states that 'it would be unethical to withhold sedation and anesthesia when necessary' and 'more harm may be inflicted if necessary treatment is withheld'. As a corollary to this statement, based on current evidence and considering the advantages of breast-feeding to both the mother and the infant, the use of short-acting sedative premedication for the nursing mother may be considered (albeit with caution as with any other medication). Further research in measuring the parent drug and any active metabolites in the infant blood and urine would be reassuring in determining which maternally administrated drugs would deliver minimal to absent exposure to the infant (5). We certainly remain concerned over any possible effect of any drug transmitted via breast milk (5).

Financial support

Department of Anesthesiology and Department of Pediatrics, Penn State Hershey Medical Center, Penn State Children's Hospital, Hershey, USA.

Conflict of interest

None for all authors.

Priti G. Dalal[1] & Cheston Berlin[2]
[1]*Department of Anesthesiology, Penn State Hershey Medical Center, Penn State Children's Hospital, Hershey, PA, USA*
[2]*Department of Pediatrics, Penn State Hershey Children's Hospital, Hershey, PA, USA*
Email: pdalal@hmc.psu.edu

doi:10.1111/pan.12376

References

1 Dalal PG, Bosak J, Berlin C. Safety of the breast-feeding infant after maternal anesthesia. *Pediatr Anesth* 2014; **24**: 359–371.
2 Nemergut ME, Aganga D, Flick RP. Anesthetic neurotoxicity: what to tell the parents? *Pediatr Anesth* 2014; **24**: 120–126.
3 Hale TW. Anesthetic medications in breastfeeding mothers. *J Hum Lact* 1999; **15**: 185–194.
4 Slikker W Jr, Zou X, Hotchkiss CE *et al.* Ketamine-induced neuronal cell death in the perinatal rhesus monkey. *Toxicol Sci* 2007; **98**: 145–158.
5 Berlin CM Jr, van den Anker JN. Safety during breastfeeding: drugs, foods, environmental chemicals, and maternal infections. *Semin Fetal Neonatal Med* 2013; **18**: 13–18.

Pain score guided morphine titration is risky and inappropriate

Sir—We read with great interest the recent article by Bernard *et al.* (1) that described, evaluated, and proposed a morphine titration protocol for children in the postanesthesia care unit (PACU). The authors concluded the efficacy and safety of their titration protocol based on reductions in pain scores to <30/100 and the purported nonserious nature of side effects in their sample of 103 children. However, we are compelled to raise several important concerns regarding their proposed protocol and findings that might, in contrast, suggest potentially risky and inappropriate morphine titration practices.

First, the use of pain score cut-points to titrate medications should be regarded as inappropriate. Experts in assessment now largely concur that pain scores alone cannot convey the information necessary to effectively treat pain (2). This is particularly true of behavioral pain scores which convey distress signals and require differentiation between pain, anxiety, hunger, or, most importantly, physiologic compromise. Interpreting self-report scores poses its own challenges. We previously found that although self-reported numeric pain scores >4/10 were statistically associated with children's perceived need for medicine; there is wide variability in the scores children associate with analgesia need, perceptions of pain severity, and pain relief (2,3). Given such variability, had we applied our own cut-point to our sample, we would have over-treated 42% of children compared to their stated needs. These data and others highlight the inappropriateness of pain score-based algorithms to achieve clinically relevant analgesia.

More importantly, data suggest an increase in opioid-related adverse events and death following implementation of pain score-guided algorithms and guidelines (4,5). Bernard *et al.*'s data highlight this risk as 20% of their sample experienced excessive sedation (the precursor to respiratory depression), one child became bradypneic, and 2 experienced oxygen desatura-

tion. This incidence of sedation is not surprising, given that some children in their sample had received as much as 350 $\mu g \cdot kg^{-1}$. Of note, several had received multiple doses of morphine, yet continued to have pain scores above the target at the end of the observation period. In these cases, children experienced both ineffective (based on study definitions) and risky outcomes, thereby emphasizing the pitfalls of a titration-to-pain-score protocol.

