

Canadian survey of the use of sedatives, analgesics, and neuromuscular blocking agents in critically ill patients*

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Objectives: To characterize the perceived utilization of sedative, analgesic, and neuromuscular blocking agents, the use of sedation scales, algorithms, and daily sedative interruption in mechanically ventilated adults, and to define clinical factors that influence these practices.

Design: Cross-sectional mail survey.

Participants: Canadian critical care practitioners.

Measurements and Main Results: A total of 273 of 448 eligible physicians (60%) responded. Respondents were well distributed with regard to age, years of practice, specialist certification, size of intensive care unit and hospital, and location of practice. Twenty-nine percent responded that a protocol/care pathway/guideline for the use of sedatives or analgesics is currently in use in their intensive care unit. Daily interruption of continuous infusions of sedatives or analgesics is practiced by 40% of intensivists. A sedation scoring system is used by 49% of respondents. Of these, 67% use the Ramsay scale, 10% use the Sedation-Agitation Scale, 9% use the Glasgow Coma Scale, and 8% use the Motor Activity Assessment Scale. Only 3.7% of intensivists use a delirium scoring system in their intensive care units. Only 22% of respondents currently have a protocol for the use of neuromus-

cular blocking agents in their intensive care unit, and 84% of respondents use peripheral nerve stimulation for monitoring. In patients receiving neuromuscular blocking agents for >24 hrs, 63.7% of respondents discontinue the neuromuscular blocking agent daily. Intensivists working in university-affiliated hospitals are more likely to employ a sedation protocol and scale ($p < .0001$), as are intensivists working in larger intensive care units (≥ 15 beds, $p < .01$). Intensivists with anesthesiology training (and no formal critical care training) are more likely to use a protocol and sedation scale, and critical care-trained intensivists are more likely to use daily interruption. Younger physicians (<40 yrs) are more likely to practice daily interruption ($p = .0092$).

Conclusions: There is significant variation in critical care sedation, analgesia, and neuromuscular blockade practice. Given the potential effect of practices regarding these medications on patient outcome, future research and educational efforts related to evidence-based protocols for the use of these agents in mechanically ventilated patients might be worthwhile. (Crit Care Med 2006; 34:374–380)

KEY WORDS: sedation; analgesia; neuromuscular blockade; practice guidelines; intensive care unit

Patients in the intensive care unit (ICU) often require life-saving treatments such as mechanical ventilation and dialysis and devices such as central venous catheters. To aid the healing process, facilitate use of life-support technology, and relieve anxiety and pain, sedative and analgesic drugs are commonly administered. Evidence is now

emerging that how much sedation we give, and when and how we stop it, are very important in determining patient outcome (1, 2). Two recent randomized trials have started to lay the scientific foundation for this important therapy: a trial evaluating a nurse-driven sedation protocol (1) and an article in the *New England Journal of Medicine* on daily sedation cessation (2). Both of these trials demonstrated reductions in the duration of ventilation and ICU stay in patients managed with the intervention, highlighting the potential effect of sedation strategies on healthcare resources.

The importance of sedation in the ICU is further emphasized by an executive report of practice guidelines produced by a multidisciplinary task force from the Society of Critical Care Medicine (3), published in January 2002. These guidelines recommend incorporation of a sedation protocol, a scoring system for both sedation and de-

lirium, and daily discontinuation of sedative/analgesic infusions. However, the impact of these trials and guidelines on physicians' practice patterns is not clear.

Therefore, we conducted a national survey of Canadian intensivists to determine the perceived utilization of various sedative, analgesic, and neuromuscular blocking agents (NMBAs) in mechanically ventilated adults. We also assessed the perceived utilization of strategies, including sedation scoring systems, sedation algorithms, and daily sedative interruption, and some important determinants to physicians' responses to these questions. We anticipated that the information would be helpful to design structured educational interventions (including, but not limited to, evidence-based practice guidelines) and health services research to evaluate these interventions.

*See also p. 556.

