



Postoperative Maladaptive Behavior, Preoperative Anxiety and Emergence Delirium in Children Undergone General Anesthesia: A Narrative Review

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Abstract

Over the years, the number of pediatric patients undergoing surgeries are increasing steadily. The types of surgery vary between elective to emergency with involvement of multidisciplinary teams. The development of day care surgery unit is expanding where the patients will only come to the hospital on the day of surgery and discharge home after such as satisfactory parameters achieved, minimal to no pain, minimal to no bleeding from surgical site and able to tolerate fluids. Hospitalization and surgery could contribute to significant psychological disturbance to the children. These issues are not being addressed as children have difficulty in conveying their problems and fear. They do however express it through negative behavioral changes.

Keywords

pediatric, general anesthesia, postoperative maladaptive behavior

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What we already know about this topic?

The high incidence of postoperative maladaptive behavior in children.

How does your research contribute to the field?

Assisting clinicians on how to recognize the risk factors and identify high risk children using validated scoring systems.

What are your research's implications toward theory, practice, and policy?

Our article provides various management strategies and also simplified tables of commonly used agents and the doses to overcome the unwanted events.

Introduction

Given the potential negative effects of preoperative anxiety particularly to the children, clinicians, and researchers attempted various interventions to prevent the occurrence. These included pharmacological, non-pharmacological,

behavioral, and psychological interventions. Besides, learning about the planned procedure and exposure to the operation theater environment allow children and parents to cognitively cope with the uncertainty of the surgical and anesthesia experience. On the other hand, emergence delirium which is an acute postoperative behavioral change is another entity that is mutually fundamental in pediatric anesthesia. Despite of its high prevalence, preoperative anxiety and emergence delirium remain as understudied topics.

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This review was written comprehensively covering the 3 essential topics namely, postoperative maladaptive behaviors, preoperative anxiety, and emergence delirium. We hoped that clinicians mainly anesthesia residents will gain substantial benefits by identifying the risk factors, applying assessment methods discussed and implementing the holistic interventions comprising pharmacological and non-pharmacological techniques via simplified tables provided. We believed that the 3 components are related and could give rise to one and another. Nonetheless, till date there is still no RCT conducted to prove the hypothesis.

Postoperative Maladaptive Behavior

Children may manifest negative behavioral changes as a result of hospitalization and anesthesia. This can lead to significant psychological impact. Several studies indicated that negative behavioral changes may persist up to 2 weeks postoperatively in 60% of the children, which are characterized by new onset enuresis, disturbed sleep, apathy and withdrawal, and feeding problems.¹⁻³

Robyn et al identified a number of contributing factors in their study. These include parental anxiety, younger age, overnight admission, lower birth order, and preparation via having a discussion with the anesthesiologists.⁴ The results of the study showed that, at day 3 postoperatively, 24% (95% CI: 21.0-26.4) of children had negative behavioral changes, whereas at day 30, the number decreased to 16% (95% CI: 13.3-18.2). This study involved children between 3 and 12 years old, with a total of 1027 subjects.

Assessment

The Post Hospitalization Behavior Questionnaire (PHBQ) (Table 1) was developed by Vernon, Schulman, and Foley in 1966. The questionnaire was subsequently used as a quantifiable assessment tool to identify children's behavioral changes post hospitalization and postoperatively.^{5,6}

It comprises of 27 parent-reported items and is currently considered as a standard tool to assess behavioral changes in children from age 1 month to 16 years undergoing surgical procedures. Parents are instructed to compare the preoperative and postoperative behavior changes noticed in their children on a scale of 1 to 5, with 1=much less than before, 2=less than before, 3=same as before, 4=more than before, and 5=much more than before. The scores range from 27 to 135. The parents answered "not applicable" if the questions

asked were irrelevant to their children's condition. The child was considered to have significant behavioral changes if there was deterioration in 7 or more items.⁵

Risk Factors

The identified risk factors include younger age group, longer hospital stay, previous unpleasant anesthetic experience, and parental level of anxiety. The association between premedication and negative behavioral changes was conflicting. The same was true for the association of pain and the development of negative behavioral changes. However, several studies indicated that there was a demonstrable association between postoperative behavioral changes and the child's anxiety during induction of anesthesia.^{2,7}

The relation between anesthetic preparation and the development of negative behavioral changes varies according to a number of studies. For smaller children between the ages of 2 and 4 years, a preoperative teaching book was found to be beneficial, while another study proved that hypnosis also worked for the same age group of patients.⁸

Preoperative Anxiety

Anxiety, as according to cognitive theories of anxiety, happens when one is overestimating the danger while underestimating the coping abilities. Preoperative anxiety, whether it involves the children or the parents, could contribute significantly to the postoperative negative behavioral changes.

