Pain and Sedation Management in Mechanically Ventilated Children

Lauren Sorce¹ Shari Simone²

¹Department of Nursing, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois, United States

²Women and Children's Service, University of Maryland Medical Center, University of Maryland School of Nursing Pediatric Acute Care, Baltimore, Maryland, United States

Address for correspondence Lauren Sorce, MSN, RN, CPNP-AC/PC, CCRN, FCCM, Ann & Robert H. Lurie Children's Hospital of Chicago, Pediatric Critical Care Box, 225 E. Chicago Avenue, Box #246, Chicago, IL 60612, United States (e-mail: lsorce@luriechildrens.org).

J Pediatr Intensive Care 2015;4:64–72.

Abstract

Keywords

- pain
- agitation
- sedation
- analgesia
- assessment
- pediatric
- pediatric critical care

Assessing and managing pain and agitation in critically ill children can be challenging. Multiple factors contribute to the challenges of management, including prior medication exposure, surgical and procedural interventions, pharmacokinetics, and age-related pharmacodynamics making the population heterogeneous. Therefore, individualizing treatment approaches embedded with frequent assessments is likely to improve the management of pain and agitation in critically ill children. Novel approaches to manage pain and agitation continue to evolve and will require ongoing evaluation prior to widespread adoption.

Introduction

Critically ill children who require endotracheal intubation and mechanical ventilation often experience pain and agitation while being treated in the pediatric intensive care unit (PICU). Exploring the currently available assessment tools and medications will provide health care team members with a repertoire of management strategies for critically ill children.

Conventional Therapies: Analgesics and Sedatives

Analgesics and sedatives are commonly used medications in the PICU and have variable mechanisms of action depending on class. Although a mainstay in the treatment of critically ill children, selecting the proper medication for the child's condition is necessary to maximize therapeutic response and reduce unintended effects. Important considerations in selecting the right analgesic for the child include his/her condition, previous exposures, current medications, desired delivery route, and targeted goal of analgesia and sedation. See ► **Table 1** for analgesics and sedatives used in the treatment of critically ill children.

Pain and Sedation Assessment

Frequent assessment is essential to optimize the management of pain and agitation in children requiring mechanical ventilation. However, assessing pain and agitation in these children can be difficult due to factors such as young age, disease process, inability to speak, and sedation. The use of a validated pain and sedation scale can provide objective data to guide the multidisciplinary team in determining effectiveness of treatment. This assessment typically requires more than one tool to evaluate comfort related to pain and sedation. Although several assessment tools exist, only a few are appropriate for the assessment of mechanically ventilated children.¹ One frequently used tool to assess pain- and non-pain-related distress in critically ill children is the COMFORT scale and its modified version the COMFORT-Behavior Scale. The COMFORT-Behavior adapted version consists of the six behavioral items in the original version but without the physiologic items that were found to have low internal consistency. Total score ranges between 6 and 30, with a desired score between 11 and 23. Higher scores suggest discomfort and need for treatment. Another tool commonly used specifically to assess pain is the Faces, Legs, Activity, Cry,

received
November 18, 2014
accepted after revision
November 25, 2014

Issue Theme Nursing in the Pediatric Intensive Care Unit; Guest Editors: Andrea M. Kline-Tilford, MS, CPNP-AC/PC, FCCM, and Lauren Sorce, MSN, RN, CPNP-AC/PC, CCRN, FCCM

Copyright © 2015 by Georg Thieme Verlag KG, Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0035-1556748>.
ISSN 2146-4618.

