Emergence Delirium in Children: Review and Rationale for the Use of Dexmedetomidine for Prevention

CE 1.5 Contact Hours

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Abstract: Pediatric emergence delirium is a problematic condition affecting children emerging from general anesthesia. Young children specifically have an increased probability of developing this condition; risk factors such as gender, surgical procedure, pain, and/or anesthetic technique pose an increased susceptibility to emergence delirium. Dexmedetomidine, an alpha-2 agonist, has been shown to be effective in reducing the incidence of pediatric emergence delirium in a variety of administrative methods. This article presents a review of emergence delirium and rationale for its prevention with dexmedetomidine. There are presently many pharmacological methods of treating and avoiding emergence delirium. However, dexmedetomidine has been shown to be a safe and effective choice above the current pharmacological alternatives in the pediatric population.

KEY WORDS: dexmedetomidine, emergence delirium, pediatrics

INTRODUCTION

Emergence delirium (ED) is defined as "a mental disturbance during the recovery from general anesthesia consisting of hallucinations, delusions and confusion manifested by moaning, restlessness, involuntary physical activity, and thrashing about in bed" (Sikich & Lerman, 2004, p. 1138). This condition is self-limiting and does not usually last for more than an hour. Voepel-Lewis, Malviya, and Tait (2003) noted a range of 3–45 minutes of duration, with an average of 14 ± 11 minutes, after general anesthesia in children 3–7 years old undergoing general surgery. The incidence of ED in children has been estimated to range from 25% to 80% depending on the assessment methods utilized (Sikich & Lerman, 2004). The exact mechanism behind ED development in children after anesthesia has not been elucidated, but several risk factors have an association with the condition (Kanaya, 2016). Although emergence agitation and ED are used synonymously, the distinction is that emergence agitation denotes physical hyperactivity versus ED, which is a psychological derangement upon wakening (Wong & Bailey, 2015). However, emergence agitation is far more prevalent than ED (Wong & Bailey, 2015). ED will be utilized throughout to denote the collective behavioral phenomenon that encompasses both states.

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DOI: 10.1097/JPS.0000000000000167

Risk Factors

There are several risk factors that have been noted to increase the predilection for emergence agitation—(a) young age, (b) gender, (c) surgical procedure, (d) pain, and (e) anesthesia method (inhalational vs. intravenous agent or regional block)—and have been associated with ED (Kanaya, 2016). Children of young age, particularly those of preschool age, are most affected by the condition (Aono, Ueda, Mamiya, Takimoto, & Manabe, 1997; Vlajkovic & Sindjelic, 2007; Voepel-Lewis et al., 2003). Preschoolers have been noted to be most vulnerable to this condition because of an inability to reorient to surroundings upon rapid emergence, therefore rendering this population most vulnerable in comparison with older counterparts (Vlajkovic & Sindjelic, 2007).

Gender

Preschool-aged boys have a greater chance of experiencing agitation upon emergence from anesthesia. Aono et al. (1997) noted a 40% incidence of ED after urological procedures in this population. A significantly greater occurrence rate for young boys compared with girls undergoing anesthesia for general surgery

was determined by Mohkamkar et al. (2014) in a ratio of approximately 2:1. In addition to general surgery, the incidence of agitation postoperatively was also notably increased in boys under 6 years old having dental procedures (Beringer, Segar, Pearson, Greamspet, & Kilpatrick, 2014).

Surgical Procedure

The specific type of surgery is also an independent risk factor for ED. Ear, nose, and throat (ENT) procedures have a markedly increased incidence of ED. Mohkamkar et al. (2014) examined the incidence of postoperative agitation in varying surgical populations: (a) ENT, (b) ophthalmology, (c) urology, (d) orthopedics, and (e) abdominal. The study showed a significant rate of an increased risk for otorhinolaryngological procedures, $p < .001$ (p. 186). A predisposition for ED after ENT procedures has been validated by current and past studies as well (Cao, Pei, Wei, & Zhang, 2016; Finkel et al., 2001). Ophthalmological procedures also promote an increased risk of emergence agitation. Joo, Lee, and Lee (2014) noted a propensity for postoperative agitation depending on the invasiveness of surgery, with invasiveness denoting the amount of surgical repair that was needed.

