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Emergence Delirium in children

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Abstract

Delirium after anesthesia, also known as emergence delirium (ED) is a clinical condition in which patients have alterations to their attention, awareness, and perceptions. In children, this often results in behavioral disturbances such as crying, sobbing, thrashing and disorientation. Emergence Agitation (EA) and Emergence Delirium (ED) are commonly used interchangeably; they describe two distinct conditions with emergence delirium being described in the anesthesia literature as a state of mental confusion, agitation, and dis-inhibition marked by some degree of hyper-excitability during recovery from general anesthesia. 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. Transient agitation - delirium from sevoflurane anesthesia can lead to a variety of adverse events, such as airway spasm, shedding or displaced tracheal tube, dehiscence, or bleeding. Volatile anaesthetics may affect brain activity by interfering with the balance between neuronal synaptic inhibition and excitation in the central nervous system. Elevated postoperative pain has been suggested to underlie ED. But given that ED is seen in patients undergoing MRI, pain cannot be the sole cause. Treatment options include the use of premedication, analgesic adjuvants, single dose of propofol at the conclusion of the case. Midazolam premedication, intraoperative dexmedetomidine and fentanyl were associated with lower incidence of ED. The incidence of ED in patients receiving propofol is markedly lower than those receiving sevoflurane, despite the similar rapid emergence profile of both agents. Paediatric Assessment of Emergence Delirium (PAED) scale, developed specifically for children, is a valid and reliable scale. Watcha score is a simpler, reliable tool to measure emergence behaviour. There has been considerable progress in the neuroscience of anaesthesia and the application of new pharmacological agents, but the mystery behind the exact mechanism of ED is elusive. ED is a diagnosis of exclusion once other causes have been dismissed. There is no strong evidence of long-term effects and outcomes in children who developed emergence delirium after anesthesia. Prevention may be the best treatment but no one medication is entirely effective.

Keywords: Emergence delirium; Agitation; Anesthesia; Volatile anesthesia

1. Introduction

Emergence delirium (ED) was first described in the literature in the early 1960s. Incidence of ED is two to three times more common in children than in adults. Current data would suggest that the incidence of ED varies from 20% to 80% of all paediatric anaesthetics with most of the literature suggesting it to be close to 20%. ED is a transient state of marked irritation and disassociation after the discontinuation of anaesthesia. Delirium and agitation can occur as a child awakens, or emerges, from anesthesia. Emergence agitation, emergence excitation, and emergence delirium are all terms utilized to describe the state of behavioral dysregulation that can happen during emergence from general anesthesia. The fact that ED is the most common in pre-schoolers does not necessarily mean that it cannot develop in different age categories. Although often used interchangeably with emergence agitation, the characteristics that make up ED include irritability, inconsolable crying, distress, uncontrolled movements and inability to cooperate. There are defined risk factors, and usually symptoms occur within 30 min of termination of anaesthesia and last for 15–30 min.

