AANA Journal Course

Current Evidence-Based Practice for Pediatric Emergence Agitation

Kristie Hoch, DNP, CRNA, RRT

This article provides a systematic review of pediatric emergence agitation, also known as emergence delirium. Major topics of this review include the incidence, risk factors, and impact of the phenomenon, in addition to current evidence-based strategies for prevention of pediatric emergence agitation. Emergence agitation causes tremendous psychological distress for the patient, family, and healthcare providers, as well as concerns for physical safety. Risk factors for pediatric emergence agitation are the child’s age, genetic profile, length and type of surgical procedure, and use of inhalational anesthesia. In an attempt to prevent this problem, anesthesia providers should consider these factors and possible interventions when implementing an anesthetic plan. Evidence-based interventions that may decrease the incidence of pediatric emergence agitation include technology, familial involvement, pharmacologic adjuncts, and alternative methods of general anesthesia.

Keywords: Delirium, pediatric anesthesia, pediatric emergence agitation.

Objectives
Upon completion of this course, the reader will be able to:
1. Describe pediatric emergence agitation (PEA) and associated features of the phenomenon.
2. Identify risk factors that contribute to cases of PEA.
3. Describe the incidence and impact of PEA.
4. Analyze the current evidence-based interventions for the prevention and management of PEA.
5. Discuss the effects of PEA on the patients’ and parents’ operative experience.

Introduction
Pediatric emergence agitation (PEA), also referred to as emergence delirium, and emergence excitation is a common occurrence following anesthesia. It is described as a state of mental confusion, agitation, hyperexcitability, crying, restlessness, and hallucinations. Pediatric emergence agitation influenced by the use of inhalational anesthetics may begin during emergence from anesthesia and last through recovery in the postanesthesia care unit (PACU). Although PEA is transient, there is the potential for psychological distress for the child, the parents, and the caregivers as well as for increased staffing requirements and costs associated with the phenomenon. Clinical ramifications suggest that the prevention and management of PEA is complex but vital for patient safety and satisfaction. Although multiple meta-analyses have evaluated the etiology and methods for prevention of PEA, there are identified gaps between current evidence and clinical practice, such as the use of preoperative distractions, various intraoperative pharmacologic adjuncts, and postoperative identification. The intent of this systematic review is to explore patient, provider, and procedural factors that contribute to the incidence of PEA and to inform anesthesia providers of current practice methods for the prevention of PEA.

Literature Review Methods
Multiple databases were used to search the literature, including the Cochrane Database, EBSCO, Cumulative Index to Nursing & Allied Health Literature (CINAHL), and PubMed. The following search terms were used: pediatric, emergence agitation, delirium, and anesthesia. Inclusion criteria were research studies on this topic published since 2012, including randomized controlled trials, meta-analyses, and systematic reviews. Three articles considered to be seminal studies were included in the review. These articles provide the definition and measurement scale frequently used in identifying and determining the occurrence of PEA. Bibliographies of research articles provided additional references for this review.

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www.aana.com/aanajournalonline AANA Journal ■ December 2019 ■ Vol. 87, No. 6 495
Causes of and Risk Factors for Pediatric Emergence Agitation
Emergence agitation was first described by Eckenhoff et al. in 1961 as a dissociated state of consciousness and excitement in patients experiencing postoperative behavioral disturbances. The causes of PEA include anxiety, stress, pain, hypoxemia, unfamiliar environment, and rapid emergence following surgery. Multiple risk factors are associated with PEA, including age, temperament, genetics, general anesthesia induction with an inhalational agent, and length and type of surgical procedure. The incidence of PEA has been correlated to be higher for preschool-aged children aged 2 to 5 years. Some authors attribute this to child behavioral development, temperament, and severe preoperative anxiety following parental separation.

Currently, there is insufficient research to thoroughly explain the link between genetic markers and the incidence of PEA. It is hypothesized from animal studies that certain genetic polymorphism regions, including interleukins 1, 6, and 10, as well as tumor necrosis factor- genes may be attributable. It is also theorized that emergence agitation is an interaction between the gene allele apolipoprotein E e4 and factors resulting from surgery and anesthesia.