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MATERIALS AND METHODS

Survey Development. We conducted a MEDLINE and an EMBASE literature search for sedation, analgesia, and NMBA administration in the ICU. From these searches we identified the most commonly used medications, methods of monitoring, sedation scoring systems, published algorithms, and clinical practice guidelines. This search allowed us to identify important questionnaire items. We also surveyed intensivists members of the Canadian Critical Care Trials Group (CCCTG) and intensivists, pharmacists, and nurses at Mount Sinai Hospital about additional domains of interest. We sampled to redundancy; that is, we terminated this phase when questionnaires failed to identify new or additional domains or items.

The initial search for potentially relevant items yielded many more items than could be included in the final questionnaire. The goal of item reduction was to retain 15–20 items that are most likely to carry an important educational message for clinician consumers of this research and that are most likely to generate important research questions. A second questionnaire was circulated to ≥ 20 adult and pediatric intensivist members of the CCCTG in October 2001. For each item, this group of intensivists was asked to comment on relevance of the item, inclusiveness of response choices, and whether they that this item would have important educational value if included in the questionnaire.

The format of the questionnaire was mainly tick boxes, with few open-ended questions. The questionnaire was formatted in three sections. Section 1 explored the use of sedation and analgesia, including the types of agents used, the route of administration, the reasons for use, whether sedation scales and algorithms are used, and whether the algorithms were developed locally. Section 2 explored similar items for NMBA, including indications for use, daily interruption, and use of reversal agents. Finally, section 3 consisted of data about the respondents and their clinical practice, such as training, years in practice, hospital setting (community vs. university-affiliated); type of ICU (medical, surgical, neurosurgical, etc); number of ICU beds; and proportion of patients ventilated at one time.

Survey Testing. To ensure clarity, realism, and validity of the survey instrument, four physician-experts with advanced training in survey methodology individually reviewed the questionnaire in a semistructured fashion, discussing and revising until no further issues arose. Fourteen additional intensivists then reviewed the survey individually for clarity and ease of completion.

Survey Administration. The survey was sent to 448 practicing adult intensivists in university- and non-university-affiliated ICUs across Canada. Intensivists were identified using the Canadian and Provincial Critical Care

Societies and the Royal College of Physicians and Surgeons of Canada. We excluded retired intensivists and pediatric intensivists. In total, 448 critical care physicians were considered eligible. The study population was surveyed between May 2002 and October 2002. The study was approved by the Mount Sinai Hospital Research Ethics Board, who waived the requirement for informed consent.

If target respondents had not returned the questionnaire within 8 wks of the initial mailing, a duplicate copy was sent. Nonrespondents to both mailings were then contacted by phone approximately 8 wks after the second mailing, to urge them to complete and return the survey.

Data Management and Statistical Analysis. Research personnel entered data from the paper survey into a database (Microsoft Access), which included range and consistency checks. Descriptive statistics, including mean values, standard deviations, distributions, and confidence intervals, were used to address our primary questions. Regression methods were used to address possible determinants of response (practice setting, size of hospital, age, sex, and years of experience). Where responses were significantly skewed, we collapsed responses into two categories and conducted step-wise forward logistic regression including all variables with p values of $<.1$ in the final multivariable model. Where variables showed reasonably uniform distributions across the response options, we used step-wise forward linear regression models including all variables with p values of $<.1$ in the final model.

RESULTS

Of the 448 surveys distributed to eligible physicians, 273 (60%) were returned. The demographic characteristics of the respondents are shown in Table 1. Fifty-one percent of respondents work in cities with a population of $>500,000$. Seventy-six percent have a clinical pharmacist attending daily ICU rounds.

Analgesics and Sedatives. Figure 1 illustrates the frequency of use of the most commonly administered sedatives, analgesics, and antipsychotics. Midazolam and lorazepam are the most frequently used sedatives, whereas propofol is the primary sedative choice for 13% of respondents. Morphine is the most commonly administered analgesic, with fentanyl a second choice. Fifty-six percent of respondents use haloperidol frequently or primarily. Ativan is primarily administered as intermittent intravenous boluses (64%), midazolam is administered by intravenous bolus (53%) or continuous infusion (45%), and 79% administer propofol as a con-

tinuous infusion. Approximately 50% of intensivists give morphine as continuous infusion and 50% as bolus doses. Fentanyl is given most commonly as intravenous boluses (51%) or infusion (39%). Eighty-nine percent of respondents administer haloperidol as intermittent intravenous boluses.

