

## Case Scenario: Severe Emergence Agitation after Myringotomy in a 3-yr-old Child

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**E**MERGENCE agitation (EA) in children, also called postanesthetic or postoperative delirium, agitation, or excitement in children, is a specific pediatric postoperative complication. Its reported incidence ranges from 2 to 80%.<sup>1,2</sup> This explains in part why it is usually considered as a part of the “normal” emergence process by many pediatric anesthesiologists. However, for those who episodically care for pediatric patients in the postanesthesia period (both medical and nursing staff), it may represent a significant source of anxiety and disappointment. Moreover, parents of children experiencing this complication might be terrorized by this event, and the motor agitation accompanying EA may cause harm to the child, such as loss of IV line, removal of surgical dressing, and so on.

In the current case scenario, we shall focus on the description of emergence agitation and the associated risk factors,

prevention, and treatment. We will also try to establish a relation between EA and other postoperative behavioral issues observed in children, such as postoperative maladaptive behaviors.

### Case Reports

A Caucasian 3 yr-old child weighing 15 kg was planned for bilateral myringotomy and tubes. The child was born at term and eutrophic. When he was 1 month old, he had been operated for congenital pyloric stenosis, and no perioperative complication had occurred at that time. Preanesthetic risk evaluation was performed 10 days before surgery. Discussion with parents and clinical examination of the child both failed to detect any pathologic finding. The child and his parents were given information about anesthesia and ambulatory surgery (anesthesia procedure including mask induction; postoperative pain and postoperative nausea and vomiting management; stay in the postanesthesia care unit or PACU; and discharge from the hospital, including postoperative complications such as emergence agitation and long-term behavior complications). No preoperative laboratory testing was indicated. The child was allowed to eat solids until 6 h and drink clear liquids until 2 h before the scheduled time for surgery (planned at 9:00 AM).

On the day of surgery, preoperative examination did not reveal any new findings as compared with the previous anesthetic consultation. The child was very anxious, however, and was particularly agitated and cried because of being separated from his mother.

According to our local protocol during this procedure, no premedication was given to the patient. Induction was performed with sevoflurane 6% (in a mixture of O<sub>2</sub>/N<sub>2</sub>O: 50%/50%). A peripheral venous line was inserted and 1 µg of sufentanil and 200 mg of IV paracetamol were administered before the onset of surgery. Duration of surgery was 10 min, and the child was kept spontaneously breathing with a 3%

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sevoflurane end-tidal concentration (in a mixture of O<sub>2</sub>/N<sub>2</sub>O: 50%/50%) given by a facemask. At the end of surgery, anesthesia was discontinued; inspiratory oxygen was increased to 100% and the child was transferred sedated (no reaction to verbal or tactile stimulation) to the PACU under spontaneous ventilation. Upon admission into the PACU, arterial oxygen saturation was 98% (without oxygen supplementation), heart rate 103 beats/min, and arterial blood pressure 90/45 mmHg.

Five minutes later, the child awakened from anesthesia. He was agitated, inconsolable, made no contact with caregivers, and needed some physical restraint in order to avoid self-injury. In response to the intensity of agitation, the child was given an IV bolus of 1 µg of sufentanil, which was followed by rapid cessation of the agitation. A Pediatric Anesthesia Emergence Delirium (PAED)<sup>2</sup> scale performed retrospectively was found to be 19 and decreased to 4, 30 min after sufentanil administration. According to the routine practice in our ambulatory PACU, the mother was allowed to enter the PACU and hold her child after a brief explanation of the clinical situation was given to her by the attending anesthesiologist (risk factor of EA, its treatment, and the potential association with postoperative maladaptive behaviors). Regarding the rapid satisfactory recovery of the agitation episode and its characteristics (following sevoflurane anesthesia in a preschool children with no contact with caregivers during agitation), the absence of hemodynamic or respiratory failure and the absence of pain, it was considered an emergence agitation, and no complementary laboratory (glycemia or natremia dosage) or imaging (cerebral computed tomography scan) were considered necessary. The child completely recovered 1 h later and could drink and eat without any nausea or vomiting. He did not exhibit any new episode of agitation and did not require additional analgesics or postoperative nausea and vomiting treatment. The patient left the PACU 75 min after admission with a good recovery profile (hemodynamic, respiratory, neurologic, and no pain), and could leave the hospital 70 min after the discharge from PACU (after eating without any nausea or vomiting).