Inhalational agents such as sevoflurane are used for pediatric anesthesia induction because of their low blood-gas solubility, thus allowing for rapid induction, improved anesthetic control, and quicker recovery. Based on several factors, such as decreased respiratory tract irritation and pungency, sevoflurane is considered the inhalational agent of choice for pediatric cases. However, compared with sevoflurane, desflurane has been shown to decrease the duration of PEA. The surgical procedures most often correlated with PEA have been identified as ear, nose, and throat surgery and ophthalmic procedures less than 60 minutes in duration. Table 1 shows the risk factors for PEA.

Incidence and Impact of Pediatric Emergence Agitation
Around the world, approximately 4 million children undergo general anesthesia each year, and PEA is a major problem in children as they recover. Estimates on the incidence of PEA range from 10% to 80% for children undergoing anesthesia. Although emergence agitation also occurs in adults, the prevalence in children has been reported at rates 3 to 8 times greater. This higher rate is largely attributed to the induction of anesthesia for children with volatile anesthetic gases rather than the IV medications commonly used with adults.

Usually PEA is self-limiting and occurs within the first 30 minutes of recovery, lasting up to 2 days. Despite the phenomenon of PEA being short-lived, it can lead to injury to the child, bleeding from the surgical site, parental dissatisfaction, and anxiety. Additionally, PEA can lead to physical damage, disconnection of intravenous (IV) catheters, dressing removal, and disruption of monitoring devices. Furthermore, the occurrence of PEA places a demand on staffing resources because the child will have a prolonged recovery time, will require full staff attention for his or her safety, and may require hospitalization. Restless recovery from anesthesia may cause harm to a child and delay patient discharge, all of which are distressing to the family and caregivers. The high prevalence, substantial financial burden, and major risks imposed on patients, families, and healthcare providers underscore the impact of PEA on an already overburdened healthcare system.

Prevention and Intervention
To date, there has been an inability to establish a standard of anesthesia practice for the prevention of PEA. Prevention and management of PEA is complex, as witnessed by years of research, but it remains vital for patient safety and satisfaction. Potential interventions for decreasing the incidence of PEA include familial involvement, alternative anesthetic methods, and pharmacologic interventions at various stages of perioperative care. A paradigm shift in today’s healthcare system necessitates the use of effective communication and multidisciplinary teams to meet current healthcare needs. Continuous team communication among family and caregivers may lead to successful interventions for PEA. This section outlines the perioperative phases and influence of communication among the multidisciplinary team members in the surgical arena.

• Preoperative Phase. Current evidence supports the use of technology and familial involvement. The author of this course suggests that a prompt in the electronic medical record could be used to highlight and identify those children at risk of PEA based on their age and surgical procedure (see Table 1). An alert would allow preoperative staff to discuss the concern with the anesthesia team, so possible interventions could be planned and implemented. Even before the child arrives at the hos-

Table 1. Factors Contributing to Pediatric Emergence Agitation

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
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<tbody>
<tr>
<td>Child temperament/personality</td>
<td></td>
</tr>
<tr>
<td>Preoperative anxiety: parental and child</td>
<td></td>
</tr>
<tr>
<td>Preschool age: 2-5 years of age</td>
<td></td>
</tr>
<tr>
<td>Inhalational anesthetic agents: sevoflurane and desflurane</td>
<td></td>
</tr>
<tr>
<td>Type of surgery: eye, ear, nose, and throat</td>
<td></td>
</tr>
<tr>
<td>Length of surgery: &lt; 1 h</td>
<td></td>
</tr>
<tr>
<td>Rapid emergence</td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td></td>
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Hospital the day of the operation, a discussion between the hospital staff and the child and parents, preparing them for the procedure, may help to alleviate some of the fear and anxiety of the child.\textsuperscript{19,20} Availability of online videos, brochures, and healthcare facility tours that demonstrate the perioperative process may improve patient and family expectations and recall of the shared information. Most parents state they can recall receiving information about their child’s anesthesia administration, but slightly more than half recall being given information about the risks of anesthesia and side effects.\textsuperscript{21} In a 2014 statement from the American Academy of Pediatrics, the inclusion of therapeutic play, expressive modalities, and psychological preparation can facilitate coping and adjustment for the family in an overwhelming circumstance such as surgery.\textsuperscript{20} Child life specialists also recommend the use of distractions, such as those via electronic devices, during the perioperative period for the same purposes.\textsuperscript{22}