Table 1 Commonly used analgesics and sedatives

Medication	Pharmacology	Route and dose	Pharmacokinetics/pharmacodynamics	Significant side effects
Analgesic medications				
Morphine	Opioid analgesic	Intravenous: Infants ≤ 6 mo: 0.025–0.03 mg/kg/dose every 2–4 h Infants > 6 mo, child: 0.5–0.2 mg/kg/dose every 2–4 h as needed Continuous infusion: 10–30 $\mu\text{g/kg/h}$ titrate to effect Oral ^a : Infants < 6 mo: 0.08–0.1 mg/kg/dose every 3–4 h Infants > 6 mo, child: 0.2–0.5 mg/kg/dose every 3–4 h as needed	Onset of action: Intravenous/continuous infusion: 1–10 min Oral: 10–20 min Duration: Intravenous: 3–5 h Oral: 3–5 h Protein binding: 20–35% (adult data) Metabolism: liver via glucuronide conjugation. Active primary metabolite Half-life: 1–10 h Elimination: Mostly urine; feces ~7–10%	Respiratory depression, central nervous system depression, hypotension, tachycardia, syncope, constipation, urinary retention, histamine release. Reduce dose in renal and hepatic disease
Fentanyl	Opioid analgesic, synthetic	Intravenous: 1–2 $\mu\text{g/kg/dose}$ Infants: every 2–4 h Child: every 30–60 min Continuous infusion: 1–3 $\mu\text{g/kg/h}$ titrate as needed to effect	Onset of action: near immediate Duration: Intravenous: 30–60 min Protein binding: 80–85% (adult data) Metabolism: liver via cytochrome P450 and hydroxylation Half-life: 2.4 h (child 5 mo to 4.5 y) 21 h (after continuous infusion) Elimination: 75% in urine; 9% in feces	May cause rigid chest with rapid injection. May cause respiratory depression, bradycardia, tachycardia, central nervous system depression, constipation, urinary retention. Reduce dose in renal and hepatic disease
Hydromorphone	Opioid analgesic	Intravenous: Infants > 10 kg: > 6 mo: 0.01 mg/kg/dose every 3–6 h as needed Child < 50 kg: 0.015 mg/kg/dose every 3–6 h as needed Child > 50 kg: 0.2–0.6 mg/dose every 2–4 h as needed Oral: Infants > 10 kg: > 6 mo: 0.03–0.06 mg/kg/dose every 4 h as needed Child < 50 kg: 0.03–0.08 mg/kg/dose	Onset of action: Intravenous: near immediate Oral: 15–30 min Duration: Oral/intravenous: 4–5 h Protein binding: ~80–19% (adult data) Metabolism: liver via glucuronidation Half-life: 2–3 h (adult data) Elimination: urine and minimally in feces	May cause respiratory depression, hypotension, hypertension. Extreme cautious use in children with head injury or intracranial lesions as may exaggerate intracranial pressure elevation. Reduce dose in renal and hepatic disease

(Continued)

Table 1 (Continued)

Medication	Pharmacology	Route and dose	Pharmacokinetics/pharmacodynamics	Significant side effects
		every 3–4 h as needed Child >50 kg: 1–2 mg/dose every 3–4 h as needed, up to 2–4 mg/dose. Continuous infusion: Infants >10 kg: >6 mo: 0.003–0.005 mg/kg/h child <50 kg: 0.003–0.005 mg/kg/h titrate as needed to effect		
Methadone	Opioid analgesic	Intravenous: 0.1 mg/kg/dose every 4 h for 2–3 doses, then every 6–12 h Intramuscular, oral, subcutaneous: 0.1 mg/kg/dose every 4 h for 2–3 doses, then every 6–12 h	Onset of action: Intravenous: within 10–20 min Oral: within 30–60 min Duration: Intravenous: 30–60 min Oral: 6–8 h up to 48 h after repeated dosing Protein binding: 80–90% (adult data) Metabolism: liver via N-demethylation Half-life: 19 ± 14 h Elimination: urine	Risk of life-threatening arrhythmias including torsade de pointes and prolonged QTc; respiratory arrest; respiratory depression
Clonidine Use as adjunct in intubated patients	Nonnarcotic analgesic	Intravenous: 0.1 $\mu\text{g/kg/h}$ ²⁶ Oral: 5 $\mu\text{g/kg}$ every 6 h ²⁵ 3–5 $\mu\text{g/kg}$ every 8 h ²⁸	Onset of action: Intravenous: rapid Oral: within 30–60 min Duration: Intravenous: 30–60 min Oral: 6–8 h (based on every 6–8 h dosing) Protein binding: 20–40% (adult data) Metabolism: liver with enterohepatic recirculation Half-life (oral dosing): Neonate: 44–72 h Child: 8–12 h Elimination: urine (40–60% unchanged)	Cannot be dialyzed. Bradycardia, hypotension, arrhythmias, hyperglycemia
Sedation medications				
Midazolam	Benzodiazepine	Intravenous: Load 0.05–0.2 mg/kg over 2–3 min followed by continuous infusion 0.06–0.12 mg/kg/h and titrate to effect	Onset of action: Intravenous: within 1–5 min Duration: Intravenous: 20–30 min Protein binding:	Hypotension, drowsiness, headache, nystagmus, apnea, laryngospasm, seizure-like activity. Careful dosing with hepatic and renal insufficiency or failure