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Sevoflurane anesthesia has advantages of rapid uptake and elimination and shows reduced opioid adverse events in pediatric ambulatory surgery. However, emergence agitation (EA) and emergence delirium (ED) are recognized as a significant complication after sevoflurane anesthesia in pediatric patients, with a reported prevalence between 10% and 80%. Emergence delirium may be distressing to the patient, parents, and caregivers, and can result in inadvertent removal of intravenous (IV) catheters, drains, and dressings, and rarely, self-harm. While pain is not the sole cause for ED, surgery associated with elevated postoperative pain has been thought to increase the risk of ED. The site of surgery has been proposed as a risk factor, as well. Otorhinolaryngological and ophthalmological procedures have been shown to increase the risk of ED in comparison with urological and general surgery procedures, pointing to the possibility that surgeries affecting the head and neck may be relatively more likely to induce ED. Children who are more emotional, more impulsive, less social, and less adaptable to environmental changes, has been identified as a risk factor for ED. Various causes of ED have been proposed, including rapid emergence after the use of short-acting volatile anaesthetics. The introduction of short-acting volatile anaesthetics has been historically associated with the increased incidence of ED. In non-surgical settings, with patients undergoing magnetic resonance imaging (MRI), sevoflurane has been shown to increase the risk of ED. Several perioperative factors may be associated with EA or ED. Volatile anesthesia exposure and depth are the major risk factors for EA/ED. Volatile agents induce EA/ED nearly four times more often than intravenous anesthetics, particular sevoflurane. The bispectral index (BIS) monitor is a common method for monitoring the depth of anesthesia. Previous studies have suggested low BIS value <40, affects postoperative recovery, including postoperative delirium, mortality. A definitive relationship between low BIS and EA- ED remains inconclusive. EA is commonly considered not always associated with significant changes in behavior or cognition. Intensity of EA can be scored using tools such as the Richmond Agitation-Sedation Scale (RASS), it is the version of typical sedation scales. Unlike EA, ED is acute brain dysfunction, which occurs in the setting of systemic disease or derangement. Due to the large range of behaviors in children, the Pediatric Anesthesia Emergence Delirium (PAED) scale was created to assess these behaviors in a reliable way. The Pediatric Anesthesia Emergence Delirium (PAED) is considered an effective tool for ED assessment and is widely used in the post-anesthesia care unit (PACU). One theory attributes ED to the unique neurodevelopmental characteristics in this age group and the effects of the newer volatile anesthetics (ie, sevoflurane, desflurane, isoflurane) on them. Another theory associates ED with the unique electroencephalographic (EEG) findings that occur with sevoflurane anesthesia. Sevoflurane but not propofol is associated with altered metabolism in some parts of the brain, which in turn is associated with a greater risk of ED. ED can be described with neurological symptoms and terms that amount to a discreet postoperative neurological state, characterised by core neurological and behavioural symptoms: motor agitation, confusion, and lack of recognition or appropriate interaction with their surrounding environment. It usually begins at the start of emergence, but the onset can be as long as 45 min after the termination of anaesthesia. ED occurs with a similar frequency after desflurane and isoflurane even though the EEG tracings during these inhaled anesthetics are quite dissimilar from sevoflurane. The EEG patterns that may predict ED have yet to be determined, and EEG monitoring cannot yet be used to predict which children might develop ED in the PACU. Postoperative pain can confound the identification of ED. It is often difficult, especially in the nonverbal child, to differentiate between pain and delirium. Patients who experience emergence delirium are at higher risk of developing postoperative maladaptive behaviours. Preoperative anxiety is recognised as a risk factor for ED. Nonpharmacologic, behavioural and distraction techniques to minimise preoperative anxiety are being studied. Delirium may also occur without signs of agitation restlessness or non-purposeful movement. This type of delirium is called hypoactive or quiet delirium. The clinical significance, cause and management of hypoactive delirium in the post-operative setting are unknown [1-8].

2. Prophylactic Measures

Sevoflurane and desflurane with their low blood-gas solubility coefficients are associated with rapid washout and emergence from anaesthesia. It remains unclear as to whether rapid emergence causes ED, or whether emergence in the presence of surgical pain and before the onset of effective analgesia is a major factor. The duration of deep anesthesia, bispectral index- BIS <45, does not correlate with the risk for developing ED. ED is as likely to occur after brief procedures, as it is after surgeries of greater duration. Children with purported agitation in the recovery room should first be assessed for potentially dangerous causes of agitation; hypoxia, hypotension, hypercarbia, hypoglycemia and for pain. If pain is a problem, treated appropriately with analgesics. The incidence of ED varies with the anesthetic agent used, age of the child, the procedure or surgery and in particular, with the criteria used to diagnose ED. Current practice routinely includes preemptive administration of analgesics, often sedatives and other adjunct agents to ensure a smooth emergence from anesthesia, which has reduced the clinical incidence of ED in the PACU. Elevated postoperative pain has been suggested to underlie ED. But given that ED is seen in patients undergoing MRI, pain cannot be the sole cause. It is worth noting that while postoperative pain is not the sole cause of ED, the degree of pain produced by a surgical procedure can change the characteristics of the observed ED and may affect the efficacy of non-analgesic adjuvants such as propofol used to treat or prevent ED. 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 and low adaptability skills. 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. Patients aged 2 to 7 years have been found to be at higher risk of ED when compared with those older than 7 years. Rapid emergence has also been identified as another possible contributing factor. It is postulated that sudden awakening in an unfamiliar environment with strangers can worsen 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. 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. Various narcotics, including fentanyl, remifentanyl, sufentanyl 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. 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. Oral melatonin doses up to 0.4 mg/kg (maximum 20 mg) is effective in reducing ED in children (age 3-7 years). 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. The addition of midazolam or an antiemetic enhanced the efficacy of other agents. Among single drugs, high dose melatonin (0.2 to 0.4 mg/kg) was the most effective preventive measure for ED. Regional anaesthesia has not been widely studied with respect to ED. Acupuncture may be an important technique in decreasing ED. Due to the rapid pharmacokinetics of propofol, a bolus of 1 mg/kg given at the end of the procedure or continuous infusion used during maintenance of anaesthesia results in increased concentrations during emergence resulting in a decreased incidence of ED. Several analgesics have been studied for the prevention of ED including: fentanyl (dose 1 µg/kg i.v. given 10 min before the end of a procedure), ketamine (0.25 mg/kg i.v. given at the end of procedure, or as a premedication 6 mg/kg orally), and α₂-adrenoreceptor agonists such as clonidine (caudally 1–3 µg/kg; i.v. 2–3 µg/kg) and dexmedetomidine (0.15–0.3 µg/kg). These preventative strategies increase sedation and therefore should be balanced against the risk of prolonging emergence or delaying discharge from the post-anaesthesia care unit. Pain is a significant confounding factor. Propofol, ketamine, fentanyl, and preoperative analgesia were effective in reducing the risk of ED presumably by delaying emergence and reducing postoperative pain. Propofol and other adjuvants may reduce the risk but may prolong recovery. Total i.v. anaesthesia (TIVA) techniques have become popular in recent years with well-described techniques that can be adapted to most surgeries. Watching cartoons, video goggles, or hand-held video games have been shown to decrease anxiety in some patients as effectively as those who received oral midazolam as premedication. Many children with ED require no treatment other than support and prevention of harm. Approximately 95 percent of cases of ED in children resolve spontaneously within 20 minutes of onset without lasting sequelae. Although ED is a self-limited condition lasting most commonly from 5 to 15 min it can lead to several complications. Children with ED have been shown to have longer recovery periods, which is particularly undesirable in the ambulatory setting. Several prophylactic strategies have been used to prevent ED including perioperative behavioral management, perioperative analgesia, and various prophylactic adjuvant medications such as midazolam, propofol, ketamine, tramadol, and dexmedetomidine, with varying degrees of success. These drugs, however, have side effects; thus, their use should be carefully considered in the ambulatory care setting, especially since ED is a self-limited disorder [9-15].

