Analgesia in Neurocritical Care: An International Survey and Practice Audit*

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Objective: To characterize analgesic administration in neurocritical care.

Design: ICU pharmacy database analgesic delivery audits from five countries. A 31-question analgesic agent survey was constructed, validated, and e-distributed in four countries.

Setting: International multicenter neuro-ICU database audit and electronic survey.

Patients: Six ICUs provided individual, anonymized analgesic delivery data in primary neurological diagnosis patients. Prescriber surveys were disseminated by neurocritical care societies.

Interventions: None.

Measurements and Main Results: Analgesic delivery data from 173 patients in French, Canadian, American, and Australian and New Zealand ICUs suggest that acetaminophen/paracetamol is the most common first-line analgesic (49.1% of patients); opiates are the "second line" in 31.5% of patients; however, 33% patients received no second agent. In the 2.3% with demyelinating disease, gabapentin was the most likely second analgesic (50.0%). Third-line analgesics were scarce across sites and neuropathologies. Few national or regional differences were found. The analgesic preference rankings noted by the 95 international physicians who completed the survey matched the audits. However, self-reported analgesic prescription rates were much higher than pharmacy records indicate, with self-reported prescribing of both acetaminophen/paracetamol and opiates in 97% of patients and gabapentin in 45% of patients. Third-line analgesic variability appeared to be driven by neuropathology; ibuprofen was preferred for traumatic brain injury, postcraniotomy, and thromboembolic stroke patients, whereas gabapentin/pregabalin were favored in subarachnoid hemorrhage, intracranial hemorrhage, spine, demyelinating disease, and epileptic patients.

Conclusions: Opiates and acetaminophen are preferred analgesic agents, and gabapentin is a contextual third choice, in neurocritically ill patients. Other agents are rarely prescribed. The discordance in physician self-reports and objective audits suggest that pain management optimization studies are warranted. (*Crit Care Med* 2016; 44:973–980)

Key Words: analgesia; intensive care; neurologic critical care; practice audit; pharmacology; survey

***See also p. 1019.**

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Current analgesic and sedation goals for the general ICU patient have shifted toward minimizing sedation, maximizing pain control, and improving patient awareness and mobility during the acute phase of their critical illness (1–3). Standardized assessment tools for pain, sedation, and delirium have made managing analgesia in general medical or surgical ICU patients more objective and goal directed (4–6). Multidisciplinary teams, including critical care pharmacists, can further reduce analgesia practice pattern variability in the ICU (7).

Although systematic pain assessments improve outcomes across all ICU patient populations (8, 9), the majority of publications describing current practice (10–12) or addressing the quality of analgesia completely exclude or include only a minority of neurocritically ill patients (13). Adequate analgesia in a neurological ICU setting is a delicate balance; providing painlessness is weighed against avoiding excessive sedation (6). Individual patient anxiety and delirium symptoms may interfere with accurate pain perception and assessment. Systematic

pain assessments and titrated pharmacological analgesia are considered challenging among the neurocritically ill patients, despite good evidence that pain assessments are feasible in the majority of these patients regardless of their underlying neuropathology (14). Furthermore, no data support outcome-driven pharmacological analgesic choices in this population (15).

Any analgesic effectiveness assessment in the neurocritically ill patients requires an evaluation of practice patterns and beliefs. We performed an international, multicenter, ICU pharmacy database audit of analgesic prescriptions in neurologically ill patients to determine true practice patterns (**Table 1**). In addition, we surveyed physicians caring for the neurologically critically ill in the same geographic areas, in order to identify potential disease-specific or regional practice differences. Our goal was to provide a descriptive pilot account of analgesic clinical practice with the international database audit to support our hypothesis that we would identify practice quality gaps, and to outline practices from which prospective evaluation of analgesic efficacy could eventually be planned. In addition, we sought clinician's perceptions with the survey results, in order to identify possible patterns in self-reported versus actual practice differences (**Table 2**).

METHODS

Practice Audit Ethics

Local institutional approval and research ethics board approval for collection of anonymous patient pharmacy data were obtained prior to the initiation of the pharmacy audit at each institution. Consent was waived, and all audited ICU patients were prescribed and received analgesics.