The specific character of a child, in particularly being shy or having high intelligence with poor adaptation to the new environment, further increases the risk. Identified variables include, age, temperament, prior hospital experience and parents' coping skills.^{9,10}

Anxiety and fear of surgery activate a human stress response similar to the other factors such as infection, pain, and cold. An increase in the circulating glucocorticoids caused by the activation of the hypothalamic-pituitary-adrenal axis enhances the susceptibility to infection, delays wound healing, and hence disrupts the overall recovery of children. The obligatory glucose requirements, larger brain tissues and restricted energy reserves make the children vulnerable to the surgical stress response.¹¹

Separation anxiety is synonymous with infants and toddlers and becomes more significant when the children are older than 1 year old. However, it declines as children grow older. At the age of 3 months, infants are able to distinguish between familiar and unfamiliar faces and

Table I. Post Hospitalization Behavior Questionnaire (PHBQ).

		PHBQ
I	4	Does your child need a pacifier?
	5	Does your child seem to be afraid of leaving the house with you?
	6	Is your child uninterested in what goes on around him/her?
	8	Does your child bite his/her finger nails?
	12	Does your child seem to avoid or be afraid of new things?
	13	Does your child have difficulty making up his/her mind?
	21	Is your child irregular in his/her bowel movements?
II	27	Does your child suck his/her fingers or thumbs?
	9	Does your child get upset when you leave him/her alone?
	16	Does your child seem to get upset when someone mentions doctors/hospitals?
	17	Does your child follow you everywhere around the house?
III	18	Does your child spend time trying to get or hold your attention?
	20	Does your child have bad dreams at night or wake up and cry?
	1	Does your child make a fuss about going to bed at night?
	19	Is your child afraid of the dark?
IV	22	Does your child have trouble getting to sleep at night?
	3	Does your child spend time just sitting or lying and doing nothing?
	2	Does your child make a fuss about eating?
V	24	Does your child has a poor appetite?
	25	Does your child tend to disobey you?
VI.	14	Does your child has a temper tantrums?
	7	Does your child wet the bed at night?
	11	Is it difficult to get your child interested in doing things (playing games, toys)
	23	Does your child seem to be shy or afraid around strangers?
	26	Does your child break toys or other objects?
	10	Does your child need a lot of help?
	15	Is it difficult to talk to your child?

respond accordingly, but separation anxiety does not start until approximately 7 to 8 months of age.^{12,13}

Assessment

The gold standard for assessing anxiety in children is the State-Trait Anxiety Inventory for Children (STAIC), which normally takes approximately 5 to 10 minutes to be completed. It is suitable to for use by children older than 5 years of age. However, with busy, rapid turnover operation theaters, it may not be feasible for routine use. Recognizing several limitations of the STAIC, a team of anesthesiologists from Yale School of Medicine came up with the modified Yale Preoperative Anxiety Scale (m-YPAS) (Table 2).^{14,15} In their study, they modified an anxiety assessment tool so that it was more reliable and friendly for use with the operation theater's staff and hectic environment. This is an observational tool rather than a self-report questionnaire, such as the STAIC, and consists of 5 domains of anxiety. Thus, it can be used for children of all ages.^{14,15}

Strategies

Behavioral modalities. The preparation modalities for children undergoing surgery are essential to minimize the unwanted consequences. When looking back into the data and psychological analysis, the introduction of the anesthetic mask and the fear of venipuncture possess the greatest risk of escalation of anxiety.¹⁶ In fact, the children who are unable to be consoled due to extreme anxiety may need to be physically restrained in order to proceed with the surgery.

A psychological preparation programmed should be conducted to suit the need of both parents and their children. To ensure that it benefits them optimally, it must be tailored to the individual's needs and age group. For instance, children more than 6 years old would benefit the most if they were exposed to the programmed 5 days earlier than the date of surgery. On the other hand, it would become less advantageous if the children were exposed only 1 day earlier than the date of surgery. It is believed that this is due to the way that preschool age

Table 2. Modified Yale Preoperative Anxiety Scale (m-YPAS).