Table 1 (Continued)

Medication	Pharmacology	Route and dose	Pharmacokinetics/pharmacodynamics	Significant side effects
Lorazepam	Benzodiazepine	Intravenous/oral: 0.02–0.1 mg/kg/dose every 4–8 h	97% bound to albumin (children >1 y and adults) Metabolism: liver via cytochrome P450 with active metabolite (α -hydroxy-midazolam) Half-life: Neonate: 4–12 h Child: 2.9–4.5 h Elimination: urine 63–80% as α -hydroxy-midazolam; feces 2–10%	Hypotension, apnea, hypoventilation, respiratory failure, anxiety. Careful dosing with hepatic and renal insufficiency or failure
Diazepam Use as adjunct to sedation in intubated patients	Benzodiazepine	Intravenous: 0.04–0.3 mg/kg/dose every 2–4 h Oral: 0.12–0.8 mg/kg/d divided every 6–8 h	Onset of action: Intravenous: within 1–3 min Oral: within 30–60 min Duration: up to 8 h Protein binding: 85–93% Metabolism: liver via glucuronide conjugation Half-life: Neonate: 18–73 h Child: 16–18 h Elimination: urine 88%; feces 7%	Cannot be dialyzed. Hypotension, apnea, bradypnea, vasodilatation, confusion, urinary retention, jaundice, paradoxical reaction. Careful dosing with hepatic and renal insufficiency or failure
Pentobarbital Use in difficult to sedate, intubated patients	Barbiturate	Intravenous: Load 1 mg/kg followed by continuous infusion 1 mg/kg/h and titrate to effect	Onset of action: Intravenous: within 3–5 min Duration: Intravenous: 15–45 min Protein binding: 45–70% (adult data) Metabolism: liver via hydroxylation and	Bradycardia, apnea, hypotension, syncope, hepatotoxicity, hypoventilation, laryngospasm

Table 1 (*Continued*)

Medication	Pharmacology	Route and dose	Pharmacokinetics/pharmacodynamics	Significant side effects
Dexmedetomidine Use as adjunct sedative in intubated patients	Adrenergic agonist, sedative	Intravenous: Load 0.5–1 µg/kg followed by continuous infusion 0.2–1.5 µg/kg/h ^a and titrate to effect	glucuronidation Half-life: 26 + 16 h Elimination: urine Onset of action: Intravenous: within 3–5 min Duration: Intravenous: 15–45 min Protein binding: 94% (adult data) Metabolism: liver via N-glucuronidation, N-methylation, and cytochrome P450 Half-life: 6 min (adult data) Elimination: urine 95% and feces 4%	Bradycardia, hypotension, hypotension, respiratory depression, apnea, hyperglycemia, oliguria, acute renal failure
Ketamine Use in difficult to sedate, intubated patients	General anesthetic	Intravenous: 0.5–2 mg/kg, continuous infusion 5–20 µg/kg/min and titrate to effect	Onset of action: Intravenous: within 30 s Duration: Intravenous: 5–10 min Protein binding: 94% (adult data) Metabolism: liver via hydroxylation, N-demethylation with active metabolite Half-life: 10–15 min (adult data) Elimination: urine	Monitor for emergence reactions, arrhythmia, hypertension, hypotension, changes in intracranial pressure, increased skeletal tone, apnea, laryngospasm, increased salivation. Decrease dose if hepatic dysfunction
Propofol Institutional policies direct use of this medication in intubated children for continuous sedation	General anesthetic	Intravenous/continuous infusion: 5 µg/kg/min titrate by 5–10 µg/kg/min until desired sedation with infusion range 5–50 µg/kg/min	Onset of action: within 30 s Duration: 5–10 min Protein binding: 97–99% (adult data) Metabolism: liver via sulfate conjugation and glucuronide Half-life: 2–8 min (adult data) Elimination: urine (88%) and feces (<25%)	Arrhythmia, bradycardia, apnea, hypertension, hypotension, tachycardia, respiratory acidosis. Mixed in lipids; monitor for hypertriglyceridemia