ICU Analgesia Practice Audit

Our audit of ICU pharmacy records in patients with neurological illness aimed to identify:

1. Commonly prescribed analgesics for patients with neurological illness, by frequency and rank order.
2. Disease-specific practices and difference between individual disease processes.
3. Administered doses of commonly prescribed drugs such as acetaminophen and opiates.
4. Avoidance of specific classes of medications in particular neuropathologies.
5. Continental, national, or regional practice patterns.

Hôpital Sacré Cœur de Montréal, the Montreal Neurological Institute, and the Montreal General Hospital in Montreal, Canada; the Carolinas Trauma and Neuro-ICU F.H. "Sammy" Ross, Jr Center, Carolinas Medical Center (CMC) in the United States; and the Prince of Wales Private Hospital in Sydney, Australia participated in the audit. Local collaborators (listed below) were asked to collect pharmacy prescription records over a continuous, convenience-based 2-week period; data collection was not simultaneous across sites and occurred between October 2013 and June 2014 in 2-week blocks. All patients admitted to ICU with a primary neurological diagnosis, and in whom the neurological diagnosis was the primary motive for analgesia (based on the site investigator's judgment;

TABLE 1. Pharmacy Audit Top First-, Second-, and Third-Line Analgesics for Individual Neuropathology

	First Line (% Patients)	Second Line (% Patients)	Third Line (% Patients)
Traumatic brain injury (30.6% of patients)	Opiates (47.2)	Opiates (47.1)	None (73.6) (acetaminophen, 41)
Subarachnoid hemorrhage (16.8%)	Opiates (51.7)	None (37.9) (acetaminophen, 31)	None (79.3)
Intracerebral hemorrhage (15.6%)	Acetaminophen (37.0)	None (51.9) (opiate, 41)	None (92.6)
Embolic stroke (11.0%)	Opiates (36.8)	None (47.4) Acetaminophen (31)	None (94.7)
Tumor	Acetaminophen (64.7)	None (58.8) Opiate (34)	None (64.7)
Postcraniotomy/craniectomy	Acetaminophen (77.8)	None (44.4) Opiates (30)	None (88.9)
Epilepsy	Acetaminophen (50.0)	None (50.5) Opiates (35)	None (100.0)
Demyelinating disease	Acetaminophen (50.0)	Antiepileptic drugs (gabapentin and pregabalin) (50.0)	None (50.0)
Spine	Acetaminophen (75.0)	Acet/Opiat/nonsteroidal anti-inflammatory drugs (25.0)	None (75.0)
Transsphen	Acetaminophen (100.0)	None (100.0)	None (100.0)
Trigeminal neuralgia/ glossopharyngeal neuralgia	Acetaminophen (100.0)	None (100.0)	None (100.0)
Anoxic brain injury	None (100.0)	None (100.0)	None (100.0)

The percentage of patients in the diagnostic column on the left is identified for pathologies of 10% or greater frequency. "None" means that no second- or third-line agent was prescribed in the highest proportion of patients in that pathology category. The most prescribed pharmacological intervention is identified in parentheses and italics below the "none" identifier when no prescription was the most frequent occurrence.

TABLE 2. Survey Responses for First-, Second-, and Third-Line Analgesics for Individual Neuropathology

	First Line (% of Respondents)	Second Line (% of Respondents)	Third Line (% of Respondents)
Subarachnoid hemorrhage	Opiates (76.9)	Acetaminophen (70.8)	Pregabalin (10.8)
Intracerebral hemorrhage	Opiates (92.2)	Acetaminophen (90.6)	Pregabalin (10.9)
Embolic stroke	Acetaminophen (87.3)	Opiates (81.0)	Ibuprofen (15.9)
Traumatic brain injury	Opiates (77.4)	Acetaminophen (72.6)	Ibuprofen (11.3)
Postcraniotomy	Opiates (82.3)	Acetaminophen (82.3)	Ibuprofen (11.3)
Complex spine	Opiates (83.9)	Acetaminophen (79.0)	Gabapentin (25.8)
Demyelinating disease	Acetaminophen (77.9)	Opiates (61.0)	Gabapentin (61.0)
Epilepsy	Acetaminophen (75.0)	Opiates (68.3)	Gabapentin (20.0)

e.g., traumatic brain injury [TBI] patients with polytrauma, or neurocritically ill patients with another confounding diagnosis for analgesic use, were excluded), were considered eligible. The primary neurological illness and all prescribed medications were recorded anonymously and stored in an electronic database. Given the limitations related to international ethics approval, only pharmacy data were accessible for study purposes. Thus, information at admission clinical status, Fischer CT grades, Hunt and Hess grades, and other past medical history/comorbid conditions was not available.