Domain: activity	
1	Looking around, curious, playing with toys, reading (or other age-appropriate behavior); moves around holding area/treatment room to get toys or go to parent; may move toward OR equipment
2	Not exploring or playing, may look down, may fidget with hands or suck thumb (blanket); may sit close to parents while waiting, or play has a definite manic quality
3	Moving from toy to parent in an unfocused manner, non-activity derived movements, frenetic/frenzied movement or play; squirming, moving on table, may push mask away
4	Actively trying to get away, pushes with feet and arms, may move whole body; in waiting room, running or unfocused, not looking at toys or will not separate from parent
Domain: vocalizations	
1	Reading (nonvocalizing appropriate to activity), asking questions, making comments, babbling, laughing, readily answer questions but may be generally quiet; child too young to talk in social situations or too engrossed in play to respond
2	Responding to adults but whispers, "baby talk," only head nodding
3	Quiet, no sound or responses to adults
4	Whimpering, moaning, groaning, silently crying
5	Crying or may be screaming "no"
6	Crying, screaming loudly, sustained (audible through mask)
Domain: emotional expressivity	
1	Manifestly happy, smiling or concentrating on play
2	Neutral, no visible expression on face
3	Worried (sad) to frightened, sad worried, or tearful eyes
4	Distressed, crying, extremely upset, may have wide eyes
Domain: state of apparent arousal	
1	Alert, looks around occasionally, notices /watches anesthesiologist (could be relaxed)
2	Withdrawn child sitting still and quiet, may be sucking on thumb and face turned in to adults
3	Vigilant looking quickly all around, may startle to sounds, eyes wide, body tense
4	Panicked whimpering, may be crying or pushing others away, turns away

children process new information. Another example is for children who have prior experience with surgery or hospitalization. They may have an exaggerated response if introduced to such a programmed.^{3,17,18}

Parental presence during induction of anesthesia (PPIA). To date, there is no formal written policy regarding parental presence during the induction of anesthesia. Data obtained have varied, and one particular study demonstrated that calm parents with calm cooperative children older than 4 years gained the most benefit from PPIA. Kain et al even showed that PPIA per se did not improve the level of preoperative anxiety or compliance during induction of anesthesia, while midazolam was proven to be more superior than PPIA alone.^{19,20}

The concern of inducing injury to anxious parents may lead to unnecessary legal consequences. The potential benefits of PPIA generally depend on the age group of the children. In infants younger than 6 months old with less marked separation anxiety, the benefit is questioned. The same goes with cooperative school aged children who preferred to be told the truth and adapted well to the new challenging

environment and were capable of building trust toward medical personnel. On the other hand, it might provide some form of relief to the accompanying parents in accordance to the biological instinct of a parent protecting their offspring from potential threat by being able to watch their children handled by the safe hands of an anesthesiologist.

Other behavioral methods. The study by Li and Lopez documented that children that took part in the play intervention group had significantly lower levels of preoperative anxiety ($P < .001$) as well as postoperative anxiety ($P < .002$) when compared to the control group. Moreover, the study also showed that the parents' level of anxiety was also reduced significantly in both the preoperative and postoperative period. In their study, the children undergoing operation participated in the visit to the operation theater prior to their surgical date and viewed a demonstration on a doll as to how the induction of anesthesia was performed.²¹

On the other hand, Kain et al conducted a more detailed and comprehensive approach whereby both the children and parents visited the Operation theater (OR)

or Post-anesthesia Care Unit (PACU) and a child life specialist assisted by exposing the children to the role-play rehearsals specific to the planned surgery. In their study, the role-play involves a doll where the children attached the electrocardiography leads. They were also able to play with the intravenous catheter, and by using the anesthesia mask, the children put the doll to sleep.²²⁻²⁴

Kain et al concluded that the behavioral programme was more beneficial to the children older than 6 years if they were exposed at least 5 to 7 days before surgery, whereas the children were noted to be more anxious if they were exposed to a shorter interval before the surgery ($P < .02$ for 1 day before surgery). The results emphasized the importance of an individual and age appropriate approach as well as the wrong assumptions of delivering the same approach for every child.^{22,23}