Clinicians were asked to rate the importance of various factors that are important in their choice of sedative or analgesic agents. The top six “extremely important” or “very important” factors, ranked in order of importance, were: clinician familiarity, rapid onset of action, adverse effects, half-life of medication, patient specific factors, and publications/evidence. Factors that ranked lower were institutional guidelines, recommendations of the nurse or pharmacist, and the cost of the medication.

Clinicians were asked, “How often do you use sedatives/analgesics for the following needs?” The most common indications for administration of sedation/analgesia were pain, agitation, anxiety/fear, to facilitate mechanical ventilation, and to facilitate procedures. Less frequent indications were to decrease metabolism, to control intracranial pressure, for transportation, and for sleeplessness.

Ninety-two percent of respondents stated that most ($>75\%$) or all of their mechanically ventilated patients receive analgesics in addition to sedatives at some time during their ICU stay. When asked about the use of continuous infusions of sedatives, 26% use infusions in few patients ($<25\%$), 38% in some patients (25–75%), and 36% use infusions in most or all patients. For analgesic infusions, corresponding percentages were 26%, 42%, and 31%. The preferred agents for sedative infusions were midazolam (50%), propofol (22%), and lorazepam (21%). For analgesic infusions, the preferred agents were morphine (85%) and fentanyl (14%).

Sedative and Analgesic Protocols and Monitoring. Twenty-nine percent of respondents indicated that a protocol/care pathway/guideline for the use of sedatives or analgesics is currently in use in their ICU, and the majority of these protocols were developed locally. In the ICUs not using a protocol, decisions regarding dosing of these agents are primarily made by the attending physician (73%), nurses (33%), and residents (22%). A sedation scoring system is used by 49% of respondents. Of these,

Table 1. Demographic characteristics of respondents (n = 273)

Characteristic	% Respondents
Male sex	85
Age in yrs	
<40	30
40–49	47
>49	22
Years of practice	
0–5	26
6–10	23
11–15	21
16–20	15
>20	15
Specialist certification ^a	
General internal medicine	56
Critical care	55
Anesthesiology	24
Respirology	24
Other/none	12
Type of hospital	
Community hospital, nonteaching	26
Community hospital, teaching	20
University hospital	54
Types of ICU patients ^a	
Medical	93
Surgical	92
Trauma	53
Neurosurgical	49
Coronary	42
Cardiovascular surgical	39
Burns	27
Residents/fellows in training in ICU	64
No. of hospital beds	
<100	5
100–400	39
401–750	44
>750	12
No. of ICU beds	
1–10	27
11–20	39
>20	28
Mechanically ventilated patients in ICU, %	
<25	14
25–50	15
51–75	27
>75	44

ICU, intensive care unit.

^aRespondents were asked to check all responses that applied to them.

67% use the Ramsay scale (4), 10% use the Sedation-Agitation Scale (5), 9% use the Glasgow Coma Scale, and 8% use the Motor Activity Assessment Scale (6). Twenty-seven percent of respondents replied that the sedation scoring system was chosen by the ICU physicians, and 21% replied that it was chosen by a multidisciplinary team. The reported frequency of monitoring with the sedation score varied: 29% use hourly scoring, 41% use scoring every 4 hrs, 10% use scoring once per shift, and 15% responded that the frequency of monitoring varies depending on the physician or patient.

Other types of monitoring reported were continuous electroencephalographic

(4%) and bispectral index monitoring (2.5%). Only 3.7% of intensivists use a delirium scoring system in their ICUs. Daily interruption of continuous infusions of sedatives or analgesics is practiced by 40% of intensivists. However, 63% of these physicians interrupt infusions in only some patients. These physicians prefer not to interrupt infusions in patients who are paralyzed or extremely ill (e.g., high intracranial pressure, difficulty ventilating, or hemodynamically unstable). Eighty-six percent of intensivists interrupt infusions before or during morning rounds. If needed, infusions are restarted at the previous dose by 20%, at half the previous dose by 19%, and 56% of respondents had no standard approach.

