Sedation Challenges in the Pediatric ICU: Is Dexmedetomidine the Solution?

R BLAINE EASLEY

Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, 600 North Wolfe Street, Blalock 941, Baltimore, MD 21287, USA. beasley@jhmi.edu

he pediatric intensive care unit (PICU) poses unique pain and sedation management challenges. Treatment of pain and anxiety in the PICU has historically been accomplished with opioids and benzodiazepines. More recently, drug therapy has been complemented with sedation scales and nonpharmacologic treatment measures, such as parental presence at the bedside and psychologic interventions (i.e. distraction, redirection, etc.), to help create more effective sedation practices and less-threatening PICU environments(1). Even with these measures, critically ill children often need prolonged sedation to facilitate respiratory management, treatment of multi-organ system dysfunction and/or performance of invasive procedures. The consequence is escalating dosages, physiologic tolerance and subsequent development of withdrawal when these agents are discontinued(2). These sedation challenges drive many PICU clinicians to seek alternative pharmacologic agents (even volatile anesthesia) to provide comfort to critically ill children(1).

Dexmedetomidine (DEX) is a highly selective α_2 -adrenergic agonist with sedative, anxiolytic, and analgesic properties. DEX provides effective sedation without the respiratory depression often seen with other agents and exhibits a synergistic sedative and analgesic effect when given in conjunction with benzodiazepines and opioid analgesics(3). The most common adverse effects associated with DEX include hypotension, brady-cardia, and even hypertension, which are usually related to rate of administration and dosage. DEX is

currently approved for use in critically ill, mechanically ventilated and intubated adults as a continuous infusion for <24 hours. To date, the drug is not approved for use in children or for prolonged infusion. Studies evaluating the pharmacology and pharmacodyamics of DEX in pediatric patients are limited in scope and number, and yet there is a growing international experience with the use of DEX for children undergoing procedural and ICUbased sedation for acute and prolonged periods of time(4,5).

The study by Reiter, et al.(6), in this issue of Indian Pediatrics, describes their experience with the usage of DEX for prolonged sedation in critically ill children. By retrospectively reviewing the charts of children receiving DEX, they characterized indications, patient demographics, and observed adverse events. DEX was initiated in 41% of children (n=12/29) to facilitate extubation and resulted in a duration of DEX treatment \geq 32 hours (n=29). Only 33% (n=10) received a loading dose of DEX prior to initiating a continuous infusion. Though there were no adverse events reported in their study population, there was a transient and statistically significant reduction in heart rate (±13 beats per min) within the first 24 hours of therapy, independent of a DEX loading dose, and no interventions were required. An important finding of this study was the clinician's expectation that DEX would help facilitate extubation, but instead DEX treatment was associated with an increase in the extubation failure rate from 6% to 30%. The authors correctly discuss the potential confounding issues that may have contributed to this finding including

INDIAN PEDIATRICS

lack of their clinical experience with how DEX might affect their "extubation readiness" evaluation. This contrasts with Carroll, *et al.*(5), who found that DEX facilitated extubation in mechanically ventilated children. One significant difference between these studies was the duration of DEX therapy (mean of 32 *vs.* 23 hours, respectively). Future studies will be required to specifically address the effect of DEX infusion duration on extubation success.

Subtle clinical differences in DEX sedation may necessitate adaptation of sedation scales when DEX is used. The current study(6) demonstrated no difference between pre-DEX infusion and during-DEX infusion sedation scores. This finding may represent a bias in the limited number of children receiving sedation scores, lack of a sedation assessment protocol or even a lack of scale validity with DEX sedation. In general, sedation scales lacking a provocative stimulus (touch, tracheal suctioning, etc) have been shown to over-estimate the sedation level of the patient when left to simple observation(7). Attempts to use DEX for procedures that are inherently stimulating (such as endocscopy or cardiac catheterization) have proven that DEX as the sole agent is inadequate to maintain an effective level of sedation and analgesia when a painful or unpleasant stimulus is present(8).

