

Pediatric Emergence Delirium: A Case Study

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The pathophysiology of emergence delirium (ED) remains a mystery. Using a case study approach, ED is discussed from a clinical perspective. The case is a 4-year-old male who had myringotomy tube placement while anesthetized with sevoflurane. The negative outcome for this child is presented. The epidemiology of the phenomena is reviewed and definitions are examined. Several methods to assess ED are presented, accompanied by a discussion of the development of assessment tools. Research findings are included that address the possible causes of ED including preoperative anxiety, rapid awakening, pain, and a predisposition for this phenomenon in certain children. Various interventions, both pharmacologic and nonpharmacologic are considered. The impact of anesthesia on pediatric brain development is discussed and finally some possible solutions are hypothesized.

Keywords: anesthesia, anxiety, emergence delirium, pain, pediatric.

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OBJECTIVES—1. List several factors that can impact on the incidence of ED in children. 2. List at least two interventions to reduce the incidence of ED in children. 3. Analyze the research that has been conducted to understand ED in children.

The pathophysiology of emergence delirium (ED) remains a mystery. Approximately 450,000 children aged less than 18 years have surgical procedures requiring anesthesia every year. Of these, 25% are aged less than 3 years. Administering anesthesia to pediatric patients is fraught with potential complications. However, mortality and morbidity in healthy children who have routine procedures with anesthesia is rare. Patterns of

brain injury have not been identified in more than 4 million children exposed to anesthesia.¹

Pediatric airways are anatomically different than adult airways and maintaining patency is vital and can become complicated. However, children are also subject to a multitude of other problems when undergoing surgery. Animal studies reveal that there are neurotoxic effects of anesthetic agents on the developing brain.² Pediatric postoperative ED is a recognized phenomenon and may occur because of this neurotoxic effect. The incidence of ED in surgical patients of all ages is 5.3% with an incidence in children of 12% to 13%.² ED is two to three times more common in children than in adults.³

Case Study

John is a 4-year-old male who was scheduled for myringotomy surgery. The Certified Registered Nurse Anesthetist (CRNA) visited John and his parents in the preoperative area. The parents described John as a healthy, well-behaved 4-year-old. He attends prekindergarten and enjoys time with other children. He obeys rules and is usually cooperative. His physical development has been normal and he can peddle a tricycle, draw a

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triangle and other shapes, use a fork and spoon, and is independent in dressing and other hygiene activities. His parents appeared to be calm and asked appropriate questions about anesthesia and postoperative pain. They were easily reassured.⁴ They accompanied John into the operating area and remained with him until he was anesthetized. A general anesthetic was performed, initiated with a smooth inhalation induction. Once John was asleep, his parents were escorted out of the operating room by the nurse, at which point an intravenous (IV) line was started in John's left hand. General anesthesia was maintained with 2% sevoflurane delivered with a 50/50 ratio of oxygen and air. John also received 25 mcg of fentanyl for pain and 4 mg of ondansetron for nausea prophylaxis. The procedure lasted 37 minutes, with the emergence process starting approximately 5 minutes before. The surgery was successful.

John was beginning to awaken before he was moved into the recovery area. His parents were waiting for him, but he did not recognize them and began to thrash, cry, and scream for his mother. This behavior lasted for 30 minutes before he became calm and was awake and oriented. In the immediate postoperative period John exhibited behaviors that were diagnosed as ED. He was considered a 5 on the Pediatric Assessment of Emergence Delirium scale. The event lasted about 30 minutes. No medication was administered postoperatively. He remained in the recovery area for 65 minutes and was discharged to Same Day Surgery, where he spent an additional 20 minutes before being discharged to home (unpublished data, M. McLaughlin, Operative Report, 2016).

John's parents have reported that he has had frequent tantrums since surgery that include screaming and throwing things. He has had a difficult time in school and has reverted to bed-wetting. John's parents relate all these behaviors to be new, starting immediately after the surgery.