Analgesics records included drug class, dosage, administration route, frequency, and order of administration in the prescription, with ranking order of the prescriptions if more than one agent was prescribed. All responses were analyzed together, as well as according to specific neurologic diagnosis, institution, and geographical region.

International Physician Survey

A 31-question electronic survey using the online software Survey Monkey was created by four of the authors (F.Z., F.A., J.T., Y.S.), whose clinical practice includes neurocritical care (13). Our goal was to identify self-reported analgesic practice patterns of physicians caring for the neurocritically ill patient population. Four neurointensive care physicians and one pharmacist then independently validated these questions, which aimed to address analgesic practice questions likely to impact the quality of analgesia and other outcomes, for construct and content validity and comprehensiveness (15, 16). The audit was then modeled according to the same themes to permit comparisons. A panel of four additional ICU physicians independently trialed the survey and provided feedback and validation of content prior to survey dissemination.

The survey included four demographic-focused questions (country of practice, role, years of experience, and ICU type) and 11 questions, with open-ended and multiple-choice formats, related to general analgesic choices for patients with neurological critical illness. The remaining 16 questions focused on particular analgesic choices for specific neuropathology. The specific neurological illnesses were as follows: subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), postcraniotomy, thromboembolic stroke, TBI, complex spine surgery, demyelinating/neuropathy, and epilepsy.

The survey (**Appendix 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/B839) was then sent internationally by email to national physician neurocritical care society specialist groups caring for neurocritically ill patients in Canada, the United States, France, and Australia/New Zealand. The anonymity required by the list-serve rules precluded identifying how many members received, or read, the survey. A reminder request was sent 2 months after the original mailing in September 2013. Responses were gathered from November 2013 to May 2014 inclusively.

Comparative Analysis

We compared self-reported versus actual practice patterns with the following questions:

1. Are there discrepancies between self-reported and actual practice for analgesic prescriptions in the neurologically ill (globally and in disease-specific circumstances)?
2. Are the self-reported and delivered analgesics provided in effective doses?
3. Are there center-specific or regional variations?
4. Are particular classes of medications avoided in specific neuropathology? If present, are these preferences clarified by the multiple-choice or open-ended questions?

Statistics

We used simple descriptive statistics, with means and percentages, for the presented data from both the database audit and the survey portions of the study.

RESULTS

ICU Pharmacy Audit

Patient Demographics. Each of the audited ICUs chose a 2-week period based on local sampling convenience; the data were collected between October 2013 and October 2014 and yielded data from 173 sequentially admitted (in each unit) neuro-ICU pharmacy patient records. Canadian critical care

units enrolling patients included 1) a specialized academic hospital with general ICU admissions, only in patients with neurological disease as a primary diagnosis and 2) two large academic regional trauma centers with specialized trauma and neuro-ICU beds (units 2–4, respectively, in **Table 3**). The American sites house the largest academic regional trauma center and a distinct neurological critical care unit. The Australian center is a large trauma and specialized neurological care academic ICU. The mean patient age was 56.9 years (range, 17–84 yr).

On an average, the number of received analgesics per patient was 1.9 (range, 0–5). Specific patient neuropathology admission diagnoses during the audit were as follows: TBI (30.6%), ICH (15.6%), SAH (16.8%), embolic stroke (11.0%), tumor (9.8%), elective craniotomy/craniotomy (5.2%), epilepsy (3.5%), demyelinating disease (2.3%), complex spine surgery (2.3%), transsphenoidal surgery (1.2%), trigeminal neuralgia/glossopharyngeal neuralgia (1.2%), and anoxic brain injury (0.6%). Figure 2 displays the patient's neuropathologies.

The majority of patients received two (44%) or three (24%) analgesics; 21% received only one and 10% received none across all pathologies. We did not record the trigger for analgesic delivery, or whether its administration occurred in response to patient-reported or behavioral (8) pain assessment scales, or because of neurocritically ill patient–specific cues (17). This information could not be gleaned from the audit; none of the ICUs had a specific protocol in place at the time of the survey.