Pain

Pain as a risk factor for the development of postoperative agitation is complex. There are multiple studies that have confirmed that the use of intravenous fentanyl, a synthetic opioid, has a positive effect on decreasing the incidence of ED (Shi et al., 2015). However, these findings are confounded by studies that have used pain-sparing techniques without success. Demirbilek et al. (2004) investigated the utilization of intravenous fentanyl in children undergoing adenotonsillectomy. The study divided study subjects into those receiving sevoflurane, an inhalational anesthetic, with fentanyl and those receiving desflurane, also an inhalational anesthetic, with fentanyl. These groups were compared with control subjects who did not receive intravenous fentanyl and received either sevoflurane or desflurane. The rate of postoperative agitation in the experimental versus control groups did not yield any clinically notable effects in the two groups. Ohashi et al. (2016) employed the use of ultrasound-guided ilioinguinal and hypogastric blocks for inguinal hernia repair. This randomized controlled trial separated the two groups into subjects receiving a block and those not receiving a block. The incidence of ED postoperatively was not different from the control group who did not receive a regional block. However, the occurrence of ED after painless procedures or adequate treatment of pain is a known phenomenon (Cravero, Surgenor, & Whalen, 2000).

Anesthetic Agents

Sevoflurane and desflurane are newer inhaled anesthetics with an increased rate of recovery compared with older inhalational anesthetics such as halothane. However, both sevoflurane and desflurane have an increased rate of ED when compared with older inhalational anesthetics (Aono et al., 1997; Sarner et al., 1995; Walker, Haugen, & Richards, 1997). Cohen, Finkel, Hannallah, Hummer, and Patel (2003) reported a decreased occurrence rate of postoperative agitation when comparing intravenous anesthetic, propofol, against sevoflurane. Patients who had received sevoflurane had 23.1% rate of ED versus subjects who received propofol 3.7%. The incidence of postoperative agitation was found to be statistically significant. The low solubilities of sevoflurane, along with desflurane, allows for a rapid emergence, therefore rendering patients susceptible to ED (Moore & Anghelescu, 2017).

Negative Consequences of ED

Impact on Children

The psychological and behavioral changes associated with ED negatively impact children, parents, and health care workers. ED "is perceived as a troublesome clinical situation by 42% of pediatric anesthesiologists" (Moore & Anghelescu, 2017, p. 11). Children can induce injury through self-extubation, removal of catheters or intravenous lines, and/or damage to the surgical site (Hudek, 2009; Mohkamkar et al., 2014). Effects from the initial episode of ED can extend beyond the postoperative period; additional surgery, hematoma formation, infection, sore throat from extubation, or urinary strictures may result (Lepousé, Lautner, Liu, Gomis, & Leon, 2006). Sequelae from ED are not limited to bodily injury, as they can exert negative psychological effects. Kain, Mayes, O'Connor, and Cicchetti (1996) reported that 54% of children were exhibiting maladaptive behaviors within the first 2 weeks of having received anesthesia. Nightmares, separation anxiety, eating problems, and increased fear of physicians were the most common problems at the 2-week follow-up. Postoperative behavioral disturbances also have been reported at 30 days postanesthetic. Stargatt et al. (2006) found that maladaptive behaviors of "general anxiety and regression, apathy or withdrawal and separation" persisted in 16% of children at 1 month (p. 850).