Neuromuscular Blocking Agents. The NMBA most commonly used are pancuronium, rocuronium, and vecuronium. All three of these agents are most commonly administered as intermittent intravenous boluses. Of clinicians that use cis-atracurium, approximately 50% administer it by continuous infusion and 50% by intermittent bolus. The most important factors in intensivists' choice of a particular NMBA are: clinician experience, duration of action, half life, mechanism of elimination, and patient-specific factors. The least important factors influencing their choices are pharmacist or nurse recommendation, cost, and publications/evidence. Figure 2 illustrates the indications for usage of NMBA. The most common indications are for endotracheal intubation, for unconventional ventilation, for reduced respiratory system compliance, and for hypoxemia. The indication for which NMBA are least commonly used is agitation. Only 22% of respondents currently have a protocol for the use of NMBA in their ICU. With regard to monitoring while patients are treated with NMBA, 61% use physical examination, 84% use peripheral nerve stimulation (train of 4 monitoring), 7% use creatine kinase levels, and 0.73% use electromyography. In patients receiving NMBA for >24 hrs, 63.7% of respondents discontinue the NMBA daily to allow patient movement. Of these latter respondents, 49% do so routinely, 40% frequently, and 10% occasionally. Reversal agents are used occasionally by 41%, frequently or routinely by <1%, and never by 58%. Only 1% of respondents have a standard protocol for the use of reversal agents. Correlates of Response.

We evaluated whether certain demographic characteristics correlate with usage of a sedation protocol, a sedation scale, a delirium scale, and daily sedative interruption. Intensivists working in university-affiliated hospitals are more likely to employ a sedation protocol and scale, but there was no difference in usage of a delirium scale or daily sedative interruption (Fig. 3). Intensivists working in larger ICUs (≥ 15 beds), who made up 53% of respondents, are more likely to use a protocol and sedation scale than those working in smaller ICUs (1–14 beds) (Fig. 4). Regarding training, intensivists with anesthesiology training (and no formal critical care training) are more likely to use a protocol and sedation scale than other intensivists. However, critical care-trained intensivists are more likely

to use daily interruption (Fig. 5). There was no association between the number of years of critical care practice and the use of any of the four strategies. However, 52% of critical care physicians <40 yrs of age practice daily interruption compared with 35% of physicians ≥40 yrs of age ($p = .0092$). There was no association between physician age and use of the other three strategies.

DISCUSSION

The goals of this national survey were to characterize the perceived utilization of sedative, analgesic, and neuromuscular blocking agents and the use of sedation

scales, algorithms, and daily sedative interruption in mechanically ventilated adults by Canadian intensivists. In January 2002, a joint task force of the Society of Critical Care Medicine and the American Society of Health-System Pharmacists published practice parameters for intravenous sedation and analgesia (3) and for sustained neuromuscular blockade in the ICU (7). The Society of Critical Care Medicine guidelines grade the evidence regarding choice of sedatives/analgesics in the ICU, sedation/analgesia assessment, and the use of scoring systems, and these guidelines provide rec-

ommendations for clinicians. However, the report acknowledges that the guidelines are based on contradictory results from few randomized trials. Performance of the current survey followed the publication of these guidelines.

Even when guidelines based on high-quality evidence are available, it is clear that wide variation in clinical practice exists. Surveys of sedation and analgesic administration in ICUs in the United States and other countries reveal widely varying practice patterns with regard to type of medications, method of administration, and sedation monitoring (8–14). In this survey of Canadian intensivists, we also found wide variation in self-reported practice patterns. Reported use of interventions, including sedation protocols, sedation scoring systems, delirium scales, and daily sedative/analgesic interruption, differed depending on clinicians' age, training, size of ICU, and whether they practice in a community or university-affiliated hospital.

