STRATEGY FOR PREDICTION AND PREVENTION OF EMERGENT DELIRIUM IN CHILDREN

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https://doi.org/10.5281/zenodo.10884825

Abstract. *Emergent excitement is a common and clinically significant postoperative complication in pediatric patients, occurring early in the postanesthesia period. The incidence of agitation varies from 0.25% to 90.5% (Lee and Sung, 2020).*

Post-anesthesia agitation may have clinically significant consequences, such as injury to the patient or his or her healthcare team, suture dehiscence or bleeding from surgical wound sites, unknowing removal of drains or intravenous catheters, inadvertent extubation and complications patient care and predisposes parents or caregivers to anxiety and additional stress. In addition, this complication increases the time of awakening and lengthens the length of stay in the post-anesthesia care unit.

Thus, there is a need for early recognition, timely prediction, and early prevention of postanesthesia delirium to avoid serious injury and disruption due to escalating behavior.

Keywords: *emergence excitement, sevoflurane anesthesia, children, anesthesia exposure, depth of anesthesia, emergence delirium.*

Introduction

Emergent delirium (ED), (post-anesthesia delirium) is an acute state of confusion during recovery from anesthesia. Patients with ED may experience confusion, agitation, hallucinations, restlessness and aimless hyperactive behavior, inappropriate movements, inconsolability, thrashing and incoherence during early recovery from general anesthesia [1].

The clinical consequences of ED are equally varied. It is usually short-lived and resolves spontaneously, with minimal clinical consequences. But clinically significant consequences may also occur, such as injury to the injured patient or his medical staff, falling from the bed, dehiscence or bleeding at surgical wound sites, unknowingly pulling out drains or intravenous catheters, unintentional extubation or dislodgement of the endotracheal tube. This leads to serious secondary complications such as respiratory depression or airway spasm, longer stays in the PACU, delayed discharge and increased costs of medical care [1,2].

The etiology of ED is multifactorial. It is important to identify the causes and risk factors of EV and modify them when applicable to reduce the incidence and prevent adverse consequences.

The mechanism of ED remains unclear. Proposed risk factors for EV include age, male gender, emergency type of surgery, use of inhalational anesthetics with low gas/blood partition coefficients (e.g., sevoflurane and desflurane), prolonged operative duration, anticholinergics, benzodiazepine premedication, postoperative pain, and the presence of invasive devices [1] ,3].

Purpose of the work: to analyze scientific publications on methods of predicting and preventing emergent delirium in pediatric clinical practice.

Materials and methods

When searching for publications on emergent agitation in children, the following keywords were used: emergence agitation, emergent delirium, childhood. A comparative analysis of 87 publications was performed, including the results of original and review articles, of which the most informative were 37 works that formed the basis of our review. Exclusion criteria included unreliable evidence without prospective registration and sample size justification. Search queries were carried out in databases/scientific electronic libraries eLibrary.ru (RISC), PubMed (MEDLINE), Cohrane, Clinicaltrials.gov, Google Scholar and Science Direct for the period from 2022 to February 2024. Despite the extensive literature search, the level of evidence to date remains limited due to the lack of randomized controlled trials. The pharmacological approach varies widely, there are no standard protocols, and the level of evidence is low.

Discussion

According to Seok-Jin Lee and Tae Yoon Song, suspected causes of ED in children may include a new environment, separation from parents, and meeting unfamiliar medical personnel. This may lead to an increase in sympathetic tone in the preoperative period and a prolongation of the arousal state during recovery from anesthesia [4].

Potential risk factors for ED in children are: preschool age (2-5 years), no previous operations or hospitalizations, a large number of previous interventions, poor adaptability, attention deficit hyperactivity disorder, psychological immaturity, preoperative anxiety, parental anxiety, poor patient communication and parents with medical professionals, lack of premedication (midazolam), paradoxical reaction to midazolam, excessively rapid awakening and pain [5,6,7,8,9,10].

ED is more common in children than in adults. In a study of children aged 2-12 years, the incidence of EB was inversely proportional to age [12,13,14].

Suggested risk factors for developing ED in adults include age, sex, obesity (body mass index ≥ 30 kg/m2), number of intubation attempts, type of surgery, emergency surgery, method of anesthesia (inhalational anesthesia), duration of surgery or anesthesia, pre-existing problems with mental health (eg, psychiatric problems or cognitive impairment), chronic pulmonary disease, substance abuse, anticholinergic drugs, doxapram, benzodiazepine premedication, urinary urgency, postoperative pain, postoperative nausea and vomiting, and the presence of invasive devices (eg, urinary catheter , chest tube or tracheal tube).