Next, Bernard *et al.*'s proposed time interval for assessment and morphine titration (i.e., every 5 min) may compound the risk for children given the known lag between plasma and brain concentrations of the drug, and, as the authors acknowledge, the accumulation of morphine-6-glucuronide (6,7). Pharmacokinetic models and clinical studies suggest that the maximum benefits and risks of morphine occur with peak brain concentrations, which are on average, 125–166 min after dosing (6,7). It is, therefore, quite possible that children in the Bernard study could have experienced additional or progressive respiratory decline after their 90-min observation period.

The high number of children with oversedation in the Bernard study cannot be overemphasized and, in fact, should have been included in their adverse events table. The study protocol required discontinuation of titration for Ramsey scores of 5 or 6 (defined as 'Patient exhibits a sluggish response to glabellar tap or loud auditory stimulus' and 'Patient exhibits no response'), and 20% achieved this excessive level during the 90-min period. We question whether even a Ramsey score of 4 (i.e., 'Brisk response to a light glabellar tap or auditory stimulus') would imply a safe level of narcosis – particularly just prior to PACU discharge. Based on procedural sedation data (8) and other recommendations (9), we suggest instead consideration of both arousability and wakefulness (i.e., ability to stay awake during assessment or conversation) to promote safe opioid use in children. The Pasero Opioid-induced Sedation Scale (POSS) combines these observations along with treatment suggestions into a four-point tool (9). A POSS level 3 (i.e., 'Frequently drowsy, arousable, drifts off to sleep during conversation') is considered unacceptable and requires increased respiratory monitoring and reevaluation of opioid dosing. Although published data have not yet described clinical outcomes following POSS implementation, we believe that compared to Ramsey arousability scores alone, such combined assessments may promote safer opioid decisions.

Regulatory agencies and the Anesthesia Patient Safety Foundation (APSF) have emphasized the need for safe opioid practices. Among other recommendations, the Joint Commission (USA) recently suggested (i) avoiding rapid dose escalation above routine dose levels; (ii) taking extra precautions when transferring patients between units or when discharging patients to home as 'drug levels may reach peak concentrations during [or after] transport'; and (iii) 'avoid using opioids to meet an arbitrary pain rating' (10). Anesthesia providers are ideally positioned to take the lead on safe opioid practices, and must therefore carefully consider the risk-benefit tradeoffs of their pain management strategies.

Disclosures

The authors declare IRB approval Not Applicable and no external funding.

Conflict of interest

The authors declare no conflicts of interest.

Terri Voepel-Lewis & Shobha Malviya
Department of Anesthesiology, University of Michigan Health System, Ann Arbor, MI, USA
Email: terriv@umich.edu

doi:10.1111/pan.12367

References

1 Bernard R, Salvi N, Gall O *et al.* MORPHIT: an observational study on morphine titration in the postanesthetic care unit in children. *Pediatr Anesth* 2014; **24**: 303–308.

2 Voepel-Lewis T. How reliable are 'valid and reliable' pain scores in the pediatric clinical setting? *Pain Management* 2013; **3**: 343–350.

3 Voepel-Lewis T, Burke CN, Jeffreys N *et al.* Do 0–10 numeric rating scores translate into clinically meaningful pain measures for children? *Anesth Analg* 2011; **112**: 415–421.

4 Lucas CE, Vlahos AL, Ledgerwood AM. Kindness kills: the negative impact of pain as the fifth vital sign. *J Am Coll Surg* 2007; **205**: 101–107.

5 Vila H Jr, Smith RA, Augustyniak MJ *et al.* The efficacy and safety of pain management before and after implementation of hospital-wide pain management standards: is patient safety compromised by treatment based solely on numerical pain ratings? *Anesth Analg* 2005; **101**: 474–480.

6 Hain RD, Hardcastle A, Pinkerton CR *et al.* Morphine and morphine-6-glucuronide in the plasma and cerebrospinal fluid of children. *Br J Clin Pharmacol* 1999; **48**: 37–42.