The paucity of data available on the choice of sedatives in the ICU was recently highlighted in a systematic review by Ostermann et al. (15), who found that only a minority of sedative agents used in the ICU have been evaluated rigorously by more than one or two randomized, controlled trials, and most of these trials were not double-blinded. Nevertheless, the Society of Critical Care Medicine report recommends midazolam and propo-

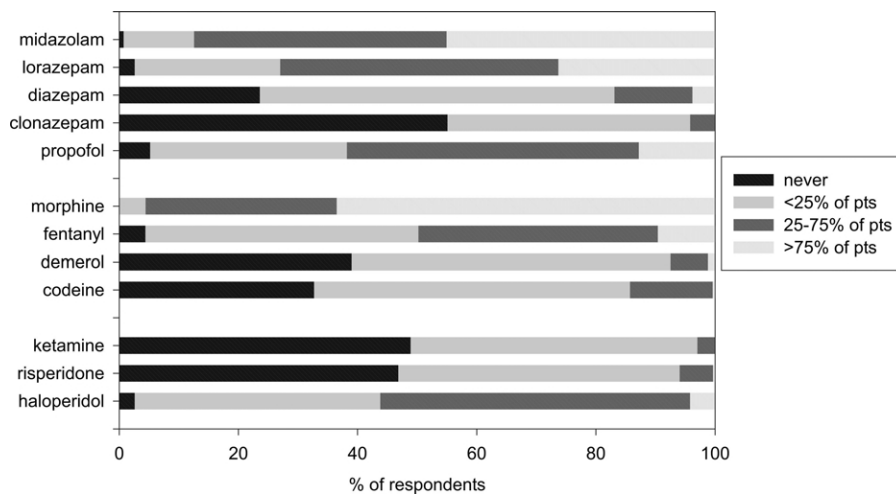


Figure 1. We asked respondents about the frequency of their use of each of these sedatives, analgesics, and antipsychotics.

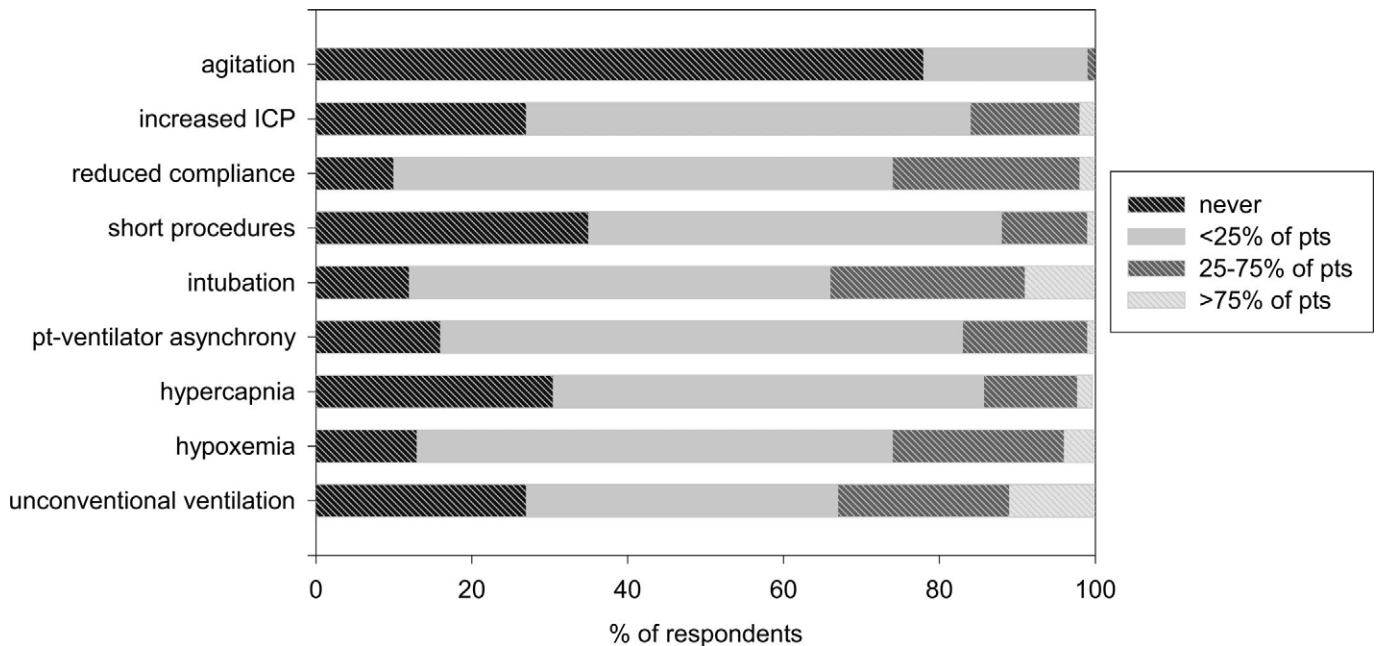


Figure 2. We asked respondents about the frequency of use of neuromuscular blockers for each of these indications. *ICP*, intracranial pressure; *pt*, patient.