We initially tallied all medications prescribed in all patients admitted to all sites. The frequency with which patients in this cohort were prescribed an agent was listed in rank order; if more than one drug was prescribed "ranking" ("first-line," "second-line," etc) was determined by the drug prescribed first and prescribed as "to be administered" first. Overall, the most commonly prescribed and administered first-line analgesic was acetaminophen/paracetamol (49.1%); no agent at all was the most likely second prescription pattern (32.7%), closely followed by opiates in frequency of administration (31.5%). Few patients (24%) received a third-line agent, and a small proportion of patients received up to six analgesic pharmacologic agents. One hundred and seventy-two of the 173 patients received an acetaminophen dose of 650 mg orally, every 4–6 hours; 81 patients received their acetaminophen as a first-line analgesic, and 47 and five patients received it as a second- and third-line analgesia, respectively. Fentanyl, morphine, hydromorphone, and hydrocodone were the most common prescribed opiates and opiate precursors. Doses and administration intervals varied, with most common fentanyl dose range being 25–75 μcg in IV bolus form; most morphine doses ranged from 2.5 to 10 mg with intervals varying from 2 to 6 hours.

Only 10 of the 173 patients received nonsteroidal anti-inflammatory drugs (NSAIDs), consisting mostly of celecoxib and ibuprofen orally. Gabapentin and pregabalin were prescribed in 9, 10, and 10 patients, respectively, with spinal surgery, demyelinating neurological illness, and SAH.

Fourteen patients were given corticosteroids, and only in the form of dexamethasone. Two patients had dexamethasone prescribed as an analgesic for meningeal irritation; the remaining 12 received it for tumor- or stroke-related edema. The analgesic and edema-related doses of dexamethasone were similar, i.e., 4 mg oral/IV every 8–6 hours. Tricyclic antidepressants were prescribed in only one patient. Other medications ordered for one or two patients were cesamet, methotrimeprazine, baclofen, methocarbamol, cyclobenzaprine, clonidine, and dexmedetomidine.

The pathologies listed as primary diagnoses in the chart across all critical care units are described in **Figure 1**.

No disease-specific differences were noted in the types of opiates prescribed although these drugs were more commonly used as first-line analgesics in TBI and embolic stroke patients. All other analgesics were prescribed infrequently. Postcraniotomy/craniotomy and TBI patients occasionally received NSAIDs, mostly oral celecoxib and ibuprofen. Antiepileptic drugs, such as gabapentin and pregabalin, were prescribed in a few ICH, spine, and demyelinating patients. These anticonvulsants were the second-line agents in demyelinating patients. Steroids, specifically dexamethasone, were administered as an analgesic in only the two SAH patients mentioned above.

Thirty-six patients were treated in a trauma ICU setting; the remaining 137 were admitted to a dedicated neuro-ICU. No practice pattern differences were identified between patients treated in trauma versus neuro-ICU settings.

Country-/Regional-Specific Prescription Patterns. The majority of audited ICU patients were hospitalized in Canada, the United States, and Australia (97.5%). Overall, and for all neuropathology categories, the first- and second-line prescribed analgesics were acetaminophen/paracetamol and opiates. Across all countries and ICU's, a third-line analgesic agent

TABLE 3. Country/Regional Differences in Analgesic Practice for Neurocritically Ill Patients

	Canada 1 + 2 + 3	Canada 4	United States 1 + 2	Australia
No. of patients	53	18	89	13
Mean no. of analgesics	2.1	1.8	2.0	1.4
First line (% of patients)	Acetaminophen (84.9)	Acetaminophen (61.1)	Opiates (58.4)	Opiates (61.5)
Second line (% of patients)	Opiates (41.5)	Opiates (27.8)	Acetaminophen (41.6)	None (69.2)
Third line (% of patients)	None (69.8)	None (88.9)	None (74.2)	None (100.0)

Canada 1 + 2 + 3 = English-speaking Canadian ICUs, Canada 4 = French-speaking Canadian ICU, United States 1 + 2 = two ICU, one trauma, and one neuro-ICU in same center.