The most commonly used preoperative medication to reduce anxiety in children is midazolam.\textsuperscript{23} The effectiveness in relation to PEA of this frequently used anxiolytic has not been definitive in the literature.\textsuperscript{4,10} Studies have revealed a strong correlation between preoperative administration of benzodiazepines and increased risk of PEA.\textsuperscript{10} A summary of commonly used pediatric preoperative medications, route, timing, and effectiveness appears in Table 2.\textsuperscript{4,6,8,10,24-30}

- **Operative Phase.** During the induction and maintenance of anesthesia, providers may influence the incidence of PEA by selecting medications known to decrease the risk. Infants and children often require an inhalational induction because obtaining preoperative IV access is forgone to limit anxiety and pain associated with IV insertion.\textsuperscript{31} Sevoflurane, the inhalational agent most commonly used for the induction and maintenance of anesthesia in younger children, is associated with the highest risk of PEA.\textsuperscript{4,8,11} Sevoflurane is commonly chosen as the inhalational anesthetic for pediatric patients based on its low pungency, low blood-gas partition coefficient, rapid onset, and rapid anesthetic recovery properties.\textsuperscript{8,52} Propofol, a short-acting hypnotic agent that interacts with the neurotransmitter γ-aminobutyric acid, is a commonly used IV anesthetic for the induction and maintenance of general anesthesia in children.\textsuperscript{33} It is widely used because of its desirable characteristics of rapid recovery and minimal postoperative side effects.\textsuperscript{34} The pharmacokinetic property of lipophilicity ensures a rapid onset of action, rapid redistribution, and quick offset of anesthetic action.\textsuperscript{35} Propofol has been shown to lower the incidence of PEA if used either for induction as a total intravenous anesthetic (TIVA) or as a maintenance anesthetic following induction with sevoflurane.\textsuperscript{4,8,14,35} In addition, a single bolus of 1 mg/kg of propofol at the end of an inhalational anesthetic has been reported to be efficacious at reducing PEA.\textsuperscript{30}

Promising results of recent research involving pharmacologic interventions for PEA evolve around the use of dexmedetomidine (Precedex). Dexmedetomidine is an α₂-adrenergic agonist that provides sedation and analgesia without substantial respiratory depression.\textsuperscript{28} Results of studies have demonstrated that dexmedetomidine given 45 minutes before induction at an effective intranasal dose of up to 1 μg/kg significantly decreases the need for fentanyl for control of postoperative pain.\textsuperscript{3,6,8,28} To date, there is no consensus defining a specific dose of dexmedetomidine for preventing PEA. Multiple studies have evaluated the use of IV dexmedetomidine for children undergoing surgical procedures. It is suggested that for tonsillectomy or adenoidectomy, the minimal IV dose range of 0.25 to 0.38 μg/kg of dexmedetomidine may be efficacious.\textsuperscript{8} Results of a meta-analysis of 12 trials comparing dexmedetomidine with placebo indicated that dexmedetomidine can be given in doses up to 1 μg/kg.\textsuperscript{6} Although dexmedetomidine is a promising agent in the prevention of PEA, it is not without limitations because it has been shown to prolong the emergence time and the time to extubation.\textsuperscript{8} Further research is indicated to validate dosing,\textsuperscript{3,6,8,28} effects on pain scores, and posthospitalization behavioral changes in children given dexmedetomidine.\textsuperscript{3,6}

<table>
<thead>
<tr>
<th>Medication</th>
<th>Route</th>
<th>Dose</th>
<th>Effectiveness</th>
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<tbody>
<tr>
<td>Midazolam</td>
<td>Oral</td>
<td>0.5 mg/kg</td>
<td>Preoperatively: Decreased anxiety</td>
</tr>
<tr>
<td></td>
<td>Intravenous</td>
<td>40 μg/kg</td>
<td>Postoperatively: Negative behaviors, eg, disorientation, excitability, and thrashing</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Intravenous</td>
<td>1-2 μg/kg</td>
<td>Prolonged emergence, time to extubation and recovery time; reduced postoperative pain; increased incidence of postoperative nausea and vomiting</td>
</tr>
<tr>
<td></td>
<td>Intranasal</td>
<td>2 μg/kg immediately after induction</td>
<td></td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>Oral</td>
<td>2.4 μg/kg</td>
<td>As effective as midazolam in anxiolysis and analgesia; decreased incidence of PEA; reduced amount of fentanyl use for postoperative pain</td>
</tr>
<tr>
<td></td>
<td>Intravenous</td>
<td>0.25-1 μg/kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intranasal</td>
<td>1 μg/kg</td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>Oral</td>
<td>0.25-6 mg/kg</td>
<td>Decreased PEA and improved postoperative pain</td>
</tr>
</tbody>
</table>

