Wild Child in the PACU: Update on Emergence Agitation

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Introduction
Though postoperative excitement has been a feature of general anesthesia since before the
development of most of our modern inhalational anesthetics, the number of studies examining
the incidence of postoperative agitation has increased exponentially since the introduction of the
poorly soluble inhalation agents sevoflurane and desflurane into routine anesthesia practice.
Eckenhoff first described the phenomenon of emergence delirium in 1961. (1) In a review of 14,436 postoperative patients he found four factors to be associated with a statistically higher incidence of emergence agitation: 1) children 3 – 9 years (13%), 2) cyclopropane or ether anesthesia, 3) tonsillectomy, and 4) barbiturate premedication. He also found that the incidence of emergence reactions was reduced in patients who had received intraoperative opioids. Though cyclopropane and ether anesthetics are no longer used, recent studies have confirmed the accuracy of many of Eckenhoff’s earlier observations as causative factors for emergence phenomena.

What is emergence agitation and why is it so important?
Emergence agitation (EA) has been defined as a state of nonpurposeful restlessness and
inconsolability that is often accompanied by thrashing, screaming, prolonged crying, and
disorientation. Often children exhibiting EA appear to be unaware of their surroundings and are
unable to be consoled by parents or other caregivers. While quite frightening for parents and
caregivers, there are often other concerns that can make either prevention or rapid control of this
behavior extremely important. Patients suffering from severe emergence reactions may harm
themselves during periods of inconsolability and thrashing as well as dislodge drains,
intravenous catheters or other medical devices essential for their care. In order to better quantify
this behavior, several scales have recently been developed to evaluate the magnitude of
emergence behavior exhibited.(2)

Etiology
No single etiology has been determined to explain this phenomenon but a number of recent
studies have examined various patient, anesthetic and surgical factors that may increase the
incidence.

Age
The highest incidence of EA has been seen in children between 2 and 5 years of age. (3,4) Aono
compared preschool children to older school age children (6 – 10 years) receiving sevoflurane
anesthesia and found a markedly increased incidence of emergence agitation in the younger age
group.(3) Przybylo using psychiatric criteria (DSM IV) for delirium found a marked increase in
altered behavior on emergence in children less than 62 months of age when compared with their older counterparts.(4)

**Preoperative anxiety**
The correlation between preoperative anxiety and postoperative agitation has been studied by a number of groups. Aono and colleagues evaluated 110 boys between 3 and 6 years of age who were to undergo circumcision under general anesthesia and divided them into an “anxious” group and a “calm” group.(5) All patients had halothane anesthesia and a caudal block. The anxious group was noted to have much more “problematic behavior” postoperatively than the calm group. More recently, Kain and colleagues at Yale University evaluated the relationship between preoperative anxiety and both postoperative emergence agitation and new maladaptive behaviors using data from several previous studies.(6) They found that higher levels of preoperative anxiety were associated with an increased risk of emergence agitation. Though this association has not been found in all studies (4,21), a recent study by Weldon and colleagues in which anxiety levels were measured preoperatively did show a strong correlation between preoperative anxiety and the severity of postoperative agitation. (7)

**Anesthetic agents**
The more insoluble agents desflurane and sevoflurane have been associated with a higher level of postoperative emergence agitation in comparison with both halothane and propofol. (7, 8-20) Multiple comparisons between sevoflurane and halothane anesthesia especially for brief anesthetics have shown a striking increase in emergence agitation.(11-17) In one study EA led to a longer PACU stay due to increased use of sedative or pain medications to control this behavior.(16) Caudal analgesia may ameliorate the duration of EA when comparing sevoflurane to halothane anesthesia (7) but the incidence is still statistically higher between these two inhalation agents.

Propofol has been shown to have a very low incidence of emergence agitation.(18-20) In one particularly compelling study, children served as their own controls when they underwent two separate eye examinations for the evaluation of retinal malignancy.(19) The children were randomized to receive either sevoflurane or propofol as the sole anesthetic for each examination. Significantly less emergence agitation was noted (0 vs. 38%) when children were anesthetized with propofol versus sevoflurane.