Emergence Delirium

In general, ED is self-limiting and in many cases, no treatment occurs. There is frequently a sense that ED is an unavoidable effect of anesthesia in the pediatric population. There is a controversy about

prevention preoperatively and the assessment and treatment of ED intraoperatively and postoperatively. In spite of these opinions, ED is not innocuous. It becomes a significant problem and can interfere with recovery and result in postoperative behavioral changes that can last up to a year. These behavioral changes have been identified in up to 50% of children after surgery.⁵

ED is defined as a dissociated state of consciousness. It is an acute brain dysfunction and should not be considered to be without unwanted side effects.⁶ Children with ED become inconsolable, irritable, and thrash, cry and moan. These children may not recognize their parents or other familiar people or objects. This is not a new phenomenon. In the immediate postoperative period this behavior can cause complications that include increased bleeding from the surgical site, interference with IV access, and in some cases has caused injury to the nurses and parents at the bedside. The postanesthesia care unit (PACU) is typically an open area and the noise level is affected by the sounds emanating from these children.

Although there are a few published data on childhood delirium, there is a suggestion that morbidity and mortality are higher in children who suffer from ED postoperatively.⁶ Huett et al conducted a survey of 1,229 anesthesia providers. Eighty-eight percent reported ED as a significant clinical problem. Only 5% reported using an assessment score to define ED and the treatment protocols varied.⁷

In an effort to standardize the identification of emergence delirium, the Pediatric Anesthesia Emergence Delirium (PAED) was developed. The emergence behavior of children was assessed and a list of items that described this behavior was developed. Fifty children were enrolled in this study. Twenty-seven items emerged and five of the items met content validity and statistical analysis criteria. Internal consistency was 0.89 and reliability was 0.84. There was a negative correlation with age ($r = -0.31, P < .04$) and time to awakening ($r = -0.05, P < .001$). Scores were greater after sevoflurane than after halothane. There was a positive correlation with clinical judgment scores. The items included are as follows: (1) the child makes eye contact with the caregiver, (2)

the child's actions are purposeful, (3) the child is aware of the surroundings, (4) the child is restless, and (5) the child is inconsolable.⁸

The Cornell Assessment of Pediatric Delirium is a rapid observational screening tool that was developed in a blind study. It is an adaptation of the PAED. It is a brief assessment tool that takes less than 2 minutes to complete. The tool has an overall sensitivity of 94.1% and specificity of 79.2%. The tool demonstrated interrater reliability when comparing results of the screen between nurses [$k = 94$]. Observations include acute change or fluctuating course of mental status, inattention, altered level of consciousness, or disorganized thinking.⁹

Factors that seem to be related to ED include younger patients, children with no surgical experience, children who have demonstrated poor adaptability to new situations, as well as children having eye and ear, nose, and throat surgery. The use of sevoflurane and isoflurane has been associated with ED. Analgesics and a short time to awakening were also factors in ED in this population.

Ketamine, fentanyl, and propofol are also used perioperatively. In a study by Almajali et al,² there was no difference in the incidence of ED in groups receiving fentanyl or propofol. Eight patients in the first group who received ketamine had severe postoperative emergence agitation. The researchers concluded that the administration of propofol or fentanyl at the end of surgery under sevoflurane anesthesia reduced the frequency and severity of ED compared with the use of ketamine.²

In another study, Wong and Bailey¹⁰ found that when intranasal ketamine in a dose of 2 mg/kg was administered preoperatively, the incidence of ED was reduced. In addition, a bolus dose of 0.25 mg/kg administered IV 10 minutes before the end of the procedure reduced ED, but also had negative effects causing an increase in postoperative nausea and vomiting, which resulted in a longer recovery time.¹⁰

Sevoflurane, the anesthetic agent of choice for children, is associated with rapid induction and emergence from anesthesia. Its high hemodynamic stability and minimal airway side effects make it a desirable agent to use. However, when sevoflurane

is used as the inhalational agent, the frequency of ED is about 80%.² The rapid awakening associated with the use of sevoflurane may cause the child to have an increase in apprehension when awakening in an unfamiliar environment and experiencing pain.