Though DEX initation, maintenance and discontinuation in the current study were at the discretion of the bedside clinicians, there were no observed adverse events (such as hemodynamic or withdrawal). Notably, 93% (n=13) patients receiving DEX infusions >72 hours had the dose tapered over a 1 to 4 day period. Such a slow taper may have eliminated a possible discontinuation syndrome (hypertension and agitation)(9). This observed absence of adverse events with discontinuation of prolonged DEX infusions is consistent with other reports(3-5).

The increased usage of DEX in critically ill children is the direct result of the bedside challenges many PICU clinicians face in sedation management. Available studies of DEX pharmacology in children have provided conflicting information, which is highlighted by two recent pharmacology studies, one suggesting infants need a higher dosage and the other saying current dosing ranges are adequate(9,10). Prospective studies of stable infants and children receiving bolus and maintenance DEX infusions are needed to resolve this issue.

The findings of the Reiter study help us understand the potential safety, efficacy and limitations of DEX sedation in children. At this time, DEX is not a single-drug solution to the complicated problem of pediatric sedation, but it appears to have a potential complementary role in the challenging task of sedating critically ill children in the ICU.

Funding: None.

Competing interests: I am a member of the National Scientific Advisory Board for Hospira Inc, USA, to address dexmedetomidine usage in children. I have neither honoraria nor financial reimbursement to disclose.

REFERENCES

- Yaster M, Easley RB, Brady KM. Pain and sedation management in the critically ill child. *In:* Nichols DG, editor. Rogers's Textbook of Pediatric Intensive Care. 4thEdition. Philadelphia, PA: Lippincott, Williams & Wilkins; 2008.p.136-165.
- 2. Easley RB, Nichols DG. Withdrawal assessment in the PICU: quantifying a morbidity of pain and sedation management in the critically ill child. Crit Care Med 2008; 36: 2479-2480.
- 3. Tobias JD. Dexmedetomidine: applications in pediatric critical care and pediatric anesthesiology. Pediatr Crit Care Med 2007; 8: 115-131.
- Walker J, Maccallum M, Fischer C, Kopcha R, Saylors R, McCall J. Sedation using dexmedetomidine in pediatric burn patients. J Burn Care Res 2006; 27: 206-210.
- 5. Carroll CL, Krieger D, Campbell M, Fisher DG, Comeau LL, Zucker AR. Use of dexmedetomidine for sedation of children hospitalized in the intensive care unit. J Hosp Med 2008; 3: 142-147.
- 6. Reiter PD, Pietras M, Dobyns EL. Prolonged dexmedetomidine infusions in critically ill infants and children. Indian Pediatr 2009; 46: 767-773.
- 7. Curley MA, Harris SK, Fraser KA, Johnson RA, Arnold JH. State Behavioral Scale: a sedation assessment instrument for infants and

INDIAN PEDIATRICS

young children supported on mechanical ventilation. Pediatr Crit Care Med 2006; 7: 107-114.

- Mester R, Easley RB, Brady KM, Chilson K, Tobias JD. Monitored anesthesia care with a combination of ketamine and dexmedetomidine during cardiac catheterization. Am J Therap 2008; 15: 24-30.
- 9. Weber MD, Thammasitboon S, Rosen DA. Acute discontinuation syndrome from dexmedetomidine

after protracted use in a pediatric patient. Paediatr Anaesth 2008; 18: 87-88.

- Vilo S, Rautiainen P, Kaisti K, Aantaa R, Scheinin M, Manner T, *et al.* Pharmacokinetics of intravenous dexmedetomidine in children under 11 yr of age. Br J Anaesth 2008; 100: 697-700.
- 11. Potts AL, Warman GR, Anderson BJ. Dexmedetomidine disposition in children: a population analysis. Paediatr Anaesth 2008; 18: 722-730.