Emergence Delirium in Pediatric Patients

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KEY POINTS

- Emergence delirium is a transient dissociated state of consciousness that occurs after discontinuation of anaesthesia. It is characterised by marked irritation and psychomotor agitation.
- The commonly reported incidence of emergence delirium is about 10% to 30% of paediatric patients.
- Risk factors associated with emergence delirium are age, preexisting behaviours, types of surgery and the use of volatile anaesthesia.
- Postoperative pain can confound the identification of emergence delirium.
- Patients who experience emergence delirium are at higher risk of developing postoperative maladaptive behaviours.
- Interventions to decrease emergence delirium include choice of anaesthetic techniques, medications and nonpharmacologic interventions. It is crucial that the anaesthesia provider review and select the most appropriate strategy for each individual patient.

INTRODUCTION

Emergence delirium (ED) was first described in the literature in the early 1960s. Although often used interchangeably with emergence agitation, it is defined as a temporary dissociated state of consciousness after discontinuation of anaesthesia. The characteristics that make up ED include irritability, inconsolable crying, distress and inability to cooperate.[1] Practically, it can be challenging to accurately identify patients who are at risk for developing ED as well as preventing and treating it. This tutorial reviews what we currently know about ED, who is at risk for developing ED and the pharmacologic and nonpharmacologic interventions that can be used to treat it.

INCIDENCE

The incidence of ED has been reported to range from 2% to 80%. The most common consensus from the literature is an incidence of 10% to 30% of all children in the postanaesthesia care unit (PACU). This wide range results from differences in study design, methodology and interpretation.[1] The incidence of ED is higher in paediatrics than that reported in the adult population (5.3%).[2]

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Criteria	Not at All	Just a Little	Quite a Bit	Very Much	Extremely	Score
The child makes eye contact with the caregiver/parent	4	3	2	1	0	
The child's actions are purposeful	4	3	2	1	0	
The child is aware of his/her surrounding	4	3	2	1	0	
The child is restless	0	1	2	3	4	
The child is inconsolable	0	1	2	3	4	
Total score						

Table 1. Pediatric Anaesthesia Emergence Delirium (PAED) Scale Score. The PAED scale consists of 5 criteria that are scored using a 5-point scale. The scores of each criterion are added to make a total score. The maximum achievable score is 20. A score of $\geq$10 has 64% sensitivity and 86% specificity for the diagnosis of ED. A score of $>$12 has 100% sensitivity and 94.5% specificity for the diagnosis of ED.[18]

CHARACTERISTICS

The signs and symptoms of ED include inconsolable crying, uncontrolled movements and uncooperativeness. These attributes can lead to both short- and longer-term negative effects on the child, parents as well as direct caregivers in the PACU. For example, children with ED can disrupt surgical repairs as a result of excessive movement; they can dislodge intravenous (IV) catheters and surgical drains or tubes. These children pose a risk of harming not only themselves but also the care staff in PACU. In addition, the care of these children often requires additional nursing staff, which can compromise staffing ability in the PACU. Parental satisfaction is becoming an important benchmark for anaesthesia care. Parents of children with ED frequently express concern, anxiety and dissatisfaction.[1] In the longer term, children with ED are 1.4 times more likely to have new onset of maladaptive behavioural changes (sleep disturbance, separation anxiety, eating disturbance) for up to 2 weeks after surgery.[2]

The challenge for caregivers is how to best identify ED by means of an objective grading system. The manifestations of ED can overlap with those expressed by children in pain, and to date, there is no such rating scale that can reliably discriminate between these 2 conditions. Various scales have been proposed, and the Pediatric Anesthesia Emergence Delirium (PAED) scale is considered the gold standard (Table 1). It was developed in 2004 and has been validated to identify ED in children older than 2 years.[3]

RISK FACTORS

Recognizing the risk factors for ED enables the anaesthesia provider to anticipate, prevent and manage ED. These can be categorised into 3 categories: patient risk factors, type of surgery and anaesthetic technique (Figure 1).

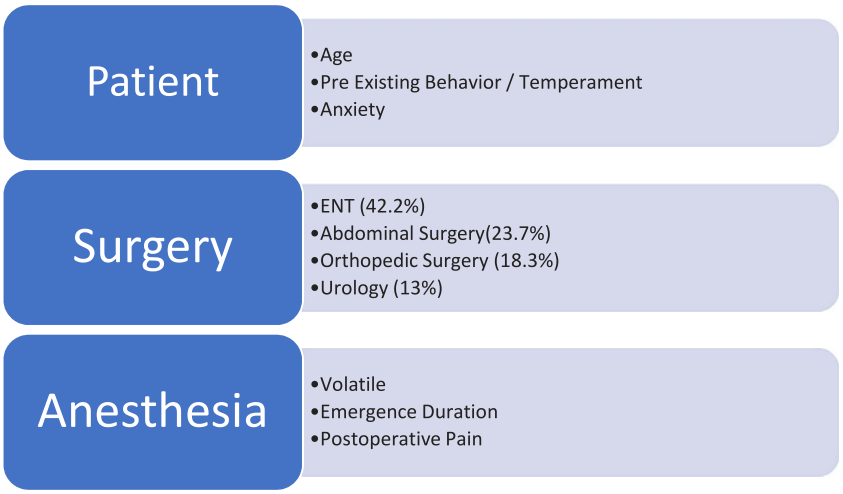

Figure 1. Risk factor categories for emergence delirium.