The surgical consultation, performed 2 weeks later and with a phone call 3 months later, did not find any evidence of postoperative adverse behaviors (no mood or temperament changes and no bed-wetting).

## Discussion

The current case might seem very familiar for many anesthesiologists who consider this complication as part of the so-called “normal” anesthesia course. However, agitation is a possible manifestation of many situations, such as pain or hypoxemia, and physicians must therefore differentiate between these causes. In addition, considering the risks of self-injury and the psychological impact of this complication on parents, every effort must be made to prevent its occurrence.

**Table 1.** Specific Signs Associated with Emergence Agitation in Children<sup>5</sup>

Predictor	OR (95% CI)	Sensitivity	Specificity
<b>Model 1</b>			
Kick	19.3 (1–373.9)	54%*	98%*
Purposefulness movement	0.03 (0–0.3)		
Consolability	0.06 (0–0.7)		
<b>Model 2</b>			
Predictor			
Eyes reverted	73.7 (0.62–97.5)	81%*	90%*
No language	0.05 (0–316)		
Purposefulness movement	93.3 (2.75–1.585)		

\* 95% confidence intervals were not displayed in the original article.

### Is Emergence Agitation Frequent in Children?

The exact incidence of EA is difficult to establish. According to different reports, it ranges from 2 to 80%.<sup>1,2</sup> Many factors can explain this wide range. First, the incidence is known to be increased by the use of the new volatile agents, namely sevoflurane and desflurane, as shown in a recent meta-analysis.<sup>3</sup> Second, there was until recently no consensus upon the diagnostic criteria for EA,<sup>2</sup> and many authors used self-made, nonvalidated tools with different thresholds to define and score it.<sup>1,2</sup> Therefore, cases of agitation caused by other etiologies such as pain could be classified as EA.<sup>4</sup> Finally, its frequency depends on the preventive strategies used to decrease its occurrence during the perioperative period.<sup>1</sup>

### What Is the Clinical Presentation of Emergence Agitation?

The typical presentation of EA is the association of agitation together with a confusion state without recognition of the surrounding environment. It typically begins soon after emergence from anesthesia (mean 14 ± 11 min), but longer delays of onset have been reported (up to 45 min).<sup>4</sup> Patients are typically kicking and tilting, holding their head backward, agitated, inconsolable, and have no eye contact with their family members or caregivers.<sup>4,5</sup> Regarding the possible confusion with other causes of agitation such as pain or tantrum, Malarbi *et al.*<sup>5</sup> have recently tried to define some specific symptoms of EA in relation with the delirium criteria as defined in the Diagnostic and Statistical Manual of Mental Diseases (DSM-IV and V). They found eyes stared or averted and nonpurposeful movement as independent signs associated with probable cases of emergence agitation in children aged 18 months–6 yr. These authors also identified kicking, nonpurposeful movements, and inconsolability as independent predictors of EA. Table 1 summarizes some findings of this study with rates of prediction for each model. However, one of the major limitations of this study was that criteria used to diagnose of EA relied on clinical agreement between observers rather than a specific and validated diagnostic tool,

**Table 2.** Pediatric Anesthesia Emergence Delirium (PAED) Scale<sup>2</sup>**Items**

1. The child makes eye contact with caregiver
2. The child action is purposeful
3. The child is aware of his surroundings
4. The child is restless
5. The child is inconsolable

Items 1, 2, and 3 are scored: 4 = not at all, 3 = just a little, 2 = quite a bit, 1 = very much, 0 = extremely. Items 4 and 5 are scored: 0 = not at all, 1 = just a little, 2 = quite a bit, 3 = very much, 4 = extremely.

such as the PAED.<sup>2</sup> In addition, no correlation between the presence of EA and other epidemiologic characteristics of this complication such as age, type of surgery, or preventive strategies was performed.