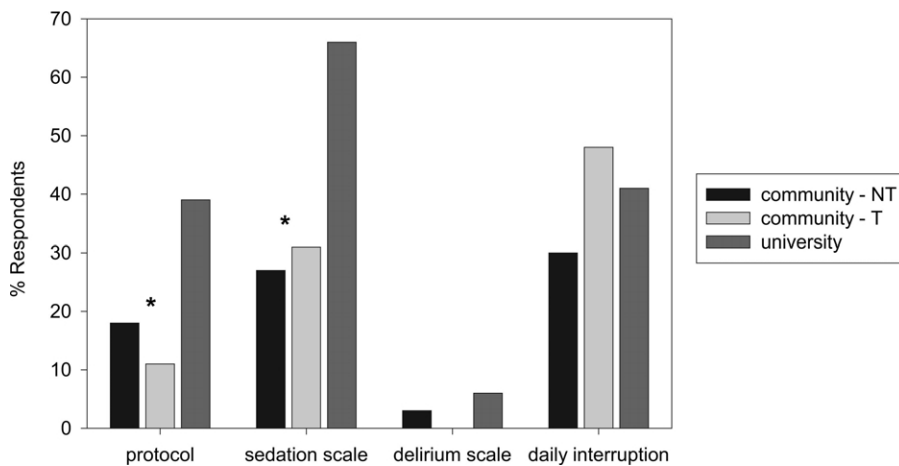


Figure 3. Use of sedation protocols, sedation scales, delirium scales, and daily sedative/analgesic interruption by respondents' practice location. *Community-NT*, community nonteaching hospital; *community-T*, community teaching hospital; *university*, university-affiliated hospital. * $p < .0001$ for the comparison between community and university-affiliated hospitals.

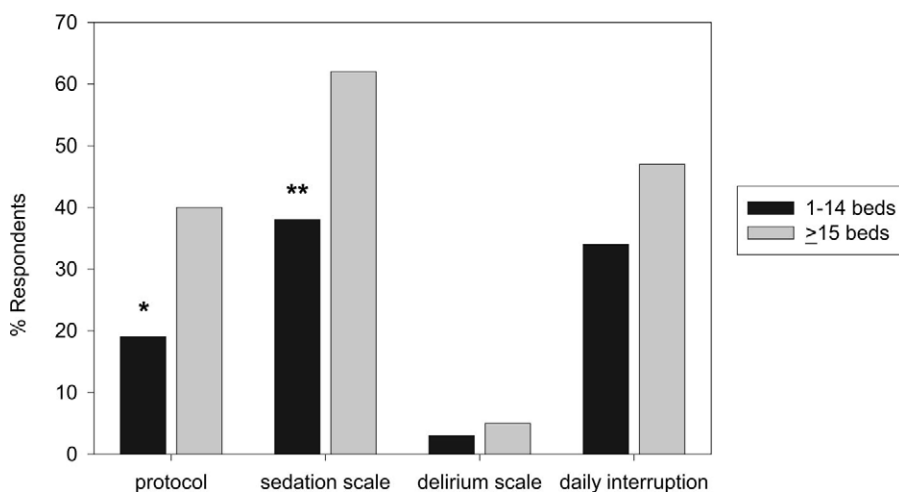


Figure 4. Use of sedation protocols, sedation scales, delirium scales, and daily sedative/analgesic interruption by size of respondents' intensive care unit. Forty-seven percent of respondents work in intensive care units with 1–14 beds, and 53% work in intensive care units with ≥ 15 beds. * $p = .0019$; ** $p < .0001$ for the comparison between 1–14 beds and ≥ 15 beds.