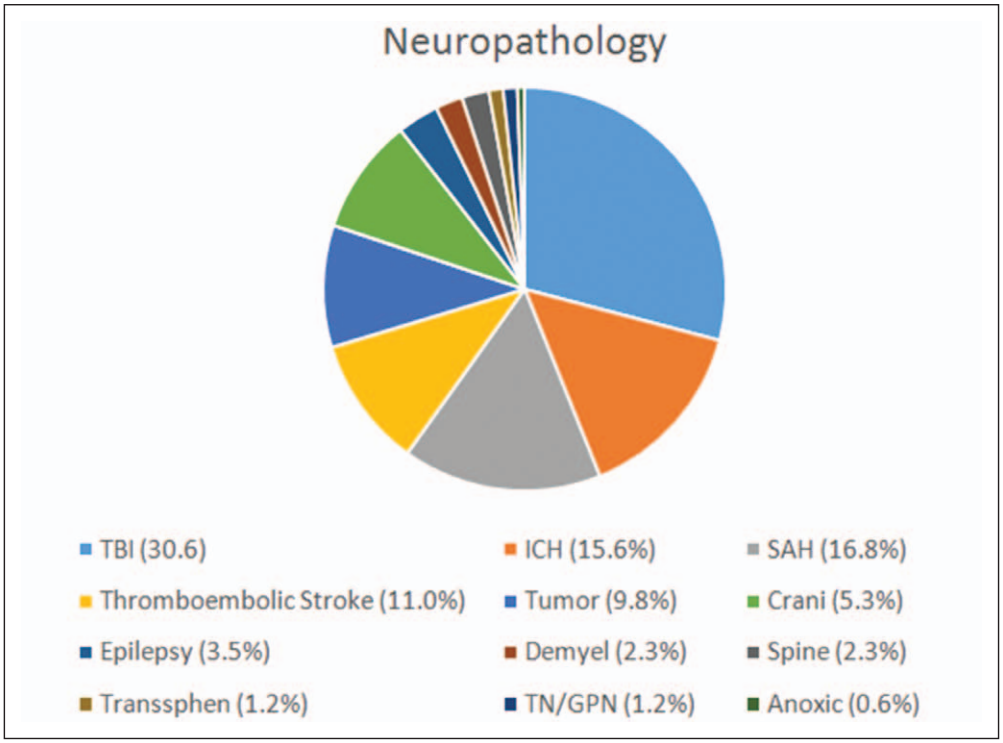

Figure 1. Pathologies are listed as primary diagnoses in the chart across all critical care units. AED = anti-epileptic drugs (gabapentin and pregabalin), Anoxic = anoxic brain injury, Crani = craniotomy/craniectomy, Demyel = demyelinating disease, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, TBI = traumatic brain injury, TN/GPN = trigeminal neuralgia/glossopharyngeal neuralgia, Transsphen = transsphenoidal.

was usually not prescribed (74.0%). A similar mean number of analgesics were prescribed per patient.

A few regional differences concordant with survey responses were identified. Paracetamol was very commonly prescribed in Australia, in contrast to other ICUs. Hydrocodone was the "usual" opiate (precursor) agent in the two American ICUs included in the audit and was not prescribed anywhere else. Celecoxib and methotrimeprazine were only prescribed in Canada to the SAH population. Finally, dexmedetomidine use as a third-line analgesic agent was seen almost exclusively in Australian patients.

Critical care units with less than a 5% difference in prescription patterns were grouped together and corresponded to geographical region and culture (sites 1 + 2 + 3 are within one academic community; site 4 is affiliated with another university). A summary of the country-/regional-specific prescription patterns can be seen in Table 3.

Survey

Demographics of Respondents. A total of 95 physicians responded to our survey during the defined time period; the denominator is unknown. Intensivists made up 94.7% of the respondents, and neurointensivists and neurologists whose practice includes care and prescribing for the neurocritically ill patients accounted for 4.2% and 1.1%, respectively. The physicians reported a mean of 16 years of ICU experience (range, 2–40 yr); 80% reported caring for the neurocritically ill patients in mixed medical/surgical ICUs, whereas those working in medical ICU, surgical ICU, and neuro-ICU constituted 1.1%, 6.3%, and 12.6% of the remaining specialized ICU profiles, respectively. Respondents were mostly Canadian (44.2%) and Australian (41.1%), with some representation from New Zealand (7.3%), France (6.3%), and America and Japan (1.1% each).

