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The use of neuromuscular blocking drugs in the intensive care unit: A US perspective

M.J. Murray, R.A. Strickland, C. Weiler

Mayo Clinic and Mayo Foundation, Rochester, Minnesota, USA

Abstract. Surprisingly little is known about the use of neuromuscular blockers (NMBs) in intensive care units (ICUs) in the USA. Recently, Klessig et al. [1] surveyed anesthesiologists/intensivists in the USA and found that the 55% who responded used NMBs in the ICU in an average of 10 patients per ICU per month. Anxiolytics and analgesics were administered concomitantly with NMBs, but a majority of respondents did not use electrophysiologic measures of the degree of blockade. Another survey of predominantly medical ICUs also demonstrated widespread use of NMBs, but internists did not use sedation/analgesia as frequently as anesthesiologists for patients receiving NMBs, and infrequently monitored the degree of neuromuscular blockade [2]. Because these were retrospective surveys, we decided to monitor prospectively the use of NMBs in our ICUs. The use of NMBs was ascertained by daily review of pharmacy records and, when use was documented, the patients' hospital records were reviewed. Where information was missing or not found, attending physicians were interviewed. On average, one patient per month per ICU received NMBs. Approximately 5% of neonatal and pediatric, and 1% of adult, ICU patients received NMBs. Eighty-three percent of patients received NMBs to facilitate mechanical ventilation, and mortality was high (51%) in those critically ill patients. More than half the patients were treated for ≤24 h, the remainder for 2 days to >3 weeks. Twitch monitors were used for monitoring the degree of neuromuscular blockade in adult patients, and all patients received sedatives/analgesics. We estimated that the risk of clinically significant, prolonged neuromuscular blockade following the discontinuation of NMBs was 5% per year. Our data demonstrate that NMBs in our practice are used less frequently than previous surveys indicate, that it is possible to change behavior with respect to the use of monitors of neuromuscular treatment, and that clinically significant prolonged blockade was an infrequent but serious problem in this population of critically ill patients.

Introduction

There have been multiple reports of prolonged muscle weakness that extended the length of time on mechanical ventilation in patients who received NMBs in the ICU [3–5]. The incidence of this complication is unknown. Nonetheless, this added concern regarding the use of NMBs in the ICU has resulted in several editorials with specific recommendations regarding the use of NMBs in the ICU [6–9]. The United States Food and Drug Administration (FDA) recently convened an Anesthetic and Life Support Drugs Advisory Committee panel to specifically discuss these concerns, especially with regard to the problem of prolonged weakness following discontinuation of a NMB [10]. Issues of who should administer these drugs, how the NMBs should be monitored, and other possible side effects were also discussed. Two recent national surveys suggest that NMBs are used by most, if not all, anesthesiologists/intensivists, and in 98% of medical ICUs [1,2]. These were retrospective surveys; and, therefore, the frequency of use cited may be unreliable (10 and 19 patients per month in adult and pediatric ICUs, respectively). Anesthesiologists/intensivists were more likely to use sedatives and analgesics concomitantly with NMBs, but neither survey demonstrated widespread use of neuromuscular blockade monitoring.

Since these surveys were published, we have instituted the routine use of twitch monitors using facile assessment of the train-of-four (TOF) in the ICUs in our hospitals. Furthermore, our ICUs are staffed by a multidisciplinary group of intensivists, each of whom has passed the appropriate certifying critical care examination of their speciality. We therefore monitored for a 3-month period the use of NMBs in the Mayo Clinic ICUs to determine if NMBs were used as frequently as reported, whether sedatives and analgesics were concomitantly given, and to determine hemodynamic side effects. We compared these patients with a control group to assess the severity of illness between the two groups, and we also reviewed the records of our chronic ventilator unit to determine the percentage of patients admitted as a result of the prior administration of NMBs.