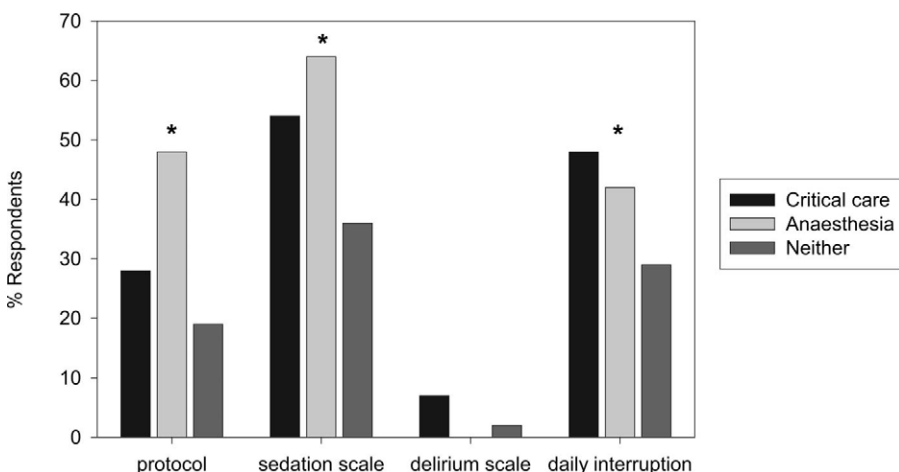


Figure 5. The use of sedation protocols, sedation scales, delirium scales, and daily sedative/analgesic interruption by respondents' training: critical care, anesthesia, or neither. * $p < .05$ for comparison between type of training.

fol as the preferred agents for short-term sedation and lorazepam for long-term sedation (3). However, published studies are controversial, and many do not support these recommendations. McCollam et al. (16) compared the safety, efficacy, and cost of infusions of lorazepam, midazolam, and propofol in critically ill patients. Although lorazepam was the most cost-effective agent, it caused the most oversedation. They concluded that midazolam is the most titratable drug, avoiding both over- and under-sedation. Similar results were observed in a study using sophisticated modeling techniques to compare the pharmacokinetics and pharmacodynamics of lorazepam and midazolam administered as infusions (17). In contrast, in one ICU, the introduction of ICU sedation guidelines promoting lorazepam rather than midazolam or propofol led to a 75% reduction in sedation drug costs and did not adversely affect weaning duration (18). Despite the recommendations, we found that Canadian physicians use midazolam most frequently, followed by lorazepam and propofol.

The guidelines also endorse the use of a sedation algorithm (grade B) or daily sedative interruption (grade A), as two separate prospective trials have shown impressive outcome benefits with each of these strategies (1, 2). However, the majority of intensivists did not report using either of these strategies. Similarly, the use of a validated sedation assessment scale is recommended (grade B), and the incorporation of sedation scales into routine ICU practice has been found in observational quality improvement studies to improve patient outcome (19–21). In the current survey, 29% of respondents employ a written protocol or guidelines for administration of sedatives and analgesics. Rates from surveys published in the last 5 yrs range from 27% in Sweden (12) to 33% in Denmark (10) and the United States (11). Forty percent of respondents employ daily interruption of sedative/analgesic infusions but only in selected patients. Previous surveys have not reported the frequency of use of this strategy; thus, it is not clear how this practice compares with other countries.

Only four sedation scales developed in adult ICU patients (4–6, 22) have been tested for reliability and validity, and only one has been tested for responsiveness, defined as the ability to detect change in sedation status over time (22). Approximately half of Canadian intensivists replied that their ICU uses a sedation scor-

ing system, and 67% use the Ramsay scale. Reported use of sedation scales is 16% in Denmark (10), 67% in the UK (8), and 16% in Sweden (12). In an international survey of 16 western European countries, the use of sedation scales ranged from 18% of ICUs in Austria to 72% in the UK (14). The Ramsay scale is the most commonly used scale. In a United States survey, Rhoney and Murry (11) reported that 78% of respondents monitor sedative usage; however, the majority used the Glasgow Coma Scale.

Delirium in the ICU is common, with an estimated rate of 20%. Delirium in critically ill patients is of particular concern because of its associated morbidity and an increased rate of self-extubation and removal of catheters (23). Ely et al. (24) found that the duration of delirium was significantly associated with length of stay in the ICU and in the hospital, and using multivariate analysis, they identified delirium as the strongest predictor of hospital length of stay. In the ICU population, the frequent inability to conduct an interview makes diagnosis of delirium difficult, and until recently, there was no easily applicable assessment tool for delirium. Recently, two delirium assessment instruments have been validated for ICU patients (25, 26). It is not yet clear whether regular monitoring for delirium or targeted treatment improves patient outcomes. Currently, very few Canadian intensivists use delirium scales, and none of the previous surveys have reported on the frequency of delirium assessment in ICU patients.