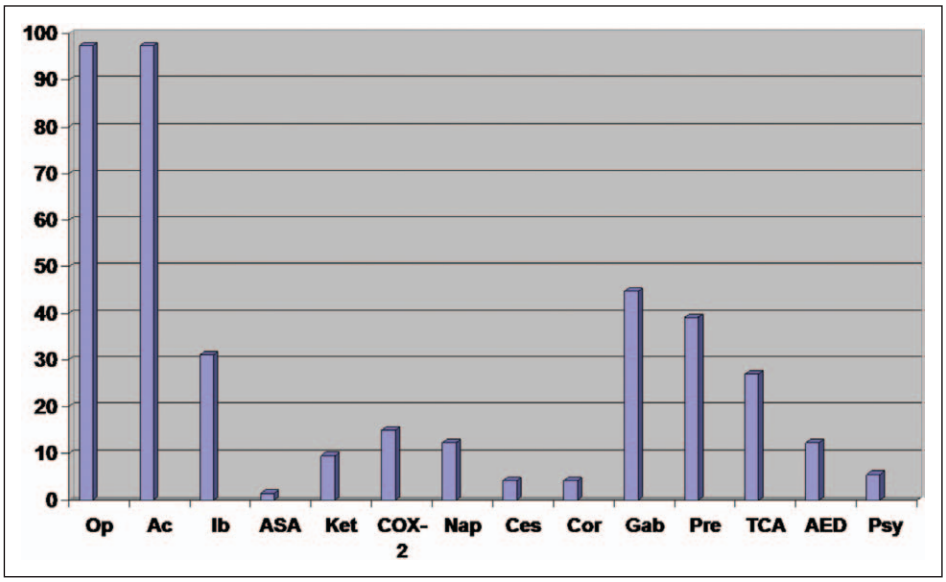

Figure 2. Patient's neuropathologies. AED = antiepileptic drugs (gabapentin and pregabalin), AC = acetaminophen/paracetamol, ASA = acetylsalicylic acid, Ces = cesamet, Cor = corticosteroids, COX-2 = cyclooxygenase 2 inhibitors, Gab = gabapentin, Ib = ibuprofen, Ket = ketotolac, Nap = naproxen, Op = opiates, Pre = pregabalon, Psy = antipsychotics, TCA = tricyclic antidepressants.

Overall Prescription Patterns. The top three medications prescribed in the neuro-ICU patient, as reported by respondents, were opiates in 97.3%, acetaminophen/paracetamol in 97.3%, and gabapentin in 44.6%. An illustration of prescription patterns for all individual medications is represented in **Figure 2**.

Preferred opiates were fentanyl (55.6%), morphine (38.8%), and hydromorphone (27.1%). Reported opiate and precursor choices were sufentanil (3.0%), remifentanil (4.5%), oxycodone (14.6%), and codeine (8.3%). Acetaminophen/paracetamol doses were most often reported as 1 g orally every 4–6 hours (68.6%); the remaining physicians prescribed 650 mg orally, every 4–6 hours.

NSAIDs were self-reported as analgesics of choice in less than 40% of the neurocritically ill patients and were never chosen as a first-line drug, even in patients with postoperative pain. The three most common analgesics were ibuprofen (54.6%), naproxen (42.1%), and celecoxib (33.3%). NSAID routes included oral, IV, and rectal in 80.7%, 12.9%, and 6.5% of patients, respectively.

Corticosteroid use for pain control was only reported by five respondents, with dexamethasone and mean dose of 3 mg orally/IV every 6 hours, specifically and only in the clinical context of meningeal irritation.

Antiepileptics were chosen as an analgesic by 41 respondents (43%) with the following medication preferences: gabapentin in 68.3%, pregabalin in 58.5%, phenytoin in 29.3%, and carbamazepine in 30.0%. Sixteen respondents (17%) indicated using tricyclic antidepressants for pain control in the neuro-ICU, with amitriptyline being the most common.

Disease-Specific Prescription Patterns. The top two commonly reported analgesics prescribed for all disease processes were opiates and acetaminophen/paracetamol. Ibuprofen was prescribed in embolic stroke, postcraniotomy, and TBI patients, whereas the gabapentin/pregabalin was the third-line medication reported in SAH, ICH, spine patients, demyelinating disease, and epilepsy. Table 3 summarizes the first-, second-, and third-line medications by neuropathology category.