Source: Adapted from <http://online.lexi.com>.^aOral dosing rarely used in critically ill, intubated children.

and Consolability scale, which is an observational scale that rates pain between 0 and 10 based on five behavioral assessment items. A score of <3 is desired. A sedation-specific tool that is commonly used to evaluate patient comfort while mechanically ventilated is the State Behavioral Scale. The State Behavioral Scale is an objective pediatric sedation scale consisting of a range from $+3$ to -3 based on comfort while mechanically ventilated. A score of 0 describes a child who is alert and calm and a score of $+1$ to $+3$ a child with increasing levels of agitation. It is important to note that none of these tools are appropriate for assessing children who are receiving chemical paralysis.

Regular nursing assessments of pain and sedation level combined with multidisciplinary consensus on target goals aide in monitoring the effectiveness of analgesia and sedation treatment and facilitating prompt modification of the plan as needed. Important considerations in setting target pain and sedation goals include age of child, indication for mechanical ventilation, and trajectory of illness. All of these factors influence the depth of sedation needed to facilitate mechanical ventilation. In addition, the comfort expectations of the parents and their understanding of the child's typical exhibited signs of discomfort must be incorporated into the management plan. Universally acceptable goals are a pain score <3 and a level of sedation at which the patient is asleep, but easily aroused and comfortable on the ventilator. However, young children may require deeper sedation to maintain safety and comfort, and target pain and sedation goals should be evaluated and adjusted with changing clinical status.

Optimizing Analgesia and Sedation Management

The use of guidelines or protocols to direct sedation management has been advocated by many organizations as a means to improve practice and achieve standardization of care. Key features of a sedation protocol include a standardized approach to assessment of pain and sedation combined with an algorithm that directs drug titration based on these assessments.² Although pediatric guidelines based on high-quality evidence are lacking,^{3,4} the American College of Critical Care Medicine found that a protocolized approach can significantly improve patient outcomes in adults.⁵ Specifically, a multidisciplinary team approach to sedation management that includes a protocol that empowers nurses to safely administer and titrate continuous infusions has been shown to improve patient outcomes.⁵ Similar evidence is beginning to emerge in pediatrics. Deeter et al⁶ examined the use of a nurse-led sedation protocol at a single pediatric center and found significantly decreased opioid and benzodiazepine continuous infusion duration of exposure. Most recently, a large cluster-randomization trial (RESTORE Trial NCT00814099) conducted in the United States examined the use of a nurse-led sedation protocol to minimize practice variation and improve patient outcomes in ventilated children. This study demonstrated that nurse led sedation is safe and children received less days of opioids and fewer classes of sedatives though they did not have reduced ventilator days.⁷

Novel Therapies

Dexmedetomidine

Dexmedetomidine is a potent, highly selective α -2 adrenergic agonist with a range of unique properties that has become increasingly used as adjunct therapy to traditional sedation regimens and as a primary sedative for children requiring short-term mechanical ventilation. Dexmedetomidine produces sedative and analgesic effects and has a relatively short half-life with minimal risk of respiratory depression. The most common adverse reactions reported are bradycardia and hypotension. However, these adverse effects have been found to occur more frequently with the administration of bolus dosing and typically resolve without intervention.⁸

Experience with the use of dexmedetomidine in critically ill children is increasing and demonstrates favorable use in general medical and surgical patients as well as specific pediatric populations including children with burns and cardiac disease.^{9–18} In the United States, dexmedetomidine is approved by the Food and Drug Administration as a short-term (<24 hours) sedative in adults only. It has been primarily used to facilitate early extubation in the postoperative period or weaning of opioids and benzodiazepines in preparation for extubation. However, as it has gained popularity, it is increasingly used as an adjunct agent in mechanically ventilated children to reduce exposure to opioids and benzodiazepines^{9,14,16,17} and to optimize sedation in children who are deemed difficult to sedate.^{11,19,20}