Until recently, most comparisons between inhalation agents were done between the more insoluble agents (desflurane and sevoflurane and halothane. Voepel Lewis and colleagues performed a prospective, cohort study of children from 3 – 7 years undergoing day surgery procedures. They found the highest incidence of emergence agitation in children receiving an inhalation induction with sevoflurane followed by anesthesia maintenance with isoflurane (p< 0.0001). (21) Three independent risk factors for emergence agitation were identified in their study: 1) short time to awakening (anesthetic agent off to eye opening), 2) isoflurane anesthesia, and 3) otolaryngologic surgery.

**Postoperative behavioral changes**
Several recent studies have further suggested a link between sevoflurane anesthesia and maladaptive postoperative behavioral changes in young children. Foesel and Reisch (22)
demonstrated a 26% incidence of such changes after a sevoflurane anesthetic versus only a 16% incidence after halothane (p = 0.015). More recently, Kain and colleagues demonstrated a correlation between marked emergence behavior and an increased risk of postoperative maladaptive behavioral changes in children who had received an anesthetic with sevoflurane.(6)

**Treatment**

A number of both prophylactic and postoperative treatments have been studied to ameliorate the disturbances caused by emergence agitation. Midazolam given as a premedication has not consistently led to a reduction in such symptoms and in one study led to an increase in emergence agitation versus placebo.(23) Cohen and colleagues found no particular advantage of either midazolam or propofol intravenously in reducing emergence agitation when a desflurane anesthetic was used for adenoidectomy.(24)

Opioids have generally been more successful in ameliorating postoperative agitation but the routine administration of morphine intraoperatively has not been shown to produce a consistent prophylactic reduction in EA.(21,24) Treatment with fentanyl (2.5 mcg/kg), however, causes a significant reduction in emergence agitation after adenoidectomy.(25) Smaller doses (1 mcg/kg) do not appear to be as effective. (25,26) However, when given 10 min before the end of an MRI scan (no surgery), fentanyl (1 mcg/kg) was shown to significantly reduce the incidence of emergence agitation after sevoflurane anesthesia.(27) Intranasal fentanyl in a dose of 2 mcg/kg has been shown to reduce the incidence of emergence reactions after bilateral myringotomy and tube placement. (28,29), though a lower dose (1 mcg/kg) appeared less effective.(29) Oxycodone given as an oral premedication was shown to reduce emergence agitation after bilateral myringotomy and tube placement when halothane was used as the primary anesthetic but not when sevoflurane was chosen.(30)

Several nonopioid agents with both sedative and analgesic properties have recently been shown to reduce EA. Intravenous clonidine and more recently dexmedetomidine have been shown to reduce the incidence of emergence agitation.(31,32) Kulka evaluated 2 mcg/kg of clonidine given IV during sevoflurane anesthesia for circumcision and found a marked reduction in EA (10% vs. 80% for placebo).(31) Ibacache and colleagues showed a significant reduction in EA when 0.3 mcg/kg of dexmedetomidine was given intravenously during lower abdominal and genital surgery.(32) This same reduction was not seen with the smaller dose of 0.15 mcg/kg. Oral ketamine (6 mg/kg) given 30 minutes before the induction of anesthesia for adenotonsillectomy led to a marked reduction in EA (18% vs. 56% for placebo, p < 0.0001).(33)

**Conclusions:**

The administration of inhaled anesthetic agents (especially sevoflurane, desflurane and isoflurane) is associated with a high incidence of emergence agitation in young children even in the absence of pain. Halothane and propofol appear to cause much less emergence agitation. Pre-emptive treatment with fentanyl, α2-adrenergic agonists (clonidine and dexmedetomidine) and ketamine appear to be effective in reducing symptoms of agitation in the postoperative period. It is unclear whether this is due to direct pharmacologic actions of these agents or whether the delay in awakening caused by the sedative actions of these drugs ameliorates postoperative excitement.
References:


**Interesting editorials on this subject:**