In a prospective cohort study by Vaupel-Lewis Terry (2003), which involved 521 children aged 3-7 years, it was found that 96 children (18%) of the total number of those studied had manifestations of post-anesthesia agitation (emergent delirium) in the postoperative period. The agitation lasted in some cases up to 45 minutes (range 3–45 minutes; mean 14 ± 11 minutes), which required drug relief in 52% of children and caused a long stay in the recovery room and intensive care unit (117 ± 66 minutes vs. 101 ± 61 min for non-arousal children; P = 0.02). ED was found to be associated with ten factors, including age, previous surgery, adaptation, ophthalmological and otorhinolaryngological procedures, sevoflurane, isoflurane, sevoflurane/isoflurane, analgesics and time to awakening [8].

Similarly, several studies of strabismus surgery and tonsillectomy have identified risk factors for ED in pediatric patients [15].

Thus, conflicting results have been reported depending on whether elective or emergency surgery was performed. The 2006 work of S. Lepuse and her co-authors described the effect of the urgency of surgical intervention on the incidence of ED development [16]. The suggestion that emergency surgery increases the risk of postoperative delirium compared with elective surgery is also evident in the results of a study by Ramroop and colleagues (2019). In which 417 patients took part. The authors believe that increased anxiety and uncorrected comorbidities may have contributed to the increased incidence of ED in patients undergoing emergency surgery [17].

The Riker Sedation Agitation Scale or the Richmond Sedation Agitation Scale is used to assess agitation-sedation and aggression in adults (Table 1).

Table 1 Richmond RASS (excitement-sedation) scale

Points	Terminology	Description
+4	Aggressive	The patient is aggressive, belligerent, and poses an immediate danger to medical personnel
+3	Extremely agitated	Pulls or removes tubes and catheters or exhibits aggressive behavior toward medical personnel
+2	Agitated	Frequent non-purposeful movements and/or desynchronization with the ventilator
+1	Restless	Excited, but movements are not vigorous or aggressive
0	Conscious and calm	Awake, calm, alert
-1	Drowsy	Loss of attention, but does not close eyes for more than 10 seconds during verbal contact
-2	Light sedation	Closes eyes during verbal contact in less than 10 seconds
-3	Moderate sedation	Any movement (other than eye contact) in response to voice
-4	Deep sedation	No response to voice, but some movement to physical stimulation
-5	No arousal	No response to voice or physical stimulation

Interpretation of the RASS (Richmond Excitation-Sedation Scale) score.

1. If he is awake, calm and attentive? — 0 points.

2. If eye contact is possible with the patient and is maintained for more than 10 seconds after verbal contact - 1 point.

3. If eye contact is possible with the patient, but this is not maintained within 10 seconds after verbal contact - 2 points.

4. If the patient makes any movement in response to the voice, with the exception of eye contact - 3 points.

5. The patient does not respond to the voice, but responds with any movements to physical stimulation - 4 points.

6. If the patient does not respond to voice or physical stimulation - 5 points.

In patients with a RASS score of -3 or less, sedation should be reduced or changed until a RASS score of -2 to 0 is achieved.

Patients with a RASS score of 2 or more are insufficiently sedated and need to establish the cause of agitation (anxiety disorder, delirium, pain) and deepen the sedation to achieve a score of -2 to 0 on the RASS scale.

If possible, excessive levels of sedation (less than -2 RASS) should be avoided unless indicated.

The pediatric behavioral pain scale (FLACC) can be used to assess the severity of EV in young children (Table 2).

Table 2. FLACC (Face, Legs, Activity, Cry, Consolability.)

Parameters	Characteristics	Points
Face	Vague expression or smile.	0
	Rarely - a grimace or knitted eyebrows. Closedness. Shows no interest.	1
	Frequent or constant trembling of the chin. Clenching of the jaws.	2
Legs	Normal position, relaxed.	0
	He cannot find a normal position and constantly moves his legs. Legs are tense.	1
	Kicking or lifting legs.	2
Motion	He lies calmly, his position is normal, he moves easily.	0
	Writhing, shifting back and forth, tense.	1
	Arches; rigidity; twitching.	2
Cry	No crying (wakeful or asleep)	0
	Moans or whines; complains from time to time.	1
	Cries, screams or sobs for a long time; complains often.	2
How reassuring is it	Satisfied, calm	0
	Calms down from touching, hugging, talking. You can be distracted.	1
	t's hard to calm down.	2
Overall point:		

This behavioral scale is used for children under 3 years of age. It takes into account the child's facial expression, the position or movement of the legs, the nature of the cry and how amenable the child is to calming. Pain is rated on a ten-point scale. The higher the score, the stronger the pain, and the more often repeated sedation is required, which delays the transfer of the child from the recovery room.

The severity of postanesthesia delirium in children can be assessed using the Pediatric Anesthesia Emergent Delirium (PAED) scale (Table 3).