Dexmedetomidine is administered as a continuous infusion with a recommended range of 0.2 to 1.5 $\mu\text{g}/\text{kg}/\text{h}$.^{8,21} Initial starting dose is 0.2 to 0.6 $\mu\text{g}/\text{kg}/\text{h}$ and titrated by 0.2 $\mu\text{g}/\text{kg}/\text{h}$ based on patient response. Although a loading dose of 0.5 to 1.0 $\mu\text{g}/\text{kg}/\text{h}$ over 10 minutes may be used prior to initiating the infusion, this practice is typically reserved for procedural sedation.^{8,21}

Preliminary data demonstrate dexmedetomidine to be well tolerated in children when used for <72 hours^{12,13,16} but evidence of withdrawal symptoms is reported when exposure is ≥ 72 hours.^{10,19,22} Although the data are retrospective, the reported presence of withdrawal symptoms with a prolonged infusion of dexmedetomidine is not surprising. However, attributing the symptoms specifically to dexmedetomidine may be difficult due to the lack of a validated assessment tool to identify withdrawal with this agent and often the symptoms may be explained by the concomitant weaning of a second agent (i.e., opioid or benzodiazepine).

Whalen et al¹⁹ found 30% of patients in their study ($n = 98$) with prolonged infusions of dexmedetomidine (>72 hours) experienced rebound tachycardia, hypertension, and withdrawal symptoms similar to opioids and benzodiazepines (e.g., agitation, vomiting, diarrhea). Sixty-nine percent of those with presumed withdrawal required weaning over a few days. Whereas, Carney et al²² found at least one symptom of withdrawal following discontinuation of dexmedetomidine after short-term use; however, these patients were simultaneously being weaned off another sedative. These studies suggest that withdrawal may be seen with

dexmedetomidine infusions and potentially earlier than expected. In addition, withdrawal symptoms seen with dexmedetomidine use are similar to those observed in withdrawal from an opioid or benzodiazepine except for rebound tachycardia and hypertension. Monitoring for these withdrawal symptoms after discontinuation of dexmedetomidine is necessary and slow weaning should be considered in patients receiving an infusion for >72 hours.

Clonidine

Similar to dexmedetomidine, clonidine is an α -2 adrenergic agonist. It has been classically used for the treatment of hypertension. However, the use of clonidine in pediatrics has expanded into anesthesia care for preoperative sedation,²³ postoperatively for pain management,²⁴ psychiatric care for treatment of attention deficit hyperactivity disorder,²⁵ and now most recently into the PICU for sedation management.^{26–28}

Clonidine has also been used in the PICU for withdrawal symptom treatment. Given current investigations into the relationship of neurocognitive development and exposure to narcotics and benzodiazepines, clinicians are seeking alternate medication strategies to promote comfort for the critically ill child. Arenas-López et al²⁹ described the safety of enteral clonidine for sedation in critically ill children and the associated decrement of morphine and lorazepam dosing. More recently, Duffett et al²⁶ performed a pilot study in two PICUs in Canada evaluating the feasibility of studying enteral clonidine for sedation. While the study was not powered to detect a difference in use of other medications, it was noted that clonidine was well tolerated, thus setting the stage for a broad randomized controlled trial.

Most recently, Hünseler et al²⁷ studied intravenous administration of clonidine starting on day 3 of intubation in infants and toddlers up to 2 years of age. The study divided the children in three strata based on age and administered the same dose of clonidine based on weight (1 μ g/kg/h). Subjects enrolled in the trial included both medical and surgical patients (including cardiac surgery). The youngest subjects who comprised stratum I ($\leq$ 28 days of age) demonstrated a significant reduction in fentanyl use compared with stratum II (29–120 days of age) and stratum III (121 days to 2 years of age). No group had a significant reduction in midazolam. Due to differences in pharmacodynamics, it has been hypothesized that the neonates had proportionately greater serum levels of clonidine compared with the other groups receiving the same dosing, thereby leading to a significant reduction in fentanyl dosing.

Although clonidine has been used via both the enteral and parenteral route, there remain many unanswered questions regarding the use of this medication for pain relief. Appropriate dosing, titration, length of therapy, and weaning strategy are unclear and, as such, careful use of clonidine is warranted until randomized controlled trials provide the necessary evidence.

Sedation Strategies

International sedation practices vary considerably, in part due to the limited high-quality evidence to guide practice.