In 2004, Sikich and Lerman<sup>2</sup> developed a specific PAED scale (table 2). The interobserver reliability was 0.84 and its internal consistency was 0.89. The sensibility and specificity analysis using the receiving operator characteristics found an area under the curve of 76.6% with a threshold of 10 or more giving a sensitivity of 64% and a specificity of 86%. Despite the great advantage of this classification and the excellent quality of the methodology used in this work, the diagnostic criterion of EA was also relying on the clinical judgment of clinicians. However, the quality of validation used in this work clearly minimizes the impact of this possible bias (correlations between the PAED scale and other epidemiologic characteristics of EA, such as age). In addition, this scale represents a major advance for comparing the preventive efficacy of strategies against this complication.

Based on these two major publications, one could describe emergence agitation as purposeless agitation with kicking, absence of eye contact with caregivers (or parents) with eyes stared or averted, inconsolability, and absence of awareness of the surroundings. The case we described was consistent with EA. It presented two characteristics of EA: inconsolability and absence of contact with caregivers. In addition, the PAED scale during agitation was quoted to 19.

**Are There Risk Factors of Emergence Agitation?**

Many factors have been identified as possible predictors of EA. However, their role in the genesis of this complication is still undetermined.

**Age of Patients**

EA occurs more frequently in preschool children. This has been shown by many studies. Aono *et al.*<sup>6</sup> have specifically investigated this factor and found EA to occur more frequently in preschool children (40% in the preschool sevoflurane group *vs.* 11.5% in the school-age sevoflurane group). This epidemiologic characteristic is considered as one of the most important predictors of this complication and has been used as a criterion for validating diagnostic scores.<sup>2</sup>

**Type of Surgery**

EA has been found to occur more frequently following ophthalmologic and ENT procedures<sup>1</sup> but also after for non-painful procedures, such as radiologic imaging.<sup>7</sup> The rapidity of these procedures and the resulting rapid emergence from anesthesia has been advocated as the underlying mechanism responsible for the high incidence of EA following those procedures. Voepel-Lewis *et al.*,<sup>4</sup> in their investigation of factors associated with EA, have found both ENT procedures and a rapid emergence from anesthesia as independent predictors of this complication. These results support the role of a rapid emergence as a potential risk factor of EA independently from the type of surgery. However, no satisfactory explanation concerning the association between ENT surgery and EA was found. Previous experience of surgery was also found to increase the incidence of EA.<sup>4</sup> However, regarding the relation between this factor and the intensity of preoperative anxiety,<sup>8</sup> one cannot exclude the role of preoperative anxiety (both in parents and child) in the genesis of EA rather than a direct long lasting effect of previous medical experience on brain functions.<sup>9</sup>

**Anesthesia-related Factors**

The increasing use of the new volatile agents (sevoflurane and desflurane) has been advocated as an explanation in the increased incidence of EA. Kuritani and Oi<sup>3</sup> have clearly demonstrated the greater incidence of EA following sevoflurane and desflurane anesthesia in comparison with halothane (odds ratio = 2.21, 95% CI [1.77–2.77]). Although rapid emergence from anesthesia was initially suspected as the underlying cause of the increased incidence of EA during sevoflurane and desflurane anesthesia, the conflicting results concerning this factor could not definitively incriminate it as a causative factor in the association between these volatile anesthetic agents and EA.<sup>4,10</sup> The second anesthesia-related factor is perioperative pain. However, EA must not be considered as a clinical manifestation of pain during recovery, because it can occur even following nonpainful procedures (imaging).<sup>7</sup> Nevertheless, regarding the efficacy of intraoperative analgesia (both opioid and nonopioid analgesia)<sup>1</sup> in preventing and treating emergence agitation, one cannot exclude the involvement of intraoperative pain in the genesis of this complication. Consequently, when facing agitation during emergence period or PACU stay, clinicians should pay attention to the specific characteristics of agitation, namely the absence of eye contact with caregivers and the absence of awareness of the surroundings.