7 Lotsch J, Dudziak R, Freynhagen R *et al.* Fatal respiratory depression after multiple

intravenous morphine injections. *Clin Pharmacokinet* 2006; **45**: 1051–1060.
8 Malviya S, Voepel-Lewis T, Ludomirsky A *et al*. Can we improve the assessment of discharge readiness?: A comparative study of observational and objective measures of depth of sedation in children. *Anesthesiology* 2004; **100**: 218–224.
9 Pasero C. Assessment of sedation during opioid administration for pain management. *J Perianesth Nurs* 2009; **24**: 186–190.
10 Joint Commission. Safe Use of Opioids in Hospitals. Chicago: Joint Commission, 2012.

Night terrors and emergence delirium

Sir—Night terrors belong to the parasomnia group of sleep disorders. They occur during the first third of night-time sleep during arousal from stage 3 of the nonrapid eye movement phase (1). Night terrors are characterized by sudden arousal followed by screaming and crying. A key feature is that the subject will be inconsolable and will not want to be touched or comforted. Additionally, they will act afraid, agitated, and anxious (1). Such an episode may last for up to 30 min, and afterward, the subject will have no recollection of the episode. This phenomenon has a prevalence of 1–6.5% in children aged 4–12 years (1).

Children suffering emergence delirium (ED) exhibit psychomotor agitation, hallucinations, misperceptions, and fluctuating behavior in the immediate postoperative period following anesthesia (2). The key characteristics of ED are nonpurposeful movement, nonresponsivity, and averted or stared eyes (2). As with night terrors, inconsolability is also a key behavior in children who display ED (2). Rates of ED vary from 25% to 80% in children, depending on the evaluation system being used (3).

The similarity in the clinical presentation of night terrors and ED as well as evidence from electroencephalograph patterns suggests these two phenomena may be linked (4). Similarly to how car sickness is predictive of postoperative vomiting, night terrors may be predictive of ED. Anesthesia may then be altered to decrease the incidence of ED in those children who have a history of night terrors.

We undertook an observational audit over a period of 4 months to determine the relationship between night terrors and ED. Healthy children aged 15 years and younger undergoing anesthesia for adenoidectomy, (adeno) tonsillectomy, and myringotomy procedures were included in the study. Multiple surgeons and anesthesiologists were involved in the procedures, and although the choice of anesthetic was left to the discretion of the anesthesiologist, total intravenous anesthesia was not used in this cohort. On admission to hospital, parents were asked whether their child ever woke in a distressed state where they were difficult to console. ED was determined in the postanesthesia care unit using the Pediatric Anesthesia Emergence Delirium (PAED) scale approximately 5 min after the patient awoke from anesthesia. A score equal to or greater than 10 was used to define ED. A comparison in the rate of ED when using a PAED scale score of 12 was also made, as this higher threshold has a greater sensitivity at detecting ED. Additional analyses were performed in which children administered clonidine were removed because this drug has been found to reduce the incidence of ED (5). All anesthesia was maintained with sevoflurane (and an opioid), and no other medications apart from clonidine were given to decrease the risk of ED. Ethics approval was received from the University of Auckland Human Participants Ethics Committee.

There were 406 patients included in this prospective observational study; those suffering pain were excluded leaving sufficient data for analysis from 330 (age 4.81 years SD 3.72 years, weight 22.61 kg SD 13.00 kg) children. A total of 66 children were administered clonidine 0.29–5.56 mcg·kg^{-1} during the surgical procedure. There were 82 children who experienced ED when using a PAED scale score ≥10, and 53 when using a PAED scale score ≥12; 149 children had a history of night terrors. The positive predictive values (PPVs) and negative predictive values (NPVs) for the correlation between night terrors and ED can be seen in Table 1.

Table 1 PPVs and NPVs for the correlation between night terrors and ED when using a PAED scale score of ≥10 or 12 to define ED and including or excluding clonidine

	Including clonidine		Excluding clonidine	
	PAED ≥ 10	PAED ≥ 12	PAED ≥ 10	PAED ≥ 12
PPV	26.8% (19.9–34.7%)	16.1% (10.6–23.0%)	26.1% (18.2–35.3%)	18.9% (12.1–27.5%)
NPV	76.8% (70.0–82.7%)	84.0% (77.8–89.0%)	77.8% (70.4–84.1%)	85.0% (78.3–90.2%)

The 95% confidence interval for each value is indicated.