Parental Concerns

Parents experience adverse effects from this condition along with their children. During an episode of ED,

children may not respond to familiar faces or objects and exhibit paranoid ideations resulting in a disconcerting experience for family members (Mason, 2004; Wong & Bailey, 2015). Parents witnessing this aberrant behavior remark "that it is unusual and uncustomary for the child" and may verbalize fears of "permanent brain damage" (Holzki & Kretz, 1999; Mason, 2004, p. 1). These negative impressions can significantly influence perceptions related to the care of the child. Vlajkovic and Sindjelic (2007) report that ED can lead to a perception of a child's anesthetic and recovery as less than satisfactory in the eyes of the parents, leading to a concern of long-lasting negative behavioral effects.

Effects on Nursing Staff

Health care workers often are the forgotten segment of those affected by ED. Children experiencing ED demand an increased acuity of care, secondary to the potential for injury to themselves and the surrounding caregivers. Cole, Murray, McAllister, and Hirshberg (2002) reported that, during moments of marked agitation and disorientation, two or more nurses were required to keep the patient injury free. It also was noted that 2.3% of patients presenting with severe ED had a prolonged course (Cole et al., 2002). Management of an unruly patient places both nursing staff and other patients at risk. Nursing staff in direct contact with uncooperative and aggressive patients place themselves at risk for bodily injury, and the distraction created by the mayhem creates a care deficit for other patients in the area (Lepousé et al., 2006). Considering the negative outcomes associated with this condition, ED is often cited as a major factor in dissatisfaction with care among health care workers and parents (Cao et al., 2016; Dahmani, Delivet, & Hilly, 2014).

Economic Implications

The unfavorable outcomes associated with ED impart financial expenses along with the distress it causes; additional nursing staff is required for adequate supervision of patients (Vlajkovic & Sindjelic, 2007). Faulk et al. (2010) noted that "extra PACU personnel were required for care in 49% of patients with EA [Emergence Agitation] as opposed to only 15% of those not experiencing emergence delirium" (p. 76). Another consequence of ED is additional manpower; the average length of time spent on a child with ED was 0.2 hour versus children without ED at 0.13 hour (Faulk et al., 2010). Costs related to patient injuries and pharmacological management is another source of economic burden. Children who have sustained an injury may require emergency surgery, treatment for aspiration pneumonia, or reintubation (Lepousé et al., 2006). Management of ED involves administration of medication that may delay discharge, thereby incurring cost for pharmaceuticals, staffing, and facility fees (Lepousé et al., 2006; Moore & Anghelescu, 2017; Sato et al., 2010). In the ambulatory setting, delayed discharges can impart a negative influence on patients and caregivers contemplating ambulatory surgery in the future (Sato et al., 2010).

Pharmacological Prevention

Various adjuncts such as fentanyl, midazolam, ketamine, and propofol have been employed to reduce or prevent the incidence of emergence agitation with mixed results. Prevention of ED is imperative as estimates can range as high as 80% (Nasr & Hannallah, 2011). Dexmedetomidine, a α2-adrenoreptor agonist, has shown marked success in recently conducted meta-analyses (Pickard, Davies, Birnie, & Beringer, 2014; Sun, Guo, & Sun, 2014; Zhu, Wang, Zhu, Niu, & Wang, 2015). Dexmedetomidine has a high affinity for the α2-adrenoreptor ($\alpha2/\alpha1 = 1620/1$) and reduces norepinephrine release in the central nervous system. Activation of the α2 receptor results in (a) analgesia, (b) sedation, (c) hypotension, and (d) bradycardia (Gertler, Brown, Mitchell, & Silvius, 2001).

Clinical effects seen with dexmedetomidine use are a "sedative effect similar to physiological sleep, with less respiratory depression, and a decrease in HR or blood pressure" (Cao et al., 2016, p. 3). A benefit of dexmedetomidine use over other pharmacological agents is its versatility in all phases of the perioperative period and methods of employment. Dexmedetomidine can be adminsistered via the mucocutaneous (nasal/oral) and intravenous routes. Zhu et al. (2015) concluded that its employment is successful when given preoperatively, intraoperatively, or at the conclusion of surgery.