Patient Risk Factors

The presence of preexisting anxiety or maladaptive behaviours was found to pose the greatest risk for the development of ED, including agitated, uncooperative behaviour; exaggerated displays of anger (temper tantrum); and low adaptability skills.[4] The degree of preoperative patient anxiety has also been found to correlate with ED. In addition, a high level of parental anxiety contributes to a higher level of preoperative anxiety in the child.[3] Patients aged 2 to 7 years have been found to be at higher risk of ED when compared with those older than 7 years.

Surgical Risk Factors

Certain types of surgical procedures have been found to be positively associated with increasing the risk of ED. Specifically, ear, nose and throat surgeries have the highest incidence of ED (42.2%), followed by abdominal, orthopaedic and urologic procedures.[4]

Anaesthetic Risk Factors

The use of volatile anaesthetics has been strongly associated with the development of ED. Isoflurane, halothane, sevoflurane and desflurane have all been associated with ED. Although the use of sevoflurane has been found to have the highest incidence of ED, this may be due to the fact that most studies have been performed using sevoflurane. Rapid emergence has also been identified as another possible contributing factor.[4] It is postulated that sudden awakening in an unfamiliar environment with strangers can worsens patients' underlying fear. In addition, preschool children have psychological immaturity and are less likely to cope with a rapid return of consciousness in a strange environment.[5]

Postoperative pain can confound the identification of ED. It is often difficult, especially in the nonverbal child, to differentiate between pain and delirium. If pain is ruled out, the diagnosis of ED, particularly with positive PAED scales, is more likely.[6] The challenge is that the descriptors for the PAED scale can be exhibited by children in pain as well as those with ED (and not in pain). A recent study examined these descriptors to determine which were the most likely to present. For example, failure of a child to make eye contact who is also unaware of his or her surroundings is more likely consistent with ED. Abnormal facial expression, inconsolability and crying while the patient is making eye contact and is aware of his or her surrounding is more likely from pain. For a case in which ED and pain cannot be discriminated, pain should be considered and treated first, followed by a reassessment for ED.[6]

PREVENTION AND TREATMENT

Inhalational Agents Versus Total IV Anaesthesia

As mentioned previously, the use of volatile agents is associated with an increased risk of developing ED. In contrast, total IV anaesthesia is associated with a lower risk of ED.[3]

Propofol is the most commonly used agent for total IV anaesthesia. The effectiveness of propofol administration on ED prevention varies depending on the timing and dose administered. A propofol-only infusion as a maintenance anaesthetic has been found to be effective in reducing the incidence of ED. However, an adequate depth of anaesthesia is not always achievable depending on the nature of the procedure. The role of a propofol bolus given as prophylaxis for ED is equivocal. There are data to support that 3 mg/kg of propofol over 3 minutes at the end of a sevoflurane anaesthetic may decrease the incidence of ED.[7]

Medications

Alpha 2 Receptor Agonists

Alpha 2 agonists such as clonidine and dexmedetomidine have been shown to be effective as a prophylactic in decreasing the frequency and severity of ED. Although both are alpha 2 receptor agonists, dexmedetomidine has a greater affinity to alpha 2 adrenoreceptors (a2/a1 = 1620/1) than clonidine (a2/a1 = 220/1) and may be more clinically effective than clonidine in decreasing the incidence of ED.[8]

In a randomised, double-blind placebo-controlled study, intranasal dexmedetomidine 1 and 2 $\mu g \cdot kg^{-1}$ administered preoperatively was found to reduce the incidence of ED.[9] In addition, dexmedetomidine 2 $\mu g\ kg^{-1}$ IV bolus followed by 0.7 $\mu g\ kg^{-1}\ h^{-1}$ intraoperatively was found to be more effective in decreasing ED than a single dose of IV fentanyl 1 $\mu g\ kg^{-1}$ in patients undergoing tonsillectomy and adenoidectomy.[10] When administered 5 minutes prior to extubation, dexmedetomidine 0.3 $\mu g\ kg^{-1}$ was more effective than propofol 1mg kg^{-1} in decreasing the incidence of ED after adenotonsillectomy.[11]

In addition to decreasing ED, there are multiple benefits associated with the use of dexmedetomidine. The pharmacokinetics and pharmacodynamics of dexmedetomidine make it acceptable for IV, intranasal and intramuscular administration.