Methods

We checked the daily logs of our ICU pharmacies to determine which patients were receiving NMBs. In our practice, NMBs are used for those patients in whom gas exchange cannot be optimized

on an FiO_2 of ≤0.6 and in whom airway pressures are excessive (peak airway pressure ≥30–40 cmH_2O, mean airway pressure ≥20–25 cmH_2O, positive end-expiratory pressure [PEEP] ≥10 cmH_2O). Using a survey tool modified from the one developed by Klessig et al. [1] (see Appendix 1), we then reviewed the patients' records to answer the survey. We abandoned a pilot attempt to interview attending physicians personally because of the potential to bias some of the endpoints of the study (hemodynamic changes; concomitant anxiolytics/analgesics). Data were also collected to determine the number of patients admitted to these ICUs over the same 3-month period. We identified other mechanically ventilated patients of the same gender and age (within the same decade), and with the same primary diagnosis, hospitalized in the same ICU at the same time (within 1 week). We calculated APACHE II scores on both groups of patients [11]. We also examined the records of our Chronic Ventilator Unit (Health Care Financing Administration funded) over the previous 3 years, looking specifically for etiologies for admission. Data were expressed as the mean ± standard deviation when appropriate. Parametric data were compared using Student's t-test; non-parametric data were compared using Chi square analysis. A p value of ≤0.05 was used to denote statistical significance.

Results

NMBs were used in 41 patients over the 3-month interval. The ICU specific data along with the number of patients admitted to those ICUs are listed in Table 1. The chances of being admitted to the ICU and receiving a NMB ranged from 0.5% in the coronary care unit to 14% in the neonatal ICU. For adult ICU patients, the chance of receiving a NMB ranged from 0.5–3.0%. The greater the severity of illness, as assessed by a higher APACHE II score, the greater the incidence of receiving a NMB. Patients on NMBs had a mean (± SD) APACHE II score of 24.4 (± 7.8), compared with a score of 11.4 (± 5.1; $p<0.0001$) for age, gender, and primary diagnosis matched patients on mechanical ventilation who did not receive NMBs. The mortality rate (at 30 days) was 51%. Using the medical ICU as an example, of the 21% of patients who required mechanical ventilation, approximately 9% required NMBs. The most frequently cited indication for the use of NMBs was to facilitate mechanical ventilation (83%) (Table 2).

Overall, pancuronium was used in 27% (70% of neonates) vecuronium in 56%, and atracurium in 17% of patients (but half of the patients in the medical/surgical/transplant ICU who received NMBs were treated with atracurium). Eighty-four percent of the patients had a heart rate greater than 100 beats per minute (bpm) at baseline, with 20% of patients demonstrating an increase in heart rate greater than 10 bpm once muscle relaxants were given, *independent* of the muscle relaxant administered. Forty-four percent of patients had a mean arterial pressure of less than 60 mmHg at baseline, with no significant differences noted once NMBs were administered, *independent* of the NMB that was administered (Table 3).

All adult and pediatric patients received sedatives or narcotics or both during paralysis; 4 of the 10 neonates did not. Twenty-eight of the 41 patients (68%) were given midazolam and morphine infusions during paralysis, 4 received midazolam alone, and 2 received morphine alone. The other 3 patients were on fentanyl infusions supplemented with a benzodiazepine (midazolam, diazepam).

Seventy-eight percent of the patients (32 out of 41) received NMBs for less than 24 h; this was in part due to the fact that 8 out of the 21 deaths occurred within this time interval. The other 22% of patients received NMBs for lengths of time ranging from greater than 1 day to greater than 3 weeks. Once the NMBs were discontinued, there appeared to be no correlation between how

Table 1. Intensive care units

	Beds	Admission	Receiving NMB (n)	Receiving NMB (%)
Neurologic/neurosurgical	18	519	0	(0.0)
Cardiac surgical	22	388	4	(1.0)
Coronary care	10	351	2	(0.5)
Medical	14	225	5	(2.0)
Shock/trauma	12	237	4	(1.7)
Cardiopulmonary transplant	7	102	0	(0.0)
Vascular/thoracic surgery	20	454	6	(1.3)
Pediatric	10	168	2	(1.2)
Neonatal	18	71	10	(14)
Medical/surgical/transplant[a]	14	271	8	(3.0)
Total	145	2816	41	(1.4)

[a]Liver, pancreas, kidney, bone marrow

Table 2. Indications for the use of neuromuscular blockers

I. To facilitate mechanical ventilation (83%)
- Presence of acute lung injury/ARDS
- Hypoxia
  Decreased S_vO_2, unresponsive to increase in FiO_2 and PEEP
- Hypercarbia (either passive hypercarbia or hypercarbia unresponsive to an increase in minute ventilation)

II. Other (17%)
- Agitation
- Tetanus

Table 3. Haemodynamic changes[a]

	Heart rate (bpm)			Mean arterial pressure[b]		
	Baseline	15 min	Change	Baseline	15 min	Change
Vecuronium (n=16)	113±11	116±18	3±14	90±26	89±19	−1±14
Atracurium (n=8)	115±23	115±26	8±4	89±26	93±28	5±6
Pancuronium (n=4)	109±17	123±5	19±19	72±21	71±22	−1±7

[a]No statistical difference for any parameter comparing the 15 min measurement with baseline. Similarly there was no difference between muscle relaxants comparing the change between baseline and 15 min
[b]Mean systemic arterial pressure measured from an indwelling arterial cannula

long the patients received NMBs and the period of time before the patient was extubated. Eight of the 32 patients (25%) who received NMBs for ≤24 h were on mechanical ventilation for over 1 week (Table 4).