Although different agents may be used, typical sedation regimens include a combination of an analgesic such as morphine or fentanyl and a sedative such as benzodiazepine or dexmedetomidine infusions at the lowest dose to achieve sedation goals.^{4,30} Factors to consider when choosing agents and method of administration include the indication for mechanical ventilation and expected trajectory of the patient's disease process (e.g., short or prolonged mechanical ventilation), organ dysfunction (e.g., renal insufficiency resulting in accumulation of drug such as midazolam or morphine causing oversedation), concomitant pharmacotherapy resulting in potential drug interactions, and risk for development of new disorders such as delirium impacting the effectiveness of the sedation regimen. In general, patients should receive a low-dose opioid infusion (e.g., fentanyl or morphine) and a low-dose sedative (e.g., benzodiazepine) by continuous infusion or intermittent dosing. A newer alternative regimen proposed is the use of a continuous infusion of low-dose dexmedetomidine with an intermittent opioid.¹⁶

Escalation or de-escalation of the sedation agents should be based on the target sedation goals, the patient's response to therapy, and changing clinical status. An acceptable approach is to ensure pain relief first, by administering an analgesic to treat or prevent a planned noxious event (e.g., endotracheal suctioning) followed by administering a sedative for anxiolysis and comfort. If the acute agitation is associated with an unprovoked event, it is critical to determine and treat the cause (e.g., hypoxia). Treatment of the acute agitation may include repeated intravenous bolus doses of the opioid or sedative (every 5 minutes up to three doses) and monitoring the response between doses to control the acute episode rather than the traditional approach of administering one intravenous bolus dose and then increasing the infusion rate, which may delay adequate treatment.⁶

Special Populations

Single versus multiple organ dysfunction and the degree of injury will impact analgesic and sedation agent(s) selection and dosing of these agents. Therefore, careful, routine evaluation of the child's clinical examination and laboratory data examining hepatic, renal, cardiac, and neurologic dysfunction are important for early recognition of changes in clinical status and to guide initial pharmacologic management strategies and modification as needed.

Hepatic Dysfunction

Critically ill children with hepatic dysfunction requiring pain and sedation management can be challenging to manage. As noted in **Table 1**, all of the pharmacologic interventions currently available are metabolized in the liver. Because there is no single laboratory value that quantifies hepatic dysfunction, determining medication dosing can be difficult. Assessment of the child with hepatic dysfunction includes measurement of transaminases, glucose, bilirubin, and coagulation, and the clinical neurological examination. The neurological examination should specifically identify the level of hepatic encephalopathy present. As the child progresses

through the stages of encephalopathy, irritability and agitation become somnolence. If medications are needed for the management of anxiety or agitation, opioids, though metabolized in the liver and commonly used to treat pain, should be considered specifically because of their sedative effects. Using benzodiazepines in children with hepatic dysfunction with already accumulating endogenous benzodiazepines may exacerbate this and lead to somnolence and inability to accurately evaluate hepatic encephalopathy.

Although an exact dosing recommendation for any given medication cannot be provided, it is recommended to start with a very small dose and titrate up until the desired outcome is achieved. Depending on the extent of hepatic dysfunction, even one dose of medication can remain in the body for an extended period of time, thereby hindering clinical assessments of neurologic function. It is critical to understand that currently available tools to quantify hepatic dysfunction may not accurately determine how the child will metabolize the medication.

Renal Dysfunction

Like children with hepatic dysfunction, those with renal dysfunction can also pose challenging pain and sedation management issues. However, clinicians can quantify renal dysfunction using glomerular filtration rate and medications can be adjusted based on the calculation. Although there are recommendations for decrements in medication dosing in children with a reduced glomerular filtration rate, precise elimination of these medications is not entirely clear. Therefore, buildup of toxic and/or active metabolites may occur. For children with renal failure requiring dialysis (either hemodialysis or continuous renal replacement therapy), close attention to medication filtration is necessary as different medications have different molecular size. The size of the molecules will determine whether the medication will be filtered out by the specific therapy. Monitoring for levels of comfort is important to titrate medication doses in the event they are not removed through the employed filtration therapy.