Dexmedetomidine does not cause respiratory depression[11] and has synergistic properties for analgesia as well as decreasing anaesthetic requirements for narcotics, volatile anaesthetics and propofol. Preliminary reports suggest it may decrease the incidence of postoperative nausea and vomiting when administered as a continuous infusion. Lastly, its metabolism is minimally affected by age or comorbidities.

Narcotics

Various narcotics, including fentanyl, remifentanil, sufentanil and alfentanil have been studied as prophylactic measures to prevent ED. The effectiveness of narcotics in preventing ED is unclear. Individual studies to date have had mixed results.

Fentanyl 2 to 2.5 $\mu g\ kg^{-1}$ intranasally or 1 to 2 $\mu g\ kg^{-1}$ IV has been shown to reduce the duration and severity of ED, without affecting the time to meet discharge criteria. However, fentanyl has been shown to significantly increase postoperative nausea and vomiting,[12] so its use should be carefully weighed. To date, there are no clear data in support of any narcotic as a prophylactic for ED. Caution should be used when evaluating the published studies, as narcotics may decrease manifestations of pain and mistakenly affect the PAED score in children who are in pain but who do not have ED.

Midazolam

Midazolam is the most commonly prescribed oral premedication in the preoperative setting. Its benefits include preoperative anxiolysis, amnesia, relatively rapid onset and short duration of action. Although most children have anxiolysis with midazolam, up to 29% may display a paradoxical agitation response.[13]

Midazolam (whether given before induction or at the end of surgery) has been widely studied for the prevention of ED. To date, there is no support for midazolam as a prophylactic, regardless of timing of administration. A meta-analysis was unable to support its value.[3]

Despite the conflicting data, midazolam should still be considered in the at-risk patient because it can provide anxiolysis and, in some studies, a decrease in maladaptive behaviours for up to 1 week.[14]

Gabapentin

Gabapentin may be an effective prophylactic in children, although it has not been shown to be effective in adults.[15] In children undergoing adenotonsillectomy, gabapentin was shown to decrease the severity of ED.[3]

Melatonin

Oral melatonin doses up to 0.4 mg/kg (maximum 20 mg) is effective in reducing ED in children (age 3-7 years).[16]

Ketamine

Premedication with ketamine is shown to be more effective than midazolam in reducing the incidence of ED during the early period of recovery (10 minutes, 20 minutes) after sevoflurane anaesthesia in children.[17] In addition, ketamine (1 $mg\ kg^{-1}$ IV bolus followed by a 1 $mg\ kg^{-1}\ h^{-1}$ infusion) is as effective as dexmedetomidine (1 $\mu g\ kg^{-1}$ IV followed by 1 $\mu g\ kg^{-1}\ h^{-1}$ infusion) in decreasing the incidence of ED.[18] However, from a practical standpoint, ketamine may not as suitable as a prophylactic for ED, as it produces unwanted side effects that counteract its effectiveness (hallucinations, confusion, nausea/vomiting). It has been shown that 5% to 30% of patients experience nightmares and hallucinations at high doses.[18]

Regional Anesthesia

To date, regional anaesthesia has not been widely studied with respect to ED. Its value as a prophylactic for ED has not been demonstrated.[3]

Nonpharmacologic Interventions

Acupuncture may be an important technique in decreasing ED. A double-blind, randomised controlled trial in Japan showed a decrease in ED in paediatric patients who received an electrical stimulation on the heart 7 (HT7) acupuncture site with a peripheral nerve stimulator.[19]

Preoperative anxiety is recognised as a risk factor for ED. Nonpharmacologic, behavioural and distraction techniques to minimise preoperative anxiety are being studied. For some children at induction, video distraction has been shown to be as effective as an anxiolytic as parental presence. Kim et al[20] found that video distraction, parental presence or a combination of both had a similar effect on ED. In addition to video distraction, the effect of a ride-on toy car transport on preoperative anxiety was studied. The ride-on toy car transport was effective in reducing preoperative anxiety in comparison with oral midazolam.[21]

To further understand the effectiveness of these nonpharmacologic interventions, we need further large-scale studies to determine their ability to reduce ED.

SUMMARY

ED has been studied for more than 60 years as a transient dissociated state of consciousness after anaesthesia that is marked by irritability and psychomotor agitation. It is commonly seen in young children aged 2 to 6 years. While self-limiting, ED can have serious consequences for some children. Patient age, disposition (maladaptive personality type), degree of preoperative anxiety, surgical procedure and anaesthetic technique have all been identified as playing important roles in ED. The challenge is the overlap of patient behaviours in the PACU displayed by patients in pain as well as those with ED. To date, the most effective prophylactic treatments are dexmedetomidine, efforts at establishing a good patient rapport and using nonpharmacologic techniques to decrease anxiety.

Other nonpharmacologic interventions such as acupuncture and video distraction have been studied in the past, but further research is required to better understand their effects. Understanding the risk factors and treatment options is critical to the management of ED.

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