A review of our chronic ventilator unit demonstrated that, over a 3-year interval, we admitted 43 patients per year, with 1 patient per annum admitted because of prolonged weakness following NMB administration. If the present data were extrapolated, we would estimate 1–2 patients annually would require admission to our chronic ventilator unit because of the prior use of NMBs. If we included only those adult survivors who received NMBs for ≥24 h (20), the annual incidence would be 5.0% (1 out of 20). In this analysis of the chronic ventilator unit, we have deleted those patients who were diagnosed with polyneuropathy associated with critical illness and those patients in whom manifestations of significant neuromuscular disease became apparent once they were admitted to the chronic ventilator unit (amyotropic lateral sclerosis, myasthenia gravis, etc.).

Discussion

Though neuromuscular blocking drugs (specifically tubocurarine) were first used clinically in the 1940s, it was not until the 1960s that their use became widespread in ICUs. This is due to a number of factors including the increasing use of mechanical ventilation in ICUs and increasing prevalence of a newly described entity, adult respiratory distress syndrome (ARDS) [12]. Pancuronium was used frequently in this circumstance [13], but in the late 1970s to 1980s, its use declined because of the awareness of side effects, primarily hemodynamic compromise [14]. In the mid-1980s, newer neuromuscular blocking agents such as vecuronium and atracurium were used more frequently in ICUs [15]. As with pancuronium, however, problems arose. These included prolonged neuromuscular blockade following discontinuation of vecuronium [3–5]; concerns with atracurium involving hemodynamic instability (hypotension secondary to histamine release) [16]; and CNS toxicity secondary to metabolites, i.e., laudanosine [17]. Despite these concerns, recent studies [1,2] have outlined how prevalent the use of NMBs is, and several review articles and editorials [6–9] have suggested that NMBs are being over-utilized and used inappropriately in ICUs.

Our study was prospective in that patients were identified at the time NMBs were administered, but it was retrospective in that we performed only a chart review to determine the indications, side effects, and how the NMBs were used. We had no protocol for determining the use of the NMBs, nor did we attempt in any way to intervene or alter the practice in our ICUs. In our adult ICUs, NMBs were used much less frequently than reported nationally. In the study of Klessig et al. [1], NMBs were reported to be used on average in 10 patients per month in ICUs. In our ICUs, 1 to 2 patients per month received NMBs. There are certainly discrepancies between our practice and that described by Klessig et al. No patient in our neurosurgical/neurologic ICU received NMBs, in contrast to other hospitals and practices where agitated patients with closed head injuries are paralyzed to facilitate management [18]. However, we do not believe that the discrepancy is due entirely to the differences in practice. Of note, several of the individuals who participated in the survey conducted by Klessig et al. practice in our ICUs, and a review of their responses indicates that they thought they were paralyzing more patients than we were able to document (they had retrospective recall of 10 patients per month, and yet the survey documented 1 to 2 patients per month).

Independent of whether or not our use of NMBs is low compared with the national average, some individuals think that no patients should receive NMB drugs without additional proof of their efficacy and safety [10]. Though the purpose of our study was not to determine if NMBs were used appropriately, it is clear from the study that NMBs were used in the majority of cases only for certain patients requiring mechanical ventilation. These patients were much sicker as assessed by APACHE II scoring than other patients also requiring mechanical ventilation. Presumably they were patients in whom gas exchange could not be optimized without paralysis and/or the institution of newer modes of mechanical ventilation, e.g. reverse inspired (I) to expired (E) ratio ventilation [19], pressure release ventilation [20], etc. Several studies have documented the positive impact of NMBs on gas exchange [21–23]. However, not all clinical practices are based on sound scientific principle. Clinical practice develops as a result of a variety of factors, including physicians' perceptions, unpublished surveys and studies, colleagues' opinions, etc. [24].

Our survey demonstrated that these patients are quite ill; less than half left the hospital alive. There is no proof, but a strong clinical impression, that patients who receive NMBs, because of concerns about side effects, receive them only as a last resort.

The survey also underscored for us how difficult a randomized, controlled, prospective study would be. It would be difficult to randomize to a control group patients who we were unable to oxygenate. Anesthetic agents such as propofol and inhalation agents are usually inadequate to produce a sufficient amount of muscle relaxation to facilitate newer modes of mechanical ventilation. Also, they have potential adverse side effects, including hypotension and sepsis with propofol [25,26], and alterations in ventilation-perfusion (V/P) mismatch with an increased shunt with inhalation agents [27].

There is concern that many patients in the ICU are not receiving sedation and analgesia. We demonstrated that in our practice, pediatric and adult patients are all receiving sedation or analgesia, or both, but 4 patients in our neonatal ICU did not. Presumably, with increased awareness of the need for analgesics in neonates in other settings [28], this too should change.

The hemodynamic findings we noted were of interest, but not surprising. Pancuronium has long been known to increase heart rate by 10 bpm (or at least by 10% over baseline) following its

Table 4. Duration of use and time to extubation

Time to extubation once NMB stopped		Duration of blockade			
Time	n	<24 h	2–8 days	9–20 days	>21 days
<24 hrs	15	10	3	1	1
2–8 days	16	14	1	1	
9–20 days	6	4	1		1
>21 days	4	4			
Total	41[a]				

[a]Mortality 51% (21/41)

intravenous administration [29]. Vecuronium has been associated with the least hemodynamic changes and even atracurium has minimal, if any, hemodynamic changes following recommended dosing: histamine release is only a problem if excessive doses are administered [30]. It is noteworthy that in this ICU population, in contrast to patients anesthetized in the operating room, there was a significant degree of tachycardia at baseline. The change in heart rate noted between baseline and 15 min was not statistically significant in the pancuronium group, but the number of patients was small. This could be a type II statistical error. If we had studied larger groups of patients receiving atracurium or vecuronium, or if we had measured vital signs more frequently (checking blood pressure and heart rate every minute as opposed to every 15 min), we may have observed more hemodynamic changes. In these critically ill patients, however, in whom there is frequently much minute-to-minute variability in heart rate, blood pressure, etc., such changes apparently were not thought to be clinically significant by the medical staff caring for these patients.

The same point might be made regarding prolonged blockade following the administration of NMBs. As mentioned above, some drugs given continuously to patients in the ICU may lead to a more prolonged recovery time compared with that which is observed in healthy patients in the operating room. For example, in the study of vecuronium by Segredo et al. [31], 7 of the 16 patients had prolonged recovery; 5 of the 7 patients took ≤2 days to recover, 2 patients died before recovery. In an ICU setting this might not be significant because many patients with ARDS, for example, will require several days of ventilatory support after discontinuing a NMB because of underlying lung disease. In our study, the majority of patients were on NMBs for less than 24 h. Instances of prolonged blockade are usually associated with more prolonged administration (≥48 h) [7]. The number of patients receiving NMBs was too small to draw significant and firm conclusions. However, it should be pointed out that for those patients who received NMBs for less than 24 h, the majority (18) were on mechanical ventilation for an additional 24 h, and several were on mechanical ventilation for 1–2 weeks.

The main factor in determining whether a critically ill patient remains on mechanical ventilation following discontinuation of the NMB has more to do with the underlying lung disease than with a previously administered NMB. In our practice, one way to determine and separate the component of the NMB and the underlying lung illness was to examine those patients who were admitted to our chronic ventilator unit. They could not be admitted to this unit unless all of their other medical conditions were stable, and they were, except for requiring mechanical ventilation, ready to be dismissed from the hospital. Patients staying longer in the ICU do not stay because of mechanical ventilation, but because of some other sequelae such as an open wound, hemodynamic compromise, multiple organ dysfunction syndrome, etc. Once the patient is truly stable, he or she can be transferred to our chronic ventilator unit. In our practice, only 3 patients over the last 3 years have been admitted to our chronic ventilator unit because of the use of NMBs. Our estimated incidence of 5% of prolonged weakness in adults surviving NMB administration for ≥24 h is not too dissimilar to the incidence of 10.2% of prolonged weakness described to the Anesthetic and Life Support Drugs Advisory Committee of the US FDA [10]. One must be aware that the different NMBs also have different incidences of prolonged blockade; the relative incidences for vecuronium, pancuronium and atracurium have been suggested as 450, 22 and 30, based on 45, 22 and 1 individual case reports, respectively [10]. We would expect different rates of prolonged blockade depending on the frequency of use of the different NMBs.

On the basis of these observations, we can state that in an ICU practice in which vecuronium is the principle NMB used, those patients who require NMB for >24 h, and who survive, stand a 5–10% chance of developing prolonged neuromuscular blockade. Patients in whom neuromuscular monitoring is not used [15] and who receive steroids [5] may have a higher incidence. Such an incidence of serious morbidity may be acceptable if the benefits of NMB, i.e., an improvement in survival in patients with acute lung or closed head injury, can be proven.

A final point in assessing our data has to do with the difficulty in studying such patients. While many examples can be used to document the incidence of prolonged blockade, few of which are applicable in the ICU setting, there are unique considerations in the ICU. These include:

1) The use of more than one NMB. The on-call team uses one NMB and the team that comes on in the morning changes to a second NMB.
2) The choice of NMBs varies not only from institution to institution, but, in this particular study, even between ICUs and, indeed, between individual practitioners (Hubmayr RD, personal communication).
3) The ethical issue of doing a controlled, randomized, prospective study in patients who are candidates for NMBs. Many times in enrolling patients for NMB studies in the ICU, there is a brief window (<1 h) of opportunity beyond which it is impossible to delay instituting the use of NMB (Murray MJ, personal communication).

Furthermore, clinical practice is rapidly evolving, as noted previously, involving the use of twitch monitors, institution of new drugs, and the relative infrequency – at least in our practice – of NMB use. Informed consent is often difficult to obtain and refusal occasionally runs as high as 50% when attempting to enroll ICU patients in clinical studies. There are multiple reasons for this, but in a critically ill patient in whom the risk of mortality is >50%, it is easy to understand why families might be reluctant to enroll a loved one in an experimental study that in and of itself would not be designed to assess outcome, but rather safety.

It is clear, however, that vis-à-vis previous editorials, such studies are necessary. On the basis of our experience and a review of the literature, however, we advise:

- Any recommendations should be based on sound scientific data. They should not be based on inappropriate use of NMBs; i.e. muscle relaxants given at several times the recommended dose [30].
- Patients should be appropriately monitored with a twitch monitor. The evidence for this is not conclusive, but there is a bias that keeping the train-of-four (TOF) at 1–3 twitches decreases the chances of an overdose and presumably of prolonged blockade.
- One must be careful in selecting patients who might benefit from NMBs. It may be inappropriate to administer NMB and steroids concomitantly.
- Sufficient sedation and analgesia is necessary to keep patients comfortable without either anxiety or recall.

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References

1. Klessig HT, Geiger HJ, Murray MJ, Coursin DB (1992) A national survey on the practice patterns of anesthesiologist intensivists in the use of muscle relaxants. Crit Care Med 20:1341–1345
2. Hansen-Flaschen JH, Brazinsky S, Basile C, Lanken PN (1991) Use of sedating drugs and neuromuscular blocking agents in patients requiring mechanical ventilation for respiratory failure. A national survey. JAMA 226:2870–2875
3. Partridge BL, Abrams JH, Bazemore C, Rubin R (1990) Prolonged neuromuscular blockade after long-term infusion of vecuronium bromide in the intensive care unit. Crit Care Med 18:1177–1179
4. Gooch JL, Suchyta MR, Balbierz JM, Petajan JH, Clemmer TP (1991) Prolonged paralysis after treatment with neuromuscular junction blocking agents. Crit Care Med 19:1125–1131
5. Griffin D, Fairman N, Coursin D, Rawsthorne L, Grossman JE (1992) Acute myopathy during treatment of status asthmaticus with corticosteroids and steroidal muscle relaxants. Chest 102:510–514
6. Miller-Jones CMH (1980) Paralysis or sedation for controlled ventilation? Lancet i:312
7. Coursin DB (1992) Neuromuscular blockade. Should patients be relaxed in the ICU? Chest 102:988–989
8. Sharpe MD (1992) The use of muscle relaxants in the intensive care unit. Can J Anaesth 39:949–962
9. Isenstein DA, Venner DS, Duggan J (1992) Neuromuscular blockade in the intensive care unit. Chest 102:1258–1266
10. Verbal evidence presented at Anesthetic and Life Support Drugs Advisory Committee (1992) Report, November 23. US FDA Center for Drug Evaluation and Research, Rockville, Maryland
11. Knaus WA, Draper EA, Wagner DP, Zimmerman JE (1985) APACHE II: a severity of disease classification system. Crit Care Med 13:818–829
12. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE (1967) Acute respiratory distress in adults. Lancet ii:319–323
13. Miller-Jones CMH, Williams JH (1980) Sedation for ventilation. A retrospective study of fifty patients. Anaesthesia 35:1104–1107
14. Anderson EF, Rosenthal MH (1975) Pancuronium bromide and tachyarrhythmias. Crit Care Med 3:13–15
15. Hansen-Flaschen J, Cowen J, Raps EC (1993) Neuromuscular blockade in the intensive care unit. More than we bargained for. Am Rev Respir Dis 147:234–236
16. Siler JN, Mager JG Jr, Wyche MQ Jr (1985) Atracurium: hypotension, tachycardia and bronchospasm. Anesthesiology 62:645–646
17. Yate PM, Flynn PJ, Arnold RW, Weatherly BC, Simmonds RJ, Dopson T (1987) Clinical experience and plasma laudanosine concentrations during the infusion of atracurium in the intensive therapy unit. Br J Anaesth 59:211–217
18. Robertson CS, Clifton GL, Taylor AA, Grossman RG (1983) Treatment of hypertension associated with head injury. J Neurosurg 59:455–460
19. Duncan SR, Rizk NW, Raffin TA (1987) Inverse ratio ventilation. PEEP in disguise? Chest 92:390–391
20. Sassoon CSH, Mahutte CK, Light RW (1990) Ventilator modes: old and new. Crit Care Clinic 6:605–634
21. Light RW, Bengfort JL, George RB (1975) The adult respiratory distress syndrome and pancuronium bromide. Anesth Analg 54:219–223
22. Bishop MJ (1984) Hemodynamic and gas exchange effects of pancuronium bromide in sedated patients with respiratory failure. Anesthesiology 60:369–371
23. Coggeshall JW, Marini JJ, Newman JH (1985) Improved oxygenation after muscle relaxation in adult respiratory distress syndrome. Arch Intern Med 145:1718–1720
24. Eddy D (1990) Practice policies: where do they come from? JAMA 263:1265–1275
25. Arduino MJ, Bland LA, McAllister SK et al (1991) Microbial growth and endotoxin production in the intravenous anesthetic propofol. Infect Control Hosp Epidemiol 12:535–539
26. Sebel PS, Lowdon JD (1989) Propofol: a new intravenous anesthetic. Anesthesiology 71:260–277
27. Marshall C, Lindgren L, Marshall BE (1984) Effects of halothane, enflurane, and isoflurane on hypoxic pulmonary vasoconstriction in rat lungs in vitro. Anesthesiology 60:304–308
28. Anand KJS, Hickey PR (1992) Halothane-morphine compared with high-dose sufentanil for anesthesia and postoperative analgesia in neonatal cardiac surgery. N Engl J Med 326:1–9
29. Coursin D, Murray M, Scuderi P, Prough D, Abou-Donia M, Miller D (1993) An evaluation of doxacurium and pancuronium in a multicenter, randomized, double-blind study in the critically ill. Crit Care Med 21:S263
30. Scott RPF, Savarese JJ, Basta SJ, Embree P, Ali HH, Sunder N, Hoaglin DC (1986) Clinical pharmacology of atracurium given in high dose. Br J Anaesth 58:834–838
31. Segredo V, Caldwell JE, Matthay MA, Sharma ML, Greunke LD, Miller RD (1992) Persistent paralysis in critically ill patients after long-term administration of vecuronium. N Engl J Med 327:524–528

Dr. M.J. Murray
Mayo Clinic
200 First Street, S.W.
Rochester
MN 55905
USA

Appendix A. Survey used for review of patient records. Modified from Klessig et al. [1].

Survey of muscle relaxant use in the ICU

1. ICU
2. What were the indications for neuromuscular blockade (NMB)?
3. Which muscle relaxants were used?
4. Mode of delivery of NMB
5. If intermittent boluses were used, who decided when the patient needed another bolus?
6. What technique was used to determine re-dosing?
7. What sedatives/narcotics were used along with NMB?
8. Infusion rates
9. Was NMB reversed? If so, with what agent(s)?
10. How was it decided to discontinue NMB?
11. Side effects, drug interactions, idiosyncratic reactions with NMB?
12. Time to extubation once NMB discontinued