Table 3 PEAD scale (Pediatric Anesthesia Emergence Delirium Scale)

Point	Description	Not at all	A little	A little more	A lot	Completely
1	The child makes eye contact with the observer	4	3	2	1	0
2	The child has purposeful actions.	4	3	2	1	0
3	The child understands his/her environment	4	3	2	1	0
4	The child is restless	0	1	2	3	4
5	The child is crying and rushing about	0	1	2	3	4

1 - calm

2 - not calm, but calms down easily

3 - moderately agitated or restless

4 - excited and restless.

The PAED scale is assessed immediately upon awakening and every 10 minutes thereafter until transfer from the recovery room. The total score of the scale is from 0 to 20 points. Patients are transferred to the ward after they regain full consciousness with stable vital signs, PAED score <10.

According to a number of studies, the development of post-anesthesia deliria may be associated with the use of inhaled anesthetics. Halothane, isoflurane, desflurane and sevoflurane can serve as triggers for ED. Volatile substances cause ED almost four times more often than intravenous anesthetics, in particular sevoflurane. This conclusion was reached by Zhang Y., Zhang Q. et al. Their prospective observational study of approximately 2000 patients aged 4–12 years reported that volatile anesthetics were associated with a higher incidence of EV [21].

The opinion that the appearance of volatile substances with low solubility in the blood, such as sevoflurane and desflurane, has led to an increase in the incidence of ED in children is also shared by Seok-Jin Lee and Marco Ronzani [4,22]. A proposed explanation for this is that sevoflurane and desflurane cause different rates of recovery of brain function due to differences in the clearance of inhaled anesthetics from the central nervous system [22]. In addition, increased concentrations of lactate and glucose in the parietal cortex due to sevoflurane anesthesia and the occurrence of clinically undetectable sevoflurane-induced epileptogenic activity have been proposed to cause ED [23, 24, 25].

Functional magnetic resonance imaging has been used to study the mechanisms underlying changes in consciousness during anesthesia. Research has shown that changes in brain network connections depend on the level of sedation. During recovery from general anesthesia, thalamocortical connections in sensory networks and the activated reticular formation of the midbrain are preserved. However, delayed recovery of impaired functionality of subcortical thalamoregulatory systems may contribute to defects in cortical integration of information, which can lead to confusion or agitation [26, 27].

However, only a few randomized controlled trials have been conducted to evaluate the effects of neuromuscular blocking agents on ED. In a prospective randomized controlled trial, Seok-Jin Lee and Tae-Yun Song compared the occurrence of agitation with succinylcholine and rocuronium-sugammadex in adult patients (n = 42) undergoing closed reduction of nasal fractures [28]. The authors suggested that increased lactate and potassium concentrations, incomplete neuromuscular blockade during surgery, increased intraocular pressure, and histamine release due to succinylcholine administration may have resulted in more negative effects on ED compared with those caused by rocuronium administration. -sugammadexa. Studies comparing the effects of sugammadex and cholinesterase inhibitors on ED have shown conflicting results. In a retrospective study of children undergoing strabismus surgery, sugammadex showed no effect in preventing ED compared with pyridostigmine + glycopyrrolate [29]. In contrast, a prospective randomized controlled trial of children undergoing adenotonsillectomy found that sugammadex reduced the severity of ED and resulted in a reduction in EB compared with neostigmine + atropine [30].

Propofol, μ-opioid agonists, N-methyl-D-aspartate receptor antagonists, α2-adrenergic agonists, regional analgesia, multimodal analgesia, parental induction, and preoperative surgical education may help prevent EV.

In order to prevent the occurrence of delirium in children, Gonçalves Gerard and colleagues used midazalam (2018). In their prospective, randomized, double-blind study, they compared the effect of midazolam 0.03 mg/kg given during induction with the same dose given 10 minutes before the end of surgery for the prevention of ED in children undergoing sevoflurane anesthesia. Eighty children were included in the study and randomized into two groups of forty people each. The average age of the children participating in the study was 4.9 years (2-8 years). The study found that the incidence of ED after sevoflurane anesthesia in children is 0–80%. Higher concentrations of sevoflurane have been reported to potentiate and lower concentrations to inhibit gamma-aminobutyric acid (GABA) receptor-mediated effects. The authors concluded that the incidence of ED in their study decreased with midazolam in both groups. But midazolam administered at the end of surgery resulted in a delay in the children's awakening and transfer from the postanesthesia care unit [31]. Similar studies with similar results were shown by J.H. Bae, et al. [32], H.J. Byon et al. [33], and J. Chen et al. [34].

On the contrary, D. Costi et al. [35] concluded in their Cochrane meta-analysis that midazolam administered orally or parenterally or as premedication did not prevent ED. Similarly, S. Dahmani and colleagues [36] also found in their meta-analysis that midazolam administered at the beginning of surgery did not play a role in the prevention of ED.

Conclusion. Despite significant interest in the issue of emergent agitation in the pediatric anesthesiology community, the evidence available regarding the efficacy and safety profile is mixed. The insufficient number of randomized controlled trials requires future prospective studies in this direction.

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