The latest recommendations for adult critical care practice suggest that patients receiving neuromuscular blockade should be appropriately assessed with peripheral nerve stimulation to assess the degree of blockade that is maintained and that daily interruption of NMBAs may decrease the prevalence of prolonged neuromuscular blockade (7). In the current survey, most (84%), but not all respondents, routinely assess the degree of neuromuscular blockade using peripheral nerve stimulation, and 64% discontinue NMBA infusions daily to allow patient movement.

The strengths of this survey lie in the rigorous survey development methodology, which optimized clarity, clinical sensibility, comprehensiveness, reliability, and responsiveness of the survey instrument. We used methods to maximize questionnaire response rates, including a stamped return envelope, follow-up with

a second mailing of the survey, and a subsequent phone call. We are confident that we have achieved a wide cross-sectional sampling of intensivists with regard to years of experience, training, and location of practice, among other variables, thus enhancing generalizability of the survey results. We reported practice patterns and their determinants through multivariable analysis.

There are some notable limitations to this survey. Although the response rate of 60.9% is high for lengthy surveys of this type, we cannot exclude the possibility that respondent bias affected our results. In addition, >50% of respondents were from Ontario. Another limitation of this survey stems from the possible differences between stated and actual practice. That is, what physicians report that they do in surveys often contrasts significantly with what they are found to do in observational studies. However, our intent was to determine the perceived sedation/analgesia/NMBA practice. Information about the actual practices would also be useful and will be captured by a future prospective observational survey.

It is clear that a large gap still exists between published evidence/guidelines and actual intensivist practice. For example, after the publication of the ARDSNet trial showing reduced mortality in ARDS patients ventilated with 6 mL/kg, an audit of one ICU that had previously enrolled patients into the trial revealed infrequent application of the low tidal volume strategy (27). Randomized trials provide the strongest evidence regarding treatment efficacy, and the methodology has been applied to sedative/analgesic agents and sedative strategies (e.g., sedation protocols, daily interruption). Nevertheless, varying degrees of uncertainty and controversy surround the use of different medications and other strategies for sedation. There are many reasons for the failure of clinicians to incorporate information from randomized trials into clinical practice. There are several possible explanations when uncertainty and controversy dominate an area of clinical practice. First, the strength of the study designs of investigations may be weak. Second, the designs may be strong, but the sample sizes inadequate, or the results variable, with no clear explanation for the variability. Third, clinicians may vary in their interpretation of the results. Fourth, clinicians may have varying levels of awareness of the available evidence.

Use of sedation strategies that have been shown to improve outcome is not widespread, and tremendous variability exists in clinicians' sedation practices throughout Canada.

If the final explanation is an important contributor to varying beliefs and practices, an educational intervention targeted at translation and dissemination of knowledge to clinicians is in order. Differences in care driven by lack of awareness or misinterpretation of data constitute a potentially important problem. Information related to physician practice at a national level may highlight discordant practices and thus stimulate clinicians to reevaluate the evidence on which their practice is based. This information may also lead us to consider structured educational interventions (including, but not limited to, evidence-based practice guidelines) and health services research to evaluate these interventions. Considering a broader perspective, understanding which clinical questions clinicians consider as unresolved will help to guide investigators in this field in decisions about the relative need for clinical trials in various areas related to sedative use in the ICU.

The majority of patients receive sedation and analgesia at some time during their ICU stay. The way in which clinicians administer these medications can have a profound impact on patient outcomes. Critical care physicians seem to have partially implemented, well-publicized guidelines for the administration of sedation, analgesia, and neuromuscular blockade. Nevertheless, the use of sedation strategies that have been shown to improve outcome is not widespread, and tremendous variability exists in clinicians' sedation practices throughout Canada. The results of this survey emphasize the need for further educational and research efforts in sedative/analgesic use in the ICU.

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