Table 2. Current Preoperative Medications for Pediatric Procedures\textsuperscript{4,6,8,10,24-30}

Abbreviation: PEA, pediatric emergence agitation.
Postoperative Phase. Up to two-thirds of children have emergence agitation upon awakening from general anesthesia. Following an anesthetic, PEA may be related to a rapid emergence, hypoxemia, or inadequate analgesia. Adverse events such as bladder distention, pain, and nausea and vomiting may also be recognized as PEA. The recognition of PEA and differentiation of it from other factors requires the collaboration of the multidisciplinary perioperative team, which is known to help solve clinical problems and improve patient outcomes. Current evidence suggests that implementing the use of a valid tool for identifying PEA may be valuable in the rapid identification and treatment of PEA in recovery. The Pediatric Emergence Delirium scale, created by Sikich and Lerman, has been validated as a reliable method of assisting healthcare providers in determining whether a child is experiencing PEA or another concern such as pain. Pain is considered to be one of the key contributors to PEA. Symptoms associated with pain, such as screaming and irritability, are difficult to distinguish from those of PEA. Concurrent use of a reliable pain scale and the Pediatric Emergence Delirium scale may decrease the error of misdiagnosing pain symptoms as PEA, but it does not guarantee clear differentiation between PEA and pain.

Identifiable confounding factors in the treatment of PEA are based on the fact that any approach to management may adversely affect satisfaction and outcomes due to unwanted side effects, such as nausea or extended sleepiness. A child may not have PEA on arrival to the PACU but because of an intervention with one of these medications may require a longer postoperative recovery time. They may ultimately stay as long as if they had not been treated. With continual improvement of the pharmacologic interventions and in the incidence and consequences of PEA, whether to require routine prophylaxis against PEA remains to be seen. Refining PEA guidelines and implementing current evidence into clinical practice are vital in allaying morbidity and mortality as well as decreasing the economic burden associated with this phenomenon.

Limitations in Identification and Management

The etiology of PEA is multifaceted; the cause may be a sole trigger or any combination of dynamic influences. The inability to establish a standard of care may be due to the individual child’s risk factors, the complexity of anesthetic pharmacologic agents, and the exact timing of an intervention. Children may be reacting to an environment they do not know, and this may cause fear, anxiety and distress. They may be in pain, which has led to their need for surgical intervention. Pinpointing the exact cause of PEA is further complicated in that each child reacts differently to each of the possible techniques for managing the situation.

A major limitation in the prevention and management of PEA lies in the economic expenditures associated with various pharmacologic interventions and anesthetic methods. In an evaluation of recovery from anesthesia, postoperative nausea and vomiting, and time to discharge from the hospital that compared inhalational anesthetics with TIVA, the costs associated with TIVA were substantially higher. Drug acquisition costs, materials, and setup costs are greater with TIVA vs inhalational agents.

Conclusion

Preschool-aged children are at the greatest risk of PEA. Two- to 5-year-olds are thought to be the most vulnerable to becoming confused and frightened by unfamiliar experiences and surroundings. The incidence of PEA is unacceptably high given the current evidence-based interventions available for possible prevention. The delivery of anesthesia has changed markedly since PEA was first identified and defined in the early 1960s, yet PEA remains a major clinical concern. Restless anesthesia recovery may cause harm to a child, require extra nursing care, and delay patient discharge, all of which are distressing to the family and caregivers. This phenomenon can place substantial healthcare costs on families, healthcare providers, and healthcare systems. Development and use of technology to develop a clinical practice guideline, identifying high-risk patients, and providing treatment protocols encompassing all phases of the perioperative period are viewed by this author as potential methods of decreasing the incidence of PEA. Further research on communication methods, pharmacologic interventions to include dosages, cost analysis, and use of a consistent postoperative PEA indemnification scale are recommended.

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AUTHOR

Kristie Hoch, DNP, CRNA, RRT, is assistant clinical professor and director of the DNP-Nurse Anesthesia program at the University of Arizona College of Nursing, Tucson, Arizona.

DISCLOSURES

The author has declared no financial relationships with any commercial entity related to the content of this article. The author did not discuss off-label use within the article. Disclosure statements are available for viewing upon request.

ACKNOWLEDGMENTS

Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.