In a different study of the randomized prospective trial type, Patel et al assessed the effectiveness of a handheld video game (VG) as a tool of interactive distraction in reducing the preoperative anxiety in children. The study involved children from 4 to 12 years of age. It compared between VG, premedication with midazolam (M) and parental presence during induction of anesthesia (PP).^{17,25}

A systemic review on audiovisual (AV) interventions and preoperative anxiety in children planned for elective surgery suggested that AV interventions were potentially effective in reducing preoperative anxiety and related perioperative complications. A reduction in preoperative anxiety was proven to be significant in 14 out of 18 studies with 1897 cases. In fact, the use of AV interventions could also be a potential cost-effective tool since it requires minimal time and number of health care resources with its reusable nature. However, the authors emphasized the need of adequately powered RCT to support the findings.²⁶

The postulations by Koller and Goldman on the mechanism of reduction of preoperative anxiety with the use of AV interventions mentioned that the tool distracts and competes the child's attention from threatening stimuli such as the introduction of a face mask. Hence AV interventions ameliorate the anxiety and stress components of the child.^{26,27}

In 2010, a team of multidisciplinary researchers from the USA conducted a family-center preoperative intervention programme through the dismantling approach, the ADVANCE Study. The study involved parental involvement with the use of an anesthesia mask to be practiced at home and the distraction method at the reception area. Again, the researchers emphasized that by reducing the incidence of preoperative anxiety, the

unwanted negative behavioral changes postoperatively could be prevented. The ADVANCE Study considered the behavioral and psychological principle of distraction, shaping, exposure and coaching techniques.²⁸⁻³⁰

Challenges on induction of anesthesia. Induction of anesthesia in pediatric patients possess its own challenges, and it doubles when it involves special needs children, such as a child with attention deficit hyperactive disorder (ADHD) or autistic spectrum disorder (ASD). The goal is to minimize the distress and aim to deliver as smooth an induction as possible. The concern of delayed awakening and discharge from the recovery unit and the need for additional staff for monitoring has led us to be more selective as to which children should receive sedative premedication (Table 3).

Table 3. Dose of commonly used sedatives agents.

Drugs	Dosage	Route
Chloral hydrate	25-50 mg/kg	Oral
Midazolam	0.5 mg/kg	Oral
Ketamine	1-1.5 mg/kg	Intravenous
	3-4 mg/kg	Intramuscular
Dexmedetomidine	0.5-1 mcg/kg half an hour before procedure	Intravenous
	1-2 mcg/kg	Intranasal
Clonidine	2.5 mcg/kg	Oral

Pharmacological Intervention

Commonly used sedative agents

Emergence Delirium

In the 1960s, Eckenhoff and colleagues described emergence delirium (ED) in children as disorientation and perceptual changes due to the alterations in a child's consciousness. These alterations include hyperactive motor response and hypersensitivity to stimuli.³¹⁻³³ All these unwanted acute behavioral changes happen immediately postoperatively. The phenomenon of ED is paid more attention to lately due to the greater risk of developing maladaptive behavioral changes.^{31,32} Nevertheless, ruling out other causes of agitation and restlessness such as hypoxia, hypoglycemia and hypotension due to fluid depletion, electrolytes imbalance, sepsis, and residual drug effects is essential before diagnosing ED.

Children are at greater risk of developing ED compared to adults. Most literature quoted the incidence as

Table 4. Pediatric Anesthesia Emergence Delirium (PAED) scale.

PAED scale	
1	The child makes eye contact with the caregiver
2	The child's actions are purposeful
3	The child is aware of his/her surroundings
4	The child is restless
5	The child is inconsolable

20%, but it can vary up to as high as 80%. The onset of ED is usually within 30 minutes after the offset of anesthesia and may take to 15 to 30 minutes to subside. However, ED can persist up to 2 days according to the reports. It most commonly affects preschool children undergoing surgery with sevoflurane as an agent.^{34,35}

Risk Factors

Volatile agents, mainly sevoflurane, have been mentioned as one of the prominent risk factors for ED.^{36,37} This is mainly due to the pharmacokinetic properties of the volatile agent and low blood solubility with rapid onset and offset. A year after the introduction of sevoflurane in 1990, the first case of postoperative agitation was first reported in Japan, followed by the USA in 1996, after obtaining approval from the US Food and Drug Administration.