Country-Specific Prescription Patterns. Although the majority of first-, second-, and third-line medications reported were the same across all respondents for most disease processes, regardless of country of origin, some regional differences in specific responses were noted. Paracetamol was almost always reported as a first- or second-line analgesic agent in Australia and New Zealand. Ketamine was seldom chosen as an analgesic, but almost all the clinicians choosing it were Australian. Finally, nefopam, an infrequently chosen agent, was selected only by respondents from New Zealand and France.

DISCUSSION

The most striking finding in this practice description lies in the low number of audited neurocritically ill patients who received analgesics while admitted to ICU with critical illness. The number of patients (173) described in the current audit represents a broad sample of a highly selected neurocritically ill population. Although 43% of patients received analgesics from two drug classes, nearly one-third received no or only one drug. Over 75% of the audited patients had diagnoses associated with moderate to severe pain (craniotomies, intracranial tumors, ICH, TBI, and SAH). We were limited, however, in stratifying analgesic patterns by pain level, neuropathological severity of injury, or clinical grade, because of the data access limitations imposed by research ethics boards across sites in the context of waived consent, in order to better preserve patient anonymity.

Observational trials clearly describe moderate to severe pain at rest in over 50% of medical and surgical ICU patients (8, 18), and pain prevalence increases of up to 80% during common care procedures (19). Tracheal suctioning, drain removal, and turning for nursing care are known to be painful and part of routine critical care delivery (20); this understanding has led to guideline recommendations of routine pre-emptive analgesic administration in these circumstances (4). Most neurosurgical ICU patients describe moderate to severe pain in the first 48 hours following admission; this is particularly true in those undergoing interventions and during the first 12 postoperative hours (21, 22). Pain from brain injury and intracranial procedures was once thought to be minimal, yet recent evidence suggests otherwise (22, 23).

Half of the patients (49%; range, 41–90%) received acetaminophen; a significant proportion received a lower (650 mg) dose despite studies and apparent physician intent suggesting a higher dose of 1,000 mg is safe and more effective in surgical ICU patients (11) and in postinterventional pain (24, 25). Almost all patients received acetaminophen orally; this drug's administration appears to provide faster and more reproducible cerebrospinal fluid levels when administered intravenously (26). Almost no patients received anti-inflammatories for pain control. Combining acetaminophen/paracetamol and anti-inflammatories is superior in postoperative pain than either drug alone (27). The safety profile for anti-inflammatories is well-established, and perhaps superior to the acetaminophen/paracetamol safety profiles for this drug class (28); furthermore, combining anti-inflammatories and acetaminophen is superior to either drug alone (or placebo) in pyretic neurocritical care patients (29). A similar number of patients, and the majority overall, received a second analgesic regardless of geographic location or institution; the most commonly prescribed second-line drug was an opiate or opiate precursor. Nearly one quarter (23%) of patients were prescribed opiate precursors.

The pharmacogenomic variability in the metabolism of these precursor molecules determines their potential ineffectiveness and risk (30); nearly 10% of Quebec's Caucasian population are slow metabolizers, making the drug ineffective since it cannot be converted into analgesic opiates. On the other hand, population (such as Ethiopians) with high prevalence (25%) of ultra-rapid metabolism of opiate precursors are at risk for respiratory arrest and other complications of high metabolism and resulting drug levels. Drug-drug interactions affecting drug metabolism and effectiveness are also common in the critically ill (31, 32).

Better education may thus improve caregiver analgesic choices for these critically ill patients. The effectiveness of the administered opiate doses cannot be commented upon given the lack of pain assessment data and the relative lack of information as to opiate effectiveness in general ICU patients and, specifically, the neurocritically ill.

Survey responses came from similar practices and geographic areas as the practice audit's. No corresponding overlap can be inferred, as the regional representation in the survey

(mostly Canadian and Australian) differs from the regional representation in the audit (mostly Canadian and American), making self-report and real-life practice comparisons challenging. Because the professional associations providing us with the neurocritical care society list-serves required anonymity, we are not able to document how many came from the audited sites. However, the majority of prescribing practitioners self-reported similar prescription patterns as those found in the audit. It is noteworthy that the survey respondents believed that analgesics were provided to most patients, whereas the audit suggested that this was an inaccurate perspective. Audits are the only way to truly evaluate the quality of care delivered to patients (33). Self-reporting "better" care is consistent with the median self-reported overestimation of adherence to guidelines of 27% noted among physicians (34). These findings support the use of neutral, data-driven, patient-focused delivery of care such as the provision of analgesia.