Cardiac Disease

Critically ill children with cardiac disease may be reliant on adequate fluid balance and vascular tone for optimal functioning. Because different cardiac diseases and lesions have very specific hemodynamics, each child with his/her specific cardiac condition requires careful thought in the selection of sedatives and analgesics. For example, children with cardiac diseases dependent on preload may become hypotensive when using a medication that relaxes vascular tone or has a related histamine release (e.g., morphine). Furthermore, selection of medications that are arrhythmogenic (e.g., methadone) in children who have arrhythmias or are at risk for rhythm disturbances requires careful consideration. These medications can be used in this population; however, the risk: benefit ratio must be evaluated prior to the administration of a medication with this known side effect profile. Although it is not the focus of this article to address postoperative pain management, it is imperative to recognize that these critically

ill children will require analgesia and that the surgical procedure may have impacted the preoperative hemodynamics.

Neurological Dysfunction

Critically ill children with neurological dysfunction require balancing the ability to assess the patient while meeting the needs for comfort. Additionally, standardized assessment of pain and sedation may be altered if the child has significant neurologic compromise. For children who have a history of neurological dysfunction (e.g., cerebral palsy), collaborating with the primary caretakers on assessment of pain and agitation/anxiety is crucial. Learning typical behaviors indicative of pain, agitation, or anxiety will help the care team more easily identify the need for prompt intervention.

In addition to assessment challenges, selecting medications with rapid action on and off is required in cases where there is a need for sedation management as well as frequent neurological assessments. For example, children with head injury require frequent examinations to determine decrement or improvements in condition; therefore, a rapid-acting sedative would be the best option. Unfortunately, medications with this profile often have hypotension and bradycardia as side effects, both of which can be deleterious to the injured brain. The key to successful sedation in a child with brain injury is dose titration, integration of nonpharmacological interventions (e.g., quiet environment, grouping care, etc.), and frequent monitoring.

In conclusion, critically ill children require close monitoring and assessment of pain and agitation states. Given the currently available tools, pediatric critical care nurses are prepared to make accurate and timely assessments of these children. Accessing protocols or algorithms to support nurse-led sedation may enhance interventions to control both pain and agitation in this at-risk population. Medication selection should be considered and selected based on the child's needs, organ function, and degree of illness. Matching the need with the treatment of pain and agitation in these children will improve their comfort while being critically ill.

References

- 1 Dorfman TL, Sumamo Schellenberg E, Rempel GR, Scott SD, Hartling L. An evaluation of instruments for scoring physiological and behavioral cues of pain, non-pain related distress, and adequacy of analgesia and sedation in pediatric mechanically ventilated patients: A systematic review. *Int J Nurs Stud* 2014;51(4):654–676
- 2 Schweickert WD, Kress JP. Strategies to optimize analgesia and sedation. *Crit Care* 2008;12(Suppl 3):S6
- 3 Poh YN, Poh PF, Buang SN, Lee JH. Sedation guidelines, protocols, and algorithms in PICUs: a systematic review. *Pediatr Crit Care Med* 2014;15(9):885–892
- 4 Hartman ME, McCrory DC, Schulman SR. Efficacy of sedation regimens to facilitate mechanical ventilation in the pediatric intensive care unit: a systematic review. *Pediatr Crit Care Med* 2009;10(2):246–255
- 5 Barr J, Fraser GL, Puntillo K, et al; American College of Critical Care Medicine. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013;41(1):263–306