**Psychologic Factors**

Psychologic factors are considered as important risk factors of EA. Two important issues have been investigated: preoperative child behaviors and anxiety. Voepel-Lewis *et al.*<sup>4</sup> found among 10 styles of behaviors explored (such as activity, rhythmicity, approachability, adaptability, persistence, distractibility, and sensitivity), adaptability as significantly

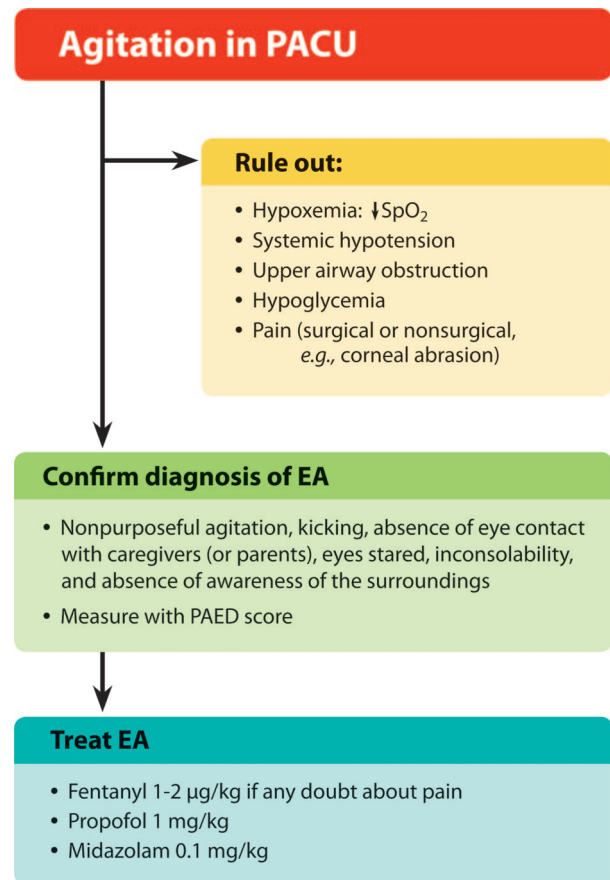
associated with EA. Although adaptability is not identified as an independent predictor by multivariate analysis, this factor might contribute to the genesis of EA, whereas a poor preoperative adaptability might trigger EA when children, especially the younger ones, are facing new anxiogenic situations such as the perioperative period. Unfortunately, there are no other studies concerning the preoperative behaviors possibly predisposing patient to EA. This challenging topic is probably one of the most promising in the elucidation of the psychological and behavioral factors associated with EA.

Because of its frequency and its intensity during the preoperative period,<sup>8,9</sup> anxiety is the second factor possibly associated with EA. Kain *et al.*<sup>8,9</sup> found a strong statistical association between the occurrence of EA and the presence of preoperative anxiety and its intensity. Predictors of preoperative anxiety in children included: younger age, parental anxiety, smaller number of siblings, poor sociability, social adaptive capability, poor quality of previous medical experience, absence of enrollment in a daycare surgery program, and low rating for activity (using the Emotionality, Activity, Sociability and Impulsivity Instrument of Child Temperament).<sup>11</sup> It is interesting to note that many of the above risk factors are similar to those associated with an increased incidence of EA. This supports the existence of a relationship between preoperative anxiety and EA.

Our patient presented most of the risk factors of EA described above: he was aged 3 yr, was scheduled for a short ENT surgery, was anxious during separation with an expected parental anxiety because of the previous surgery during infancy, and received sevoflurane as intraoperative anesthetic.

### When and How to Treat Emergence Agitation?

The diagnosis of EA is clinical. It relies on specific signs, summarized in the PAED scale, the presence of risk factors, and the elimination of other potential causes of agitation, especially pain, respiratory failure (airway obstruction: foreign body in the upper airway, bronchospasm, or laryngospasm; pulmonary edema) and hemodynamic instability (hypotension). Figure 1 highlights their diagnosis and management in case of agitation in PACU. There are no clear recommendations about the indication of pharmacologic treatment of EA. In case of intense agitation with high risk of self-injury, pharmacologic intervention seems reasonable. In case of less intense agitation without self-injury risk, caregivers must first try to reassure patients. Pharmacologic treatments become indicated when agitation continues or increases. Pharmacologic treatment of emergence agitation relies on the administration of IV sedative agents (IV midazolam 0.1 mg/kg<sup>12</sup> or propofol 0.5 or 1 mg/kg<sup>13</sup>) or opioid agents (IV fentanyl 1 or 2 mcg/kg<sup>14</sup>). However, these treatments are empirical and were extrapolated from pharmacologic preventive studies performed at the end of surgery or from personal experience. To our knowledge, there is no risk of recurrence of EA after a first episode. Consequently, EA is