Among the regional differences we identified, some may be attributable to drug or formulation availability. The consistency with which paracetamol was reported as an analgesic therapeutic choice in Australia and New Zealand may be related to its availability in IV form, whereas its use has just been approved in the United States and is not available in Canada. Nefopam was selected by few respondents, all of whom were from New Zealand and France, possibly reflecting recent opinion-leader publications (35); regional availability may have also played a role because the molecule is not currently used in North America due to lack of regulatory body approval.

Evaluating current practice patterns offers opportunities to identify areas for study and improvement. This practice audit and survey represent highly specialized neurocritical care practice in several geographic areas, and is, to our knowledge, the only such survey and audit to date.

Neurocritically ill patients are underrepresented in comparison to "general ICU patients" in most studies; the paucity of evidence as to optimal analgesic management in this population is no exception (36). In a recent systematic review (17), we identified 27 studies addressing pain management in the neurocritically ill patients. Only 38% used a validated pain assessment scale despite analgesia being the primary study goal. Of the 16 studies retained because of their reasonable quality, 13 compared interventions for postcraniotomy or spinal surgery patients; TBI, neuropathy, and intracranial hemorrhage–related analgesia were described in one publication each, respectively. None included heterogeneous populations (with epileptic, SAH, and craniotomy patients) such as ours.

The database audit and practice survey were affected by limited access to admission diagnoses, precluding subcategorization of analgesic patterns based on illness severity or grade. Whether administered analgesic doses were effective is also uncertain; potential comorbid conditions (e.g., chronic pain) and interventions (intraoperative analgesics) may have affected the prescription patterns we describe and individual patient requirements. The survey data may have been subject to the recall and self-report bias inherent to survey-based studies. Finally, our descriptions may have been influenced by local "best practice" or local "expert" influence, which may explain regional variability more than geography or drug availability. These limitations are balanced by the strength of having had each approached institution with neurosurgical ICU patients provide anonymized patient data with waived consent, minimizing bias, and providing us with an accurate reflection of the number of patients and agent distribution across centers. In addition, the practice patterns we identified were consistent across multiple sites, and during different 2-week sampling times, minimizing sampling and temporal bias. The potential practice shortcomings we identified suggest a need for research addressing analgesic requirements and effectiveness in the neurocritically ill patients.

It is estimated that it takes an average of 17 years for scientific evidence to get translated into practice. In Canadian ICU patients, the median proportion of selected best practices delivered was 57% and ranges from 8% to 95% (35); the most seriously ill patients had the lowest likelihood of being its recipients. However, little is known about effective analgesia in the neurocritically ill. No pharmacological agent or class of drug has been shown to provide better analgesic effectiveness in the neurologically critically ill (6). In a single center's analgesia titration study that included neuro-ICU patients, opioids were the most commonly used analgesic (13). Systematic pain assessments showed that 30–40% of patients (half of whom were surgical) experienced no pain and required no or minimal pharmacological intervention; however, titrated analgesia protocols quadrupled the dose range of administered opiates in those patients receiving them. Pain control in the critically ill with nonsteroidal anti-inflammatories has only been studied in postoperative cardiovascular patients (36). Acetaminophen, despite the facility with which physicians prescribe it, has not been prospectively evaluated for its analgesic effects in the ICU. The paucity of studies in this area of care is all the more surprising and disappointing when one considers the frequency with which pain occurs, on one hand, and the value patients place on effective analgesia on the other.

CONCLUSIONS

Our audit of neurocritically ill patients suggests that opiates and acetaminophen are the preferred current practice of analgesic agents, with gabapentin ranking as a contextual third choice. Despite the study's limitations, the discordance described between its physicians' self-reports and objective audits are troubling. The dearth of pain assessment, analgesic effectiveness, and comparative and outcome studies make specific recommendations challenging. However, our findings suggest that the systematic proactive analgesia practice assessments are warranted.

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