There is a suggestion that perioperative pain may be a major factor in severe ED. This rapid emergence from sevoflurane may be a double-edged sword as the patient may awaken before any intraoperative analgesics have reached peak effect. In a randomized, double-blinded study using 40 boys undergoing inguinal hernia repair, the hypothesis was that intraoperative pain management would reduce the incidence of ED. The children did not receive premedication and anesthesia was induced with 60% nitrous oxide, 40% oxygen, and 5% sevoflurane. Group A received an intraoperative nerve block and group B did not. ED was assessed postoperatively using the PAED scale. There was no difference in ED or postoperative pain but the children who received the nerve block needed less sevoflurane intraoperatively.¹¹

There are other predictors of ED related to preoperative anxiety. Kain et al⁵ examined data obtained over a period of 6 years from children who underwent surgery using sevoflurane, O₂, and N₂O who did not receive midazolam perioperatively. Midazolam is a benzodiazepine that produces sedation and has some effect on anxiety in pediatric patients. Dahmani et al compared the use of midazolam and ketamine to reduce preoperative anxiety in children. Results indicated that there was no statistically significant difference between the drugs in reducing anxiety and inducing sedation.¹²

Preoperative anxiety was assessed using the modified Yale Preoperative Anxiety scale. ED was assessed in the PACU by observation and postoperative behavioral changes were assessed with the Post-Hospital Behavior Questionnaire. Anxiety scores and marked symptoms of ED were directly related to higher scores in the child's state anxiety score. In addition, increases in state anxiety scores led to an increase in new-onset maladaptive behavioral change postoperatively.⁴ ED and subsequent postoperative behavioral changes may be predicted based on levels of preoperative anxiety.

Prevention and Treatment

Nonpharmacologic interventions have been somewhat successful in reducing anxiety in patients and parents preoperatively. These strategies include education and preparation using written materials, videos, and interactive games.¹ Allowing parents to remain with the child until they are anesthetized has been effective in reducing preoperative anxiety, which may reduce postoperative ED.

The use of dexmedetomidine, an alpha-2 receptor agonist, may induce analgesia and sedation and be useful in the management of ED. In a study by Shukry et al,¹³ group 1 received an infusion of 0.2 mcg/kg of dexmedetomidine and group 2 received an equal volume of saline started immediately after intubation and maintained for 15 minutes after PACU admission. Group 1 demonstrated a statistically significant difference in the incidence of ED. The number of episodes of ED was lower in group 1 ($P < .017$). In a retrospective record review of children who had myringotomy tube insertions or removal, comparisons were made between a group treated with intranasal dexmedetomidine and a control group that did not receive this medication; there were no statistically significant differences.¹³

Discussion

In the case presentation, John did not exhibit signs that he was at risk for ED. He did not receive any medications perioperatively except sevoflurane. Postoperatively he was assessed as a 5 (severe) on the PAED scale. His behavior change remained from moderate to severe for approximately 9 months. He was placed in a therapy program and his parents report a slight decrease in the maladaptive behavior.

Could this have been avoided? The literature is mixed. On the basis of the work done by Loepke and Hansen¹⁴ there may be some basis for concern about pediatric brain development

and its relation to the use of anesthetic agents and sedatives in young children undergoing surgical procedures. There have been epidemiologic studies that establish an association between learning disabilities and behavioral and developmental disorders when children in the first 3 to 4 years of life undergo surgical procedures that require anesthesia. Anesthetic agents have a potent effect on glutamate's *N*-methyl-D-aspartate and/or γ -aminobutyrate receptors. These receptors have a critical role in brain development.¹⁴

It becomes important to identify the population most at risk and determine if mitigating strategies can be applied. Several strategies are already in place in many cases, which include nonpharmacologic interventions, preoperative medication, perioperative medication, and medication to intervene when emergent agitation and ED are present. Although inconclusive, there is indication that anesthesia can have a long-term impact in children aged 3 to 4 years. Further study is vital to determine which agents are effective. The induction procedures are generally inhaled anesthesia. Sevoflurane has been associated with an 80% incidence of ED. In many cases, IV medication is not used as cannulation does not occur until the child is anesthetized. With the use of ultrasound guided IV insertions preoperatively and the administration of a sedative agent, the incidence of ED might be reduced.

There is also the emphasis on efficient and effective use of the operating and PACU areas. It is considered desirable to focus on rapid induction and emergence as a cost saving mechanism. More comparative studies are needed to determine if overall perioperative time is actually impacted by use of these agents. Emergence delirium is not an innocuous event. It is important for anesthesia providers to continue to explore more effective means of anesthetizing children with a focus on reduction of the incidence of ED.

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1. List several factors that can impact on the incidence of emergence delirium (ED) in children.
2. List interventions to reduce the incidence of ED in children.
3. Review the research that has been conducted to understand ED in children.

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