuscular block in the ICU may provide advantages, the use of muscle relaxation in the critically ill is not benign.

Discussion

NMB drugs have been used widely in the ICU since the 1960s, probably because of the increasing use of mechanical ventilation and the increasing prevalence of adult respiratory distress syndrome (ARDS) [9]. The goal of our survey was to assess the practice patterns of the use of NMB drugs in the ICU in the 1990s, especially with the advent of newer muscle relaxants. The 58.2% response rate was more than we expected from a single mailing survey, for which response rates of about 40% are the norm [10]. However, we need to take into account the possibility that the 42% of non-responders may or may not have similar clinical practice characteristics. Statistically, the non-responders tend to be less familiar with and/or less interested in the subject of the survey. Our survey represents the views of multispeciality intensivists, regarding the use of NMBs in the ICU. The results may be biased by the responses of the large number of anaesthetist-intensivists (more than 80%), but this only reflects the fact that most ICUs in Great Britain are anaesthetist-led.

Long-term neuromuscular block in the ICU is provided most commonly to facilitate mechanical ventilation. In critically ill patients neuromuscular block may be needed to decrease catabolism and the work of breathing, if ventilation cannot be supported adequately with sedation alone [11, 12]. Some of the newer forms of mechanical ventilation, such as high-frequency jet ventilation, airway pressure-release ventilation, pressure-controlled inverse-ratio ventilation, permissive hypercapnia and extracorporeal membrane support, may require sedation with the addition of a NMB drug in order to optimise their effectivity [12, 13]. These NMB drugs may be of benefit as they increase chest wall compliance, allow synchronisation of mechanical ventilation, lower peak pressures and decrease oxygen consumption [14].

While they may be benefits in terms of more efficient mechanical ventilation and better gas exchange, the use of NMB drugs is not without risks: catastrophic hypoxia if there is unrecognised disconnection or ventilator malfunction, increase in ventilation-perfusion mismatch [15], inability to cough with the accumulation of secretions, severe disuse muscle atrophy with delay in weaning and residual weakness persisting for periods of up to 6 months [16]. In addition, neurological examination is impaired, thus focal or localising signs might be missed leading to a delay in treatment which could be serious in some circumstances (e.g. the spread of a subdural haematoma). Thus, despite the numerous advantages provided by the use of neuromuscular blockade in the critically ill, the casual use of NMB agents in the ICU is not without problems.

In our study, most ICUs used exclusively the intermediate acting NMB drugs, such as atracurium and vecuronium, because of their pharmacokinetic properties and relative lack of side effects [16]. This contrasts with the U.S. study, but may reflect the fact that most British ICUs are anaesthetist-led. However, the use of these drugs has not been without problems, such as paralysis following

prolonged neuromuscular blockade with vecuronium [17], haemodynamic instability because of histamine release [18] and potential central nervous system toxicity secondary to metabolites [19, 20] with atracurium. Several responders reported that they had switched from vecuronium to using atracurium, in the light of recent case reports and studies showing the association of vecuronium with prolonged paralysis in patients with renal failure and hepatobiliary disease [21, 22] and also the onset of a "severe myopathy" after prolonged treatment with vecuronium and glucocorticosteroids [23].

Particularly noteworthy are the numerous reports describing otherwise healthy asthmatic patients who remains quadriparetic for many days after simultaneous treatment with a corticosteroid and vecuronium for acute respiratory failure [24, 25]. Thus, the use of atracurium for long-term neuromuscular block in the ICU has been advocated because of the relative lack of published reports of severe muscle weakness lasting for more than 12 h after the discontinuation of prolonged use of atracurium. However, recently Coursin and colleagues have reported two cases of prolonged paralysis after infusion of atracurium [26]. We also found out that in a great majority of units (>90%), neuromuscular block was monitored only clinically. Although clinical signs are important, the standard of care in assessing neuromuscular block should be evaluated using a peripheral nerve stimulator [27]. Indeed, the degree of block required differs for each patient, as it is often not necessary to provide complete and total neuromuscular block in each patient. A regimen to monitor neuromuscular block has been recommended recently [2], which allows for titration of NMB agents according to the appearance of one or two twitches following "train of four" stimulation. This method also allows for the detection of residual paralysis and may thus eliminate overdosing of NMB agents, particularly in patient with organ system failure. A majority of practitioners (52.8%) thought that it was important to stop neuromuscular block every 24 h for a comprehensive neurological assessment, but only 2% routinely antagonised to neuromuscular block of their paralysed patients.

In summary, the pattern of the use of NMB drugs in ICUs varies considerably. The question of the optimal use of NMB drugs in the ICU remains a challenging one. Objective criteria and guidelines for the long-term use the NMB agents in the ICU do not exist, and there are few data in adults to confirm that outcome is improved by their use. Consequently, it is strongly recommended that maximum effort should be made to achieve effective ventilation with a combination of sedatives and opioid analgesics before the addition of NMB drugs [28]. There will always remain a subgroup of patients whose management is dependent on the judicious use of NMB agents. The challenge is to identify this group, evaluate their therapy and select the most appropriate NMB drug.

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