3. Discussion

ED is an altered state of consciousness, which begins with emergence from anesthesia and continues through the early recovery period. ED is a disturbance of awareness of, or attention to, the child's environment, and manifests as disorientation, hyperactive behavior, and hypersensitivity in the immediate period after anesthesia. Particularly in the stressful pre- or postoperative period, any child may exhibit behaviours that do not reflect his usual behaviour. The child's preoperative psychological condition was also reported to affect the incidence of ED, with a higher incidence among children exhibiting preoperative anxiety as well as among those who were surrounded by parental anxiety. Emergence delirium is a problematic condition in children. Studies that reported an association between specific surgical procedures and ED (eg, tonsillectomy, urologic surgery without neuraxial analgesia, strabismus surgery) may have conflated postoperative pain-related behavior with ED. The cause for higher prevalence of ED among children may be related to brain maturation. Younger children are in general more prone to behavioral changes upon recovery from anesthesia, particularly the 2–5 age group. This may be due to the fact that they are more easily frightened and confused by unfamiliar experiences. In addition to their psychological immaturity, waking up in a strange environment can also be a factor that contributes to the higher incidence of ED among preschool children. Inhalation anesthetics, particularly desflurane and sevoflurane, were confirmed to be triggers of ED in children. Postoperative pain has been shown to cause agitation in children, and it is considered a potential confounder in all studies that investigate ED, however, during strabismus surgery pain is usually mild and easy to control. The wide range in incidence as per different studies may be due to a need for standardised measurement tools and confounding factors like pain. Some possible risk factors are age,

preoperative anxiety, shorter-acting inhalational agents, cultural differences and certain surgeries. ED is often a diagnosis of exclusion, and it is important to rule out other causes of altered mental status before ED is established. Elevated postoperative pain has been suggested to underlie ED. But given that ED is seen in patients undergoing MRI, pain cannot be the sole cause. It is worth noting that while postoperative pain is not the sole cause of ED, the degree of pain produced by a surgical procedure can change the characteristics of the observed ED and may affect the efficacy of non-analgesic adjuvants such as propofol used to treat or prevent ED.

4. Conclusion

Although we know that there are some predisposing factors to emergence delirium, we still are unable to predict accurately those who are at greatest risk. Emergence delirium should be considered as a vital sign, which should be followed and documented in every child in the postanaesthesia recovery period. Sudden emergence from anaesthesia into a disordered state of consciousness or into an unfamiliar environment has been proposed as a cause of ED. However, the incidence of ED in patients receiving propofol is markedly lower than those receiving sevoflurane, despite the similar rapid emergence profile of both agents. The challenge lies in determining how to modify the perioperative experience in order to decrease the incidence of ED. Strategies for improving outcomes range from non-pharmacological techniques, such as behaviour management and distraction techniques, to modification of the delivery of anaesthesia. While emergence delirium remains poorly understood in terms of mechanism and causes, detecting risk factors preoperatively and using evidence-based prevention methods can significantly help to reduce the incidence of ED. The most effective measure for prevention of ED is to supplant potent inhalation anesthetics, during general anesthesia with total intravenous anesthesia -TIVA. Combination of preventive medications may be more effective than individual medications alone.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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