In animal studies, sevoflurane was found to have the ability to excite neurons in the locus coeruleus, where it is involved with adrenergic excretion. Hence, it is believed that it may contribute to the development of ED.^{38,39} Ophthalmology and otorhinolaryngology procedures such as tonsillectomy and adenoidectomy are recognized as having a higher incidence of ED. Other factors identified include parental anxiety, patient anxiety and younger age group (2-5 years old). Baseline personality traits such as temperament, coping skills and cognitive skills were also important determinants for developing ED.^{31,40,41}

Assessment

The behavioral changes of ED patients may mimic those of patients who deal with postoperative pain. To conclude whether the child is having ED, pure pain or a combination of both, assessment tools such as the Face

Table 5. Watcha Scale for ED.

Behavior	Score
Asleep	0
Calm	1
Crying but can be controlled	2
Crying but cannot be controlled	3
Agitated and thrashing around	4

Legs Activity Cry Consolability (FLACC) scale, Pediatric Anesthesia Emergence Delirium (PAED) (Table 4), Cravero scale, and Watcha scale (Table 5) are used.^{40,41}

The PAED scale is a validated and reliable assessment tool developed in 2004 by Sikich and Lerman. It is widely used in various types of research. However, it is difficult to use routinely in a clinical practice, such as in a busy operation theater with rapid patient turnover. Many anesthetists would prefer the use of the Watcha scale, as it is a simpler and more practical tool. Both the Watcha and Cravero scales detect the presence of ED, whereas the PAED scale reports the severity of ED.^{3,40,41}

Strategies

The recent introduction of the Paedfusor and Kataria model for target-controlled infusion (TCI) of propofol for the pediatric population has been widely accepted and adapted by anesthetists in many parts of the world. Advantages of using the technique include reduced postoperative nausea and vomiting, reduced environmental pollution and reduced incidence of laryngospasm and bronchospasm. On the other hand, even a single bolus of propofol 1 mg/kg given at the termination of sevoflurane anesthesia has been shown to reduce the incidence of ED in a pediatric population.⁴²⁻⁴⁴

Several studies have shown that both dexmedetomidine and clonidine contributed to a significant impact on reduction of ED, but it does expand on the recovery time of patients. Several doses that have been used in the clinical trials include infusion of dexmedetomidine 0.2 to 1 mcg/kg/h throughout the surgery or a single dose of 0.3 mcg/kg at the end of surgery. The results showed significant a reduction of ED from 47% to 5%. When compared to a single dose of propofol or dexmedetomidine, it was shown that dexmedetomidine was superior in reducing the incidence of ED (Table 6).⁴⁵⁻⁴⁷

Commonly Used Drugs

Table 6. Dose of drugs used to reduce incidence of ED.

Drugs	Dosage	Route
Propofol	TCI (Paedfusor/Kataria) 3-6 mcg/ml Single dose toward the end of surgery (1 mg/kg)	Intravenous
Dexmedetomidine	Infusion throughout surgery (0.2-1 mcg/kg/hour) Single dose 0.3 mcg/kg toward the end of surgery	Intravenous
Ketamine	2 mg/kg as premedication Single bolus 0.25 mg/kg 10 minutes before the end of surgery	Intranasal Intravenous
Midazolam	0.5 mg/kg as premedication	Oral
Clonidine	2.5 mcg/kg as premedication	Oral
Gabapentin	15 mg/kg as premedication	Oral

Conclusion

If we observe carefully, there is an interchangeable relation and confounding effects on each component of post-operative maladaptive behaviors, preoperative anxiety, and emergence delirium in children. The risk factors contributing to each component are mostly similar as parental attitude and level of anxiety played a significant role. However, to date, there have not been many studies relating these 3 components in a population of children. Identifying the risk factors during preoperative visits using suggested assessment tools that are more practical for clinical use is prudent to save time. Preventive measures must be taken that are suitable to individual age groups and choosing the most cost-effective balanced anesthesia technique is also important. In short, being a child-friendly anesthesiologist while adapting smooth induction and emergence of anesthesia will obviously help in many aspects.

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Author Contributions

ZAH: contributed to conception and design; COS: contributed to conception and design.

MMZ: drafted the manuscript; IR: critically revised the manuscript for important intellectual content; AS: Agree to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved; MA: critically revised the manuscript for important intellectual content; gave final approval.

HSK: critically revised the manuscript for important intellectual content

HMH: drafted the manuscript

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