**Fig. 1.** Managing agitation in children during stay in the postoperative care unit. EA = emergence agitation; PACU = postanesthesia care unit; PAED = Pediatric Anesthesia Emergence Delirium scale; SpO<sub>2</sub> = oxygen saturation measured by pulse oximetry.

not *per se* a factor of increased duration of PACU stay, but sedative or opioid agents administered postoperatively to alleviate it might prolong this stay. This is supported by the study of Voepel-Lewis *et al.*<sup>4</sup> that found EA to require pharmacologic intervention in 52% of children and significantly increased the duration of PACU stay. In addition, a recent study using midazolam at the end of surgery has shown this treatment to prevent EA but delay PACU discharge.<sup>12</sup> Of note is that optimal postoperative doses of sedative or opioid agents allowing relief of agitation without a significant impact on recovery from anesthesia and discharge from PACU remain to be determined.

Finally, the symptomatic management of agitation might not fully alleviate the underlying psychotic compound of the confusion state that might induce a long-lasting effect. Once EA is highly suspected, the presence of parents must be discussed. Some authors recommended parental presence during the active treatment of EA. However, this must be balanced with the anxiety that can be developed by parents and transmitted to their child during future contacts with medical or surgical environments.<sup>15</sup> In addition, a recent evaluation of the parental presence during PACU stay did find

neither a significant reduction in the crying during PACU stay nor a decreasing in the incidence of postoperative maladaptive behavior changes during the late postoperative period.<sup>16</sup> The case we presented was treated after assessing the absence of other complications, such as absence of hypoxia or hypotension. This was indicated because the intense agitation exhibited by the child and risks of self-injury. Regarding the low intensity of postoperative pain after myringotomy, propofol (1 mg/kg) would be a good choice. However, we usually use sufentanil as the standard treatment of EA in our institution because it allows relieving pain without impacting the duration of PACU stay.<sup>14</sup>

Interestingly, EA in children presents some similarities with postoperative delirium in adults patients, especially the most elderly<sup>17</sup>. Both are observed during the early postoperative period (with a more delayed onset for postoperative delirium), occur in specific populations (preschool children *vs.* aged patients), and both might be triggered by neurobiological effects of anesthetics. Although EA represents a specific clinical entity with a specific clinical presentation, it is necessary to rule out some early postoperative complications (fig. 1). Conversely, postoperative delirium is not a specific entity, and is considered as the neurologic manifestation of many postoperative complications (wound, deep surgical infections, or metabolic disorders) that require diagnosis and treatment.

### Basic Science: Etiology of EA

Despite its high prevalence, EA is still of unknown origin. Observing four cases of EA (three were pediatric cases), Wells *et al.*<sup>18</sup> found that these patients expressed paranoid ideation and fear from anesthesiologists and surgeons during their episodes of delirium. Interestingly, all patients did not report postoperative pain after the recovery from the confusion state. Other authors have also found emergence agitation to occur following nonpainful procedures such as pediatric imaging.<sup>7</sup> Although pain, whether related to surgery or not, can participate to the genesis of EA, it is a well known cause of postoperative agitation.

One interesting hypothesis about EA involved the difference of clearance of volatile agents from the central nervous system, leading to varying recovery rates of brain function after anesthesia.<sup>4,19</sup> The late emergence of cognitive function in comparison with other brain functions (such as audition, locomotion, and sensibility) has been hypothesized to cause the confusion state. This hypothesis is supported by the increased incidence of EA since the introduction of less soluble (and thus more rapidly eliminated) volatile agents, namely sevoflurane and desflurane.<sup>3</sup> However, the rapidity of emergence from anesthesia was inconsistently found associated with a greater incidence of EA.<sup>10</sup> Moreover, studies comparing propofol, a short-acting IV anesthetic agent, administered during the intraoperative period and sevoflurane or desflurane found a preventive effect of propofol against EA.<sup>1</sup> Thus, the specific pharmacologic properties of sevoflurane

and desflurane in the nervous system might be involved in the differential recovery of brain functions leading to EA. Finally, preventing postoperative pain either systemically (opioid and nonopioid analgesics) or regionally (caudal analgesia) has been shown to decrease the incidence of EA.<sup>1</sup>