The ability to effectively reduce or prevent the incidence of postoperative agitation is one of many reasons to use dexmedetomidine. The greatest strength of dexmedetomidine is the favorable side effect profile. Reduced nausea and vomiting, analgesia-sparing properties, and low risk of respiratory depression make dexmedetomidine an attractive choice above other approaches (Cao et al., 2016; Chen, Jia, Liu, Qin, & Li, 2013; Moore & Anghelescu, 2017).

Nursing Care Considerations

Children who are most likely to experience ED need to be identified during the perioperative phase of care. During this period, nurses must focus on parental education and reassurance that unruly and combative behavior upon recovery from anesthesia is a normal

phenomenon. Particularly for preschoolers, the process of recovery from anesthesia can be complicated by a developing brain that is unable to cope with reorientation to surroundings upon emergence, thereby predisposing them to ED (Vlajkovic & Sindjelic, 2007). Children who emerge from anesthesia in a combative and emotional state need to be provided reassurance by caretakers with "constant reality orientation" (Hudnek, 2009, p. 512). Parents should be advised that regressive behaviors may persist up to 2 weeks postoperatively (Kain et al., 1996).

Patient and nursing staff safety is also a concern during an episode of ED. In addition to padding side rails and physical restraint, nurses should consider asking anesthesia staff for pharmacological intervention. Dexmedetomidine, as discussed previously, has a favorable side effect profile without the danger of severe respiratory depression as seen in opioids, barbiturates, and sedative hypnotics.

Assessment Tools

The Pediatric Anesthesia Emergence Delirium Scale, developed by Sikich and Lerman in 2004, is an intuitive tool by which to measure the presence of ED. A 4-point scale for five different behaviors is scored for a maximum score of 20. Behaviors 1–3 address the cognitive component of ED, whereas Behaviors 4–5 denote the psychomotor changes seen in ED. It is important to note that scoring for the first three behaviors is inversely related to scoring +Behaviors 4 and 5 (refer to Table 1).

Scores of ≥10 have been used throughout the literature to indicate the presence of ED (Bong & Ng, 2009; Hauber et al., 2015; Locatelli et al., 2013). However, Bajwa, Costi, and Cyna (2010) found greater sensitivity and specificity when utilizing scores of ≥12 versus scores of ≥10. Therefore, a cutoff of ≥12 will yield a greater probability of ruling in (sensitivity) children who are positive for ED while also ruling out those who do not have ED (specificity).

1. The child makes eye contact with the caregiver.
2. The child's actions are purposeful.
3. The child is aware of his/her surroundings.
4. The child is restless.
5. The child is inconsolable.

Items 1, 2, and 3 are reversed scored as follows: 4 = not at all, 3 = just a little, 2 = quite a bit, 1 = very much, 0 = extremely. Items 4 and 5 are scored as follows: 0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much, 4 = extremely. The scores of each item were summed to obtain a total Pediatric Anesthesia Emergence Delirium (PAED) scale score. The degree of emergence delirium increased directly with the total score.

TABLE 1. The Pediatric Anesthesia Emergence Delirium Scale. Reprinted with permission from "Development and Psychometric Evaluation of the Pediatric Anesthesia Emergence Delirium Scale," by N. Sikich and J. Lerman, *Anesthesiology, 100*, p. 1142. Copyright 2004 by the American Society of Anesthesiologists

CONCLUSION

Estimates for the incidence of ED have been reported to range from 25% to as high as 80% (Sikich & Lerman, 2004). Children represent a vulnerable segment of society in which the occurrence of ED can result in physical and mental health consequences. A careful examination of risk factors and appropriate assessment tools coupled with pharmacological prevention is critical in avoiding the deleterious effects of emergence agitation. Dexmedetomidine represents a safe and effective method of decreasing the incidence of postoperative agitation when employed throughout the perioperative period.

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