- 6 Deeter KH, King MA, Ridling D, Irby GL, Lynn AM, Zimmerman JJ. Successful implementation of a pediatric sedation protocol for mechanically ventilated patients. *Crit Care Med* 2011;39(4):683–688
- 7 Curley MAQ, Wypii D, Watson S, et al. Protocolized sedation vs usual care in pediatric patients mechanically ventilated for acute respiratory failure: a randomized clinical trial. *JAMA* 2015;313(4):379–389
- 8 Hoy SM, Keating GM. Dexmedetomidine: a review of its use for sedation in mechanically ventilated patients in an intensive care setting and for procedural sedation. *Drugs* 2011;71(11):1481–1501
- 9 Fagin A, Palmieri T, Greenhalgh D, Sen S. A comparison of dexmedetomidine and midazolam for sedation in severe pediatric burn injury. *J Burn Care Res* 2012;33(6):759–763
- 10 Gupta K, Gupta VK, Jayashree M, Singhi S. Randomized controlled trial of interrupted versus continuous sedative infusions in ventilated children. *Pediatr Crit Care Med* 2012;13(2):131–135
- 11 Burbano NH, Otero AV, Berry DE, Orr RA, Munoz RA. Discontinuation of prolonged infusions of dexmedetomidine in critically ill children with heart disease. *Intensive Care Med* 2012;38(2):300–307
- 12 Lam F, Ransom C, Gossett JM, et al. Safety and efficacy of dexmedetomidine in children with heart failure. *Pediatr Cardiol* 2013;34(4):835–841
- 13 Le KN, Moffett BS, Ocampo EC, Zaki J, Mossad EB. Impact of dexmedetomidine on early extubation in pediatric cardiac surgical patients. *Intensive Care Med* 2011;37(4):686–690
- 14 Lin H, Faraklas I, Sampson C, Saffle JR, Cochran A. Use of dexmedetomidine for sedation in critically ill mechanically ventilated pediatric burn patients. *J Burn Care Res* 2011;32(1):98–103
- 15 Hosokawa K, Shime N, Kato Y, et al. Dexmedetomidine sedation in children after cardiac surgery. *Pediatr Crit Care Med* 2010;11(1):39–43
- 16 Czaja AS, Zimmerman JJ. The use of dexmedetomidine in critically ill children. *Pediatr Crit Care Med* 2009;10(3):381–386
- 17 Buck ML, Willson DF. Use of dexmedetomidine in the pediatric intensive care unit. *Pharmacotherapy* 2008;28(1):51–57
- 18 Chrysostomou C, Di Filippo S, Manrique AM, et al. Use of dexmedetomidine in children after cardiac and thoracic surgery. *Pediatr Crit Care Med* 2006;7(2):126–131
- 19 Whalen LD, Di Gennaro JL, Irby GA, Yanay O, Zimmerman JJ. Long-term dexmedetomidine use and safety profile among critically ill children and neonates. *Pediatr Crit Care Med* 2014;15(8):706–714
- 20 Walker J, MacCallum M, Fischer C, Kopcha R, Saylor R, McCall J. Sedation using dexmedetomidine in pediatric burn patients. *J Burn Care Res* 2006;27(2):206–210
- 21 Phan H, Nahata MC. Clinical uses of dexmedetomidine in pediatric patients. *Paediatr Drugs* 2008;10(1):49–69
- 22 Carney L, Kendrick J, Carr R. Safety and effectiveness of dexmedetomidine in the pediatric intensive care unit (SAD-PICU). *Can J Hosp Pharm* 2013;66(1):21–27
- 23 Dahmani S, Brasher C, Stany I, et al. Premedication with clonidine is superior to benzodiazepines. A meta analysis of published studies. *Acta Anaesthesiol Scand* 2010;54(4):397–402
- 24 Lambert P, Cyna AM, Knight N, Middleton P. Clonidine premedication for postoperative analgesia in children. *Cochrane Database Syst Rev* 2014;1:CD009633
- 25 Hirota T, Schwartz S, Correll CU. Alpha-2 agonists for attention-deficit/hyperactivity disorder in youth: a systematic review and meta-analysis of monotherapy and add-on trials to stimulant therapy. *J Am Acad Child Adolesc Psychiatry* 2014;53(2):153–173
- 26 Duffett M, Choong K, Foster J, et al. Clonidine in the sedation of mechanically ventilated children: a pilot randomized trial. *J Crit Care* 2014;29(5):758–763
- 27 Hünseler C, Balling G, Röhlhig C, et al; Clonidine Study Group. Continuous infusion of clonidine in ventilated newborns and infants: a randomized controlled trial. *Pediatr Crit Care Med* 2014;15(6):511–522
- 28 Long D, Erickson S; for the ANZICS Paediatric Study Group. Baby spice: sedation practice in paediatric intensive care evaluation in Australia and New Zealand. *Pediatr Crit Care Med* 2014;15(4, Suppl):19 (Abstract)
- 29 Arenas-López S, Riphagen S, Tibby SM, et al. Use of oral clonidine for sedation in ventilated paediatric intensive care patients. *Intensive Care Med* 2004;30(8):1625–1629
- 30 Vet NJ, de Wildt SN, Verlaet CW, et al; SKIC (Dutch collaborative PICU research network). Daily interruption of sedation in critically ill children: study protocol for a randomized controlled trial. *Trials* 2014;15:55