Recent studies have emphasized the importance of changes in the connectivity of brain areas (such as thalamocortical or corticocortical connections) in the mechanisms of anesthesia. Interestingly, in a rodent model of anesthesia comparing medetomidine and isoflurane, Williams *et al.*<sup>20</sup> found these agents to produce different patterns of functional connectivity mapping with isoflurane (5% for induction followed by 2 to 3% through a nosecone) causing a more diffuse activation of brain areas than medetomidine (approval for animal use only:  $0.1 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ ). This result supports differential effects of these two anesthetics on brain connectivity, which might account in the genesis of different reactions to these anesthetics agents. The immaturity of nervous system of preschool children, in whom EA is more frequent,<sup>6</sup> might also contribute to the genesis of EA. This has been hypothesized to occur through the lack of adaptation of the younger children to the perioperative stress and anxiety perceived during this period. This also can explain the important role of this factor in the etiology of EA. This hypothesis is also supported by recent studies using functional imaging comparing the pattern of activation of brain regions involved in the cognitive control between children and adults.<sup>21</sup> In their experiments, Rubia *et al.*<sup>21</sup> tested three situations with one exploring a cognitive function. They found this test to activate predominantly the left hemispheric network of prefrontal cortex, insula, anterior cingulate gyrus, and temporal lobes in adult patients, whereas the same test in adolescents induced right hemispheric brain region activation, including temporal and parietal lobes. These results clearly support the involvement of different neuronal networks between adults and pediatric patients for a same activity, and might address some specific complications regarding EA.

### Prevention of Emergence Agitation

Regarding the potential negative issues of EA on patients (confusion state, traumatic injuries), parents, and caregivers, treatment of EA should be ideally preventive. Many strategies have been proposed in order to decrease the occurrence of this complication. They can be classified as pharmacologic and nonpharmacologic.

**Pharmacologic Prevention of EA.** A recent meta analysis has reviewed the pharmacologic preventive strategies against EA.<sup>1</sup> Interestingly, many sedative and analgesic agents given either systemically or by regional route were found efficient in the prevention of EA (table 3). In addition, their side effects and impact on PACU stay and postoperative recovery are well characterized. These preventive treatments included: propofol given at the end of surgery; intraoperative fentanyl; and ketamine, clonidine, dexmedetomidine, and hydroxyzine-

