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SCIENTIFIC ARTICLE

The incidence of emergence delirium and risk factors following sevoflurane use in pediatric patients for day case surgery, Kingston, Jamaica

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KEYWORDS
Emergence delirium;
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Abstract
Background and objectives: Emergence delirium is a distressing complication of the use of sevoflurane for general anesthesia. This study sought to determine the incidence of emergence delirium and risk factors in patients at a specialist pediatric hospital in Kingston, Jamaica.
Methods: This was a cross-sectional, observational study including pediatric patients aged 3–10 years, ASA I and II, undergoing general anesthesia with sevoflurane for elective day-case procedures. Data collected included patients' level of anxiety pre-operatively using the modified Yale Preoperative Anxiety Scale, surgery performed, anesthetic duration and analgesics administered. Postoperatively, patients were assessed for emergence delirium, defined as agitation with non-purposeful movement, restlessness or thrashing; inconsolability and unresponsiveness to nursing and/or parental presence. The need for pharmacological treatment and post-operative complications related to emergence delirium episodes were also noted.
Results: One hundred and forty-five (145) children were included, with emergence delirium occurring in 28 (19.3%). Emergence delirium episodes had a mean duration of 6.9 ± 7.8 min, required pharmacologic intervention in 19 (67.8%) children and were associated with a prolonged recovery time (49.4 ± 11.9 versus 29.7 ± 10.8 min for non-agitated children; $p < 0.001$). Factors positively associated with emergence delirium included younger age ($p = 0.01$, OR 3.3, 95% CI 1.2–8.6) and moderate and severe anxiety prior to induction ($p < 0.001$, OR 5.6, 95% CI 2.3–13.0). Complications of emergence delirium included intravenous line removal ($n = 1$), and surgical site bleeding ($n = 3$).

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Conclusion: Children of younger age with greater preoperative anxiety are at increased risk of developing emergence delirium following general anesthesia with sevoflurane. The overall incidence of emergence delirium was 19%.
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PALAVRAS-CHAVE
Delírio de emergência;
Agitação;
Sevoflurano;
Anestesia pediátrica

Incidência de delírio ao despertar e fatores de risco após o uso de sevoflurano em pacientes pediátricos para cirurgia ambulatorial, Kingston, Jamaica

Resumo
Justificativa e objetivos: Delírio ao despertar é uma complicação preocupante após o uso de sevoflurano em anestesia geral. Este estudo procurou determinar a incidência de delírio ao despertar e os fatores de risco em pacientes de um hospital pediátrico especializado, em Kingston, Jamaica.
Métodos: Estudo transversal e observacional, incluindo pacientes pediátricos com idades entre 3-10 anos, estado físico ASA I-II, submetidos à anestesia geral com sevoflurano para procedimentos eletivos em regime ambulatorial. Os dados coletados incluíram nível de ansiedade no pré-operatório medido com a Escala de Ansiedade Pré-operatória de Yale modificada, cirurgia realizada, duração da anestesia e analgésicos administrados. No período pós-operatório, os pacientes foram avaliados para verificar a incidência de delírio ao despertar, definido como agitação com movimentos não-intencionais, inquietação ou debatimento; inconsolável e apático à presença de enfermeiros e/ou dos pais. A necessidade de tratamento farmacológico e as complicações pós-operatórias relacionadas a episódios de delírio ao despertar também foram registradas.
Resultados: 145 crianças foram incluídas, com incidência de delírio ao despertar em 28 (19,3%). Os episódios de delírio ao despertar apresentaram uma média de duração de $6,9 \pm 7,8$ min; a intervenção farmacológica foi necessária em 19 pacientