INTENSIVE CARE NURSES’ KNOWLEDGE ABOUT USE OF NEUROMUSCULAR BLOCKING AGENTS IN PATIENTS WITH RESPIRATORY FAILURE

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Background The recent increase in use of neuromuscular blocking agents (NMBAs) in patients with acute respiratory distress syndrome is set against a backdrop of concerns about harm associated with use of these high-risk drugs. Bedside nurses play a pivotal role in the safe and effective use of these agents.

Objective To describe critical care nurses’ knowledge of the therapeutic properties, adverse effects, and monitoring parameters associated with NMBAs.

Methods A prospective, multicenter survey of medical intensive care unit nurses between July 2012 and May 2013. The web-based survey instrument was designed, pretested, and administered under the direction of a multidisciplinary group of individuals.

Results Responses from 160 nurses (22% of eligible nurses) were analyzed. Most respondents were able to identify NMBAs correctly as nonanalgesic (93%) and nonanxiolytic (83%). The perceived durations of action of NMBAs varied widely, and few nurses were familiar with patient-specific considerations related to drug elimination. Most (70%) recognized the independent associations between NMBAs and footdrop, muscle breakdown, and corneal ulceration. Pressure ulcers and a history of neuromuscular disease were the characteristics of patients perceived to most heighten the risk of NMBA use.

Conclusions Critical care nurses are knowledgeable about the importance of concurrent analgesia and sedation during use of NMBAs. Routes of elimination, duration of action, and adverse effects were less commonly known and represent areas for focused education and quality improvement surrounding use of NMBAs in the intensive care unit. (American Journal of Critical Care. 2015;24:431-439)
A knowledgeable critical care nurse is essential to the effective and safe use of neuromuscular blocking agents (NMBAs) in intensive care units (ICUs). The Institute for Safe Medication Practices considers NMBAs to be high-alert medications because of the robust historical documentation of harm associated with their use. Indeed, prolonged use of these agents contributes to an increased risk for corneal ulcers, skin breakdown, venous thromboembolism, ventilator-associated pneumonia, and musculoskeletal debility. Furthermore, reports of patients recalling being paralyzed and the independent association between NMBAs and posttraumatic stress disorder raise concerns about the safety of routine use of these agents.

Despite these previously documented risks, interest in the routine use of NMBAs among medical ICU patients has been renewed in the past several years. Specifically in patients with acute respiratory distress syndrome (ARDS), we now know that early continuous infusion of an NMBA improves oxygenation, inflammation, and mortality. As epidemiological evidence shows, this practice shift in support of NMBA use could affect many critically ill patients. To minimize risks for patients, critical care nurses must have a keen understanding of the importance of adequate concurrent analgesia and sedation when an NMBA is used and an appreciation for the factors that contribute to selection of patients, choice of agent, dose titration, and adverse effects.

Studies on nurses’ knowledge about the use of NMBAs are more than a decade old and do not completely assess all aspects of competency. They also predate recent efficacy publications in support of using NMBAs for certain subgroups of patients. Therefore, to promote the safe and effective use of NMBAs, we sought in this study to describe critical care nurses’ knowledge and beliefs about NMBAs in the modern medical ICU and identify opportunities for targeted educational initiatives and to improve practice homogeneity in the future.

Methods

In this multicenter, prospective, cross-sectional study, ICU nurses at 5 sites (Mayo Clinic, Rochester, Minnesota; Cleveland Clinic, Cleveland, Ohio; New York Presbyterian Hospital, New York, New York; Vanderbilt University Medical Center, Nashville, Tennessee; and The Ohio State University Wexner Medical Center, Columbus, Ohio) completed a web-based survey between July 2012 and May 2013. The study protocol was reviewed and approved by the institutional review board at each participating site. The questionnaire responses are a subset of a larger database of survey responses from licensed providers in multiple disciplines, including nurses, physicians, nurse practitioners, physician assistants, pharmacists, and respiratory therapists. For their responses to be eligible for inclusion in this study, more than 25% of the individual’s clinical practice must have been in an ICU consisting of more than 50% medical patients at 1 of the 5 large, academic medical centers involved in the study. The included academic medical centers each have approximately 700 to 1400 adult hospital beds and 24 to 65 medical ICU beds. At the time of the study, all included institutions had an electronic medical record and used computerized provider order entry (CPOE). Two centers had clinical protocols for NMBA use that were helpful in selection of patients, dosing, and monitoring.

A 16-question web-based survey was designed expressly for this study in conjunction with the Mayo Clinic Survey Research Support Center. Study
data were collected and managed in REDCap (Research Electronic Data Capture) survey software version 1.3.9. REDCap is a secure, web-based application designed to support data capture for research studies, providing (1) an intuitive interface for validated data entry, (2) audit trails for tracking data manipulation and export procedures, (3) automated export procedures for seamless data downloads to common statistical packages, and (4) procedures for importing data from external sources.

The survey instrument (see Appendix, available online only, at www.ajcconline.org) was subdivided into 2 distinct sections; the first pertained to general knowledge about NMBA s and the second involved perceptions of the role of NMBA s in patients with ARDS. All participants were asked to complete both sections of the survey. Development of the content domains included a thorough review of published reports and input from a multidisciplinary group of experts. Specific to the knowledge section presented here, the survey instrument was focused on NMBA pharmacology, pharmacokinetics (duration of action, methods of elimination), adverse effects, and titration. Questions referenced both types of NMBA s: aminosteroidal compounds (eg, vecuronium and pancuronium) and benzylisoquinolinium compounds (eg, cisatracurium and atracurium).

Response options were closed-ended and used statements of agreement and Likert scales where possible. Items pertaining to analgesia and anxiolysis asked nurses to mark agree, disagree, or unsure/no opinion for a series of statements about NMBA drug properties. Unsure/no opinion and missing responses were combined and classified as incorrect responses for these analyses to identify knowledge gaps. Pharmacokinetic items asked nurses to describe medications’ duration of action in the absence of end-organ compromise. Response options included short, intermediate, or long duration of action and unsure/no opinion. Correct responses identified atracurium and vecuronium each as intermediate duration according to current guidelines. Also, we probed respondents about the risk of NMBA accumulation in patients with clinically significant end-organ dysfunction. In this case, a correct response identified the altered elimination of the aminosteroids (vecuronium and pancuronium) in patients with hepatic and renal dysfunction, respectively, and the end-organ neutrality of both benzylisoquinolinium NMBA s. Agents that affect the central nervous system (CNS-active agents) but are not NMBA s (eg, fentanyl, hydromorphone, lorazepam, propofol) were included in survey questions to provide a reference agent for descriptive comparisons to NMBA s.

Similar to the method of Rhoney and Murry, after development, 20 ICU providers (including physicians, nurses, and pharmacists from a nonincluded surgical ICU at the primary site) reviewed and pretested the questionnaire. A structured critique form was given to each of these individuals upon survey completion, with specific probes designed to examine question clarity, response options, missing or superfluous survey items, and overall length. Two investigators reviewed the deidentified critiques to identify themes. Questions and responses were modified to address areas of ambiguity. Concerns about length and redundancy resulted in removal of several survey items.

The study team involved investigators from each of the included sites. These site representatives individually contacted the local medical directors, subspecialty managers (ie, nurse managers), and administrative staff at their center to acquire the e-mail addresses of eligible study participants. The members of the investigative team had various degrees of preexisting professional relationships with the local ICU leaders. All known members of the population were surveyed. Eligible individuals were contacted via e-mail and invited to participate in the survey. By following the survey link in the electronic communication, providers indicated their consent to participate. Reminder communication occurred electronically 2 weeks, 3 weeks, and 4 weeks after the initial e-mail, and the study concluded on day 30.

The only demographic identifiers collected pertained to the provider’s self-reported role in the ICU (eg, nurse, physician, pharmacist) and study site. Herein we reported the data from all eligible respondents who identified themselves as nurses, including licensed practical nurses, registered nurses, clinical nurse specialists, and nurse educators. Information from nurse practitioners was not included, because their additional education (formal and informal) and prescriptive authority may predispose them to an altered familiarity with medication selection, clinical protocols, and guideline recommendations. Responses were otherwise anonymously gathered in the electronic database and described in aggregate.

Descriptive statistics were used for all survey responses, with results expressed as frequencies and percentages. The Pearson χ² test or the Fisher exact test was used to analyze independent binary outcomes. Assuming 60% concordance with the correct response, we calculated that at least 150 responders...
Therapeutic Properties

The aminosteroidal and benzylisoquinolinium NMBAs studied were correctly identified as nonanalgesic by 95% and 94% of survey respondents, respectively. In a combined analysis, 148 respondents (92%) were able to identify both agents correctly as nonanalgesic (see Table). A similar number of participants correctly identified lorazepam as nonanalgesic (n = 144, 90%). The absence of anxiolytic properties among NMBAs was significantly less commonly identified by respondents (n = 132, 82%) than the absence of analgesic properties (P = .007). Unsure/no opinion was the most common answer among incorrect responses regarding anxiolytic properties of NMBAs (pancuronium: 19 out of 25 incorrect responses; atracurium: 13 out of 20 incorrect responses).

Pharmacokinetics

Marked inconsistencies existed among respondents in the perceived duration of action of each Nalb (Figure 2). Less than half of respondents correctly identified the intermediate duration of action of atracurium (46%) and vecuronium (40%), and the responses showed marked heterogeneity. In contrast, homogeneity was increased among the responses to the reference analgesic and sedative agents under study, hydromorphone (65% perceived it to be intermediate duration of action) and

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Table

Correct identification of pharmacological properties of neuromuscular blocking agents (NMBAs)

<table>
<thead>
<tr>
<th>Survey item</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Analgesic</strong></td>
<td></td>
</tr>
<tr>
<td>Correctly identified the following Nalb as nonanalgesic</td>
<td></td>
</tr>
<tr>
<td>Vecuronium</td>
<td>152 (95)</td>
</tr>
<tr>
<td>Cisatracurium</td>
<td>150 (94)</td>
</tr>
<tr>
<td>Both NMBAs correct</td>
<td>148 (92)</td>
</tr>
<tr>
<td><strong>Anxiolytic</strong></td>
<td></td>
</tr>
<tr>
<td>Correctly identified the following NMBAs as nonanxiolytic</td>
<td></td>
</tr>
<tr>
<td>Pancuronium</td>
<td>135 (84)</td>
</tr>
<tr>
<td>Atracurium</td>
<td>140 (88)</td>
</tr>
<tr>
<td>Both NMBAs correct</td>
<td>132 (82)</td>
</tr>
<tr>
<td><strong>End-organ elimination</strong></td>
<td></td>
</tr>
<tr>
<td>Correctly identified drug elimination properties of the following NMBAs</td>
<td></td>
</tr>
<tr>
<td>Aminosteroidis</td>
<td></td>
</tr>
<tr>
<td>Vecuronium (primarily hepatic)</td>
<td>66 (41)</td>
</tr>
<tr>
<td>Pancuronium (primarily renal)</td>
<td>68 (42)</td>
</tr>
<tr>
<td>Both aminosteroidal NMBAs correct</td>
<td>44 (28)</td>
</tr>
<tr>
<td>Benzylisoquinolinumis</td>
<td></td>
</tr>
<tr>
<td>Atracurium (end-organ neutral)</td>
<td>89 (56)</td>
</tr>
<tr>
<td>Cisatracurium (end-organ neutral)</td>
<td>103 (64)</td>
</tr>
<tr>
<td>Both benzylisoquinolinum NMBAs correct</td>
<td>65 (41)</td>
</tr>
</tbody>
</table>
propofol (82% perceived it to possess a short duration of action). Given the importance of ICU nurses in individualizing treatment plans and weaning patients off of CNS-active agents, survey items were included to investigate the perceived risk of NMBA accumulation in patients with hepatic or renal dysfunction. Only 8 respondents (5%) correctly identified all 4 NMBA drugs’ elimination considerations. The end-organ neutrality of benzylisoquinolinium NMBAs was identified more commonly than were the implications of renal or hepatic dysfunction on elimination of aminosteroidal NMBAs (41% vs 28%, respectively; \( P = .01 \); see Table).

**Adverse Effects**

Four out of every 5 nurses recognized independent associations between NMBAs and both footdrop and muscle breakdown. In only 34% of cases, nursing staff recognized the independent association between use of an NMBA and consciousness (Figure 3). We studied whether nurses attributed other likely unrelated biochemical and clinical effects to the use of NMBAs. Few nurses inaccurately reported a relationship between NMBA use and hyperglycemia (8%), infection (11%), or hypomagnesemia (16%). Lactic acidosis and delirium were incorrectly identified as independently related to NMBA use in 28% and 32% of responses, respectively.

Respondents were also asked to classify the degree to which a series of baseline factors and concurrent therapies modified the risk profile of continuous infusion of an NMBA. As this pertains to providers’ perceptions and beliefs, no answers for these items were considered incorrect. Respondents could select from the following options: substantial increase in risk, slight increase in risk, no change in risk, or unsure. Among the factors under study, respondents believed that pressure ulcers and a history of a neuromuscular disorder most increased the risks associated with NMBA therapy (Figure 4). Although concomitant corticosteroids were perceived to heighten the risk associated with continuous infusion of an NMBA by 77 respondents (48%), the majority classified this increase in risk as slight (58 “slight increase” out of 77 responses for increased risk).

**Titration**

When asked to select the best primary method to guide titration of a continuous infusion of an NMBA in patients with ARDS, 82 nurses (51%) preferred degree of ventilator synchrony or other oxygenation/ventilation parameters. Train-of-4 (TOF) monitoring with peripheral nerve stimulation (PNS) was selected less often \(( n = 65, 41\% )\), although this difference was not statistically significant \(( P = .06 )\).
ulceration, and venous thromboembolism). With respect to monitoring, nurses preferred to use ventilation/oxygenation parameters rather than TOF monitoring to guide dose titration in patients with ARDS.

Although the evidence is limited, researchers in previous studies have described nurses’ knowledge about NMBA pharmacology. In early work by Loper and colleagues,14 258 ICU nurses at a single center were surveyed to assess their knowledge about NMBA. Ninety percent of respondents were either unsure or believed that pancuronium provided anxiolysis. With respect to pain control, one-third of ICU nurses reported a lack of familiarity or believed that pancuronium provided analgesia. A separate structured needs assessment pertaining to analgesia, sedation, and paralysis in a surgical ICU revealed frequent insufficiency of sedation and analgesia during use of NMBA. The authors identified this as a key clinical issue that adversely affected patient care and outcomes.15 In contrast to previous work, nurses in the present study more frequently recognized the absence of analgesic properties among NMBA, but 1 in 5 still failed to note the absence of anxiolysis. The explanation for this partial improvement is unknown, but it may relate to increased awareness of pain, agitation, and delirium in critically ill patients with the recent release of updated guidelines.21 Also, the abundant educational resources and advanced credentials now available to ICU nurses through national organizations such as the American Association of Critical-Care Nurses and the Society of Critical Care Medicine may have resulted in an increased understanding of the importance of concomitant analgesia/sedation when NMBA are used. The heightened emphasis on pain assessment and control by The Joint Commission may also explain the difference in familiarity with analgesia and anxiolysis.22

In addition to the therapeutic effects, reviews and continuing education modules on NMBA also highlight the importance of nursing competency in drug pharmacokinetics, selection of patients and agents, adverse effects, and titration.16,23-25 Unfortunately, we are unaware of published studies measuring such knowledge. In our study, ICU nurses commonly misidentified the correct mechanism of drug elimination, perceived durations of action of NMBA varied widely, and certain adverse effects were underrecognized. The bedside nurse is the multidisciplinary team member most closely involved with weaning ICU patients off of CNS-active agents. In failure to predict the offset of paralytic activity correctly, particularly in the setting of end-organ dysfunction, may place patients at increased risk of exposure to insufficient analgesia and sedation during the NMBA weaning process. Our findings suggest that an opportunity also exists to heighten the emphasis on screening for muscle breakdown, corneal ulceration, and venous thromboembolism in the nurses’ daily clinical assessments. Future quality improvement and educational initiatives should seek to address these knowledge gaps.

Unlike previous studies in which nurses were surveyed about the NMBA titration practice at their sites, we instead inquired about NMBA titration preference, specifically in patients with ARDS because of the recent favorable reports on use of NMBA for this indication; the differences were revealing. Foster and colleagues24 did a survey of 483 critical care nurse managers across the United States, asking about NMBA use and titration with a particular focus on PNS. Of the 185 centers that reported NMBA use, 116 (63%) monitored NMBA with PNS, and 111 of those also used the TOF technique. Eighty-three percent of respondents reported dose titration of NMBA to PNS response, which is in line with guideline recommendations from 2002.3,15 Although the difference did not reach statistical significance, in the present evaluation, we found that more nurses favored using titration to respiratory criteria (51%) rather than TOF (41%) for monitoring effects of NMBA in patients with ARDS. Studies that have compared TOF-guided NMBA titration to titration based on subjective clinical assessments in patients with mixed indications for paralysis have yielded disparate results. Rudis et al26 reported that lower doses of NMBA were used and recovery from paralytic agents was faster in patients randomized to TOF-guided therapy, whereas 2 other studies27,28 showed no difference between groups in total paralysis time, recovery time, and amount of drug used. In a randomized controlled trial29 of 102 patients with ARDS who were given cisatracurium,
researchers reported no difference in plateau pressure, ratio of PaO₂ to fraction of inspired oxygen, Paco₂, or pH between patients titrated to a TOF of 0/4 versus 2/4, but the authors did note a reduction in total drug used and recovery time among patients titrated to a TOF of 2/4. On the basis of these data, we suggest that providers pair TOF with clinical criteria to develop individualized titration plans that consider the indication for NMBA therapy. Indeed, management of an ICU patient with severe respiratory failure most likely requires a different approach to titration than management of a patient with elevated intracranial pressure.

This study had several possible limitations. Although the focus of the study is ICU nurses, many other members of the multidisciplinary team share responsibility for ensuring safe use of NMIBs in practice. Coverage error may have existed between the target population of all medical ICU nurses and the sampling frame used in this study. The study was performed at 5 large academic medical centers. Facilities with fewer than 150 hospital beds or fewer than 10 ICU beds provide conceptural analgesia and sedation during NMIB less often and use PNS less often than larger centers do.13 If present, this bias most likely resulted in conservative estimates of NMIB knowledge gaps, but caution should still be used when generalizing these findings to smaller institutions. The results of this study may also be affected by nonresponse error. The response rate in this web-based survey was 22%, even after 3 reminder notifications were distributed to study participants by a local representative. We cannot exclude the possibility that nonresponders systematically differed from responders, but our findings are similar to the 25% response rate documented in a paper-and-pencil questionnaire distributed to physicians on a similar topic.20 Last, we did not measure baseline academic training, years of practice experience, postgraduate advanced credentialing in critical care, or involvement in national organizations (eg, American Association of Critical-Care Nurses, Society of Critical Care Medicine) and thus cannot comment on how these factors may have influenced the responses.

Conclusion

Current medical ICU nurses demonstrated a keen understanding of the importance of analgesia and sedation during therapeutic paralysis. Future educational efforts to improve the safe and effective use of NMIBs should address the knowledge gaps identified in this study, including adverse effects and NMIB pharmacokinetics, which may directly affect dose adjustment and concomitant interventions. Last, a reappraisal of therapeutic goals of NMIB and titration strategies in patients with ARDS is warranted because ventilation and oxygenation should be considered in conjunction with PNS response.

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REFERENCES


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