**Table 3.** Pharmacologic Prevention of Emergence Agitation (EA) in Children<sup>1</sup>

Agent	Route and Timing of Administration	Efficacy	Doses	Onset Time	Adverse Effects	Postoperative Effects
Midazolam	OR, IV, IR	No	OR: 0.5 mg/kg	OR: 20–45 min	No adverse effects	Possible delayed recovery and PACU discharge
	Preoperative	—	IV: 0.1 mg/kg	IV: 15 min	—	—
	—	—	IR: 0.5 mg/kg	IR: 30 min	—	—
Midazolam	IV, end of surgery	Yes	IV: 0.1 mg/kg	—	No	Delayed recovery and PACU discharge
Hydroxyzine combined to midazolam	OR, preoperative	Yes	1 mg/kg	60 min	No adverse effects	No delayed recovery or discharge from PACU
Propofol	Continuous intraoperative	Yes	Induction 2–3 mg/kg Maintenance: 3–12 mg · kg <sup>-1</sup> · h <sup>-1</sup>	—	No	No prolonged PACU stay in comparison with desflurane or sevoflurane anesthesia
Propofol	End of surgery	Yes	1 mg/kg	—	No	No prolonged duration of PACU stay
Ketamine	IV, preoperative	Yes	0.25 mg/kg	10 min	No	No prolonged duration of PACU stay
	IV, end of surgery	Yes	0.25 mg/kg	—	No	—
α 2 Adrenoceptors	OR, preoperative	Yes	6 mg/kg	30 min	No	—
Clonidine	OR or IR, preoperative	Yes	or 4 μg/kg	45 min	Decrease of arterial pressure and heart rate	No prolonged duration of PACU stay; prolonged postoperative sedation
α 2 Adrenoceptors	IV after induction	Yes	2, 3, or 4 μg/kg	—	Decrease of arterial pressure and heart rate (intraoperative and PACU)	Delayed recovery and PACU discharge; prolonged postoperative sedation
Clonidine	CAU	Yes	3 μg/kg	Intraoperative	Decrease of arterial pressure; no effect on heart rate (intraoperative and PACU)	No prolonged PACU stay
α 2 Adrenoceptors: Dexmedetomidine	IV, preoperative	Yes	0.2 μg/kg	10 min	Decrease of arterial pressure and heart rate	No delayed recovery or discharge from PACU
α 2 Adrenoceptors: Dexmedetomidine	IV, intraoperative	Yes	0.3 μg/kg	After induction	Decrease of arterial pressure and heart rate	No delayed recovery. No delayed discharge from PACU
α 2 Adrenoceptors: Dexmedetomidine	IV, intraoperative	Yes	1 μg/kg	After induction	Decrease of arterial pressure and heart rate	Delayed recovery.
α 2 Adrenoceptors: Dexmedetomidine	IV, intraoperative	Yes	0.5 μg/kg	5 min before the end of surgery	Decrease of arterial pressure and heart rate	No delayed from PACU
α 2 Adrenoceptors: Dexmedetomidine	CAU	Yes	1 μg/kg	Intraoperative	Decrease of arterial pressure and heart rate (intraoperative and PACU)	Delayed recovery
Fentanyl	IV, intraoperative	Yes	2.5 μg/kg 1 μg/kg	After induction 10 min before the end of anesthesia	Increased PONV	Sedation in PACU
Transcutaneous fentanyl	Preoperative	Yes	10–15 μg/kg 100 μg	30 min	Loss of spontaneous ventilation, increased incidence of PONV	No prolonged stay in PACU
Intranasal fentanyl	Intraoperative after induction	Yes	2 μg/kg	—	No effect	Postoperative respiratory depression and delayed discharge
Nalbuphine	IV, end of surgery	Yes	0.1 mg/kg	—	No adverse effects	No delayed discharge from PACU
Intraoperative nonopioids analgesia: Ketorolac	IV, during surgery	Yes	1 mg/kg	—	No adverse effects	No prolonged stay in PACU
Caudal Analgesia	After induction	Yes	1 ml/kg Bupivacaine (0.25%)	—	No hemodynamic effects Urinary retention	No prolonged stay in PACU

CAU = caudal; IR = intrarectal; OR = oral; PACU = postanesthesia care unit; PONV = postoperative nausea and vomiting.

midazolam association<sup>22</sup> (table 3). However, propofol given as an induction bolus or premedication with midazolam were not found efficient in decreasing EA occurrence.<sup>1</sup> This is

probably related to their short elimination half-life, which makes their blood and effect site concentration below its therapeutic effect at recovery from anesthesia. Moreover,

premedication with clonidine and melatonin have been found to decrease the incidence of EA, when compared with midazolam.<sup>23,24</sup> Given the role of anxiety in the occurrence of EA,<sup>9</sup> the lack of efficacy of midazolam in the prevention of EA seems paradoxical. An interesting study performed by Kain *et al.*<sup>25</sup> investigated patients not responding to midazolam premedication. They found that nonresponders exhibited a higher level of preoperative anxiety, were younger, and were more emotive than responders. Interestingly, these characteristics are similar to those associated with EA. Finley *et al.*<sup>26</sup> also found that a high level of impulsivity was associated with adverse reactions during induction of anesthesia, making midazolam inefficient or even more unsuitable for children. Altogether, these findings suggest that in addition to the rapid pharmacokinetics of midazolam, a high level of anxiety and a greater immaturity and emotivity are involved in the inconstant efficacy of midazolam in preventing preoperative anxiety and therefore EA.

Pharmacologic methods to prevent EA can be easily applied without a great impact on the duration emergence from anesthesia (table 3). By contrast, the postoperative treatment of this complication with sedative agents such as opioids, midazolam, propofol, or fentanyl has been shown to increase the duration of PACU stay. This highlights the financial impact of this complication in addition to its traumatic and psychologic side effects.

**Nonpharmacologic Prevention of Emergence Agitation.** Most nonpharmacologic prevention strategies against EA rely on decreasing preoperative anxiety. An important amount of work is now available on the preoperative predictors of anxiety in children and its prevention. Many strategies have been successfully found to decrease children's and parents' anxiety: a quiet induction with decreased sensory stimuli, music therapy, distraction and hypnosis, clown doctors, acupuncture, informational films before induction, and information for parents.<sup>27</sup> Parental presence during induction of anesthesia has been thought to decrease children anxiety. However, this factor has been found inconsistently efficient in reducing children anxiety.<sup>16,28,29</sup> Parents' anxiety transmitted to the child is the main cause of the inefficacy of parental presence during induction in alleviating anxiety.<sup>30</sup> Consequently, rather than preparing parents and children separately, Kain *et al.* evaluated a family-based preparation named the ADVANCE strategy.<sup>31</sup> This consists of information to parents about the methods to decrease their child's anxiety and the distraction of children by their parents in the holding area and during induction of anesthesia. This preparation has been found to decrease both preoperative anxiety and postoperative emergence agitation. Moreover, this strategy has been found more effective on EA prevention than premedication with midazolam.<sup>31</sup> However, considering the time- and cost-consuming effect of the ADVANCE strategy, Fortier *et al.* investigated the most accurate compounds of this strategy in decreasing preoperative anxiety. Their study revealed that practicing mask induction at home and parental

use of distraction in the preoperative holding area were most efficient in relieving preoperative anxiety in children.<sup>32</sup>

Concerning the case presented, we did not administer a premedication before this short procedure fearing that it might delay recovery from anesthesia and discharge from PACU. However, we usually prevent EA and postoperative pain by either systemic opioids (such as sufentanil in our case) or regional analgesia (caudal or regional analgesia for abdominal or urological procedures). Regarding the preoperative preparation, all parents and children receive detailed information about anesthesia. However, regarding the conflicting results concerning the efficacy of parental presence during induction of anesthesia in decreasing both preoperative anxiety and postoperative EA, we do not use this technique in our institution.

### ***Is There a Relationship between EA and Other Postoperative Behavioral Complications?***

Children have been shown to develop behavioral complications during the late postoperative period, named the postoperative maladaptive behavioral changes.<sup>33</sup> These can manifest as sleep disturbances, bedwetting, temper tantrums, attention seeking, and fear of being alone.<sup>33</sup> Risk factors for developing these manifestations include: a younger age, a lower birth order, an inhibited temperament, the presence of preoperative anxiety (in parents and children), the noninclusion in a daycare surgery program, a sevoflurane-based anesthesia, and the presence of postoperative pain and emergence agitation.<sup>34</sup> Prevention of this complication has been shown to be achieved using preoperative premedication with midazolam and family-centered preparation.<sup>31</sup> Regarding the similarities between risk factors and preventive strategies against EA and postoperative maladaptive behavioral changes, one cannot exclude the possibility that both events can be linked. However, at this time, no study can clearly support this hypothesis, and parents should probably be warned of the increased probability of this late postoperative complication.

### ***Knowledge Gap***

Emergence agitation is a common early postoperative complication after pediatric anesthesia. Regarding the possible injury to the patients and anxiety to parents and caregivers, it deserves active preventive and/or curative treatments. However, many issues concerning EA have to be elucidated. First, the etiologies of this complication remain unknown, although intrinsic pharmacologic properties of sevoflurane and desflurane are very likely to be involved in its genesis. Regarding the recent development of functional imaging, one can expect that these tools will help in elucidating the mechanism of EA. Second, the optimal treatment of EA has to be precisely determined, especially its effects on the quality and speed of discharge from PACU. Finally, the long-lasting effect of EA and the hypothetical causative relation between this complication and postoperative behaviors changes in children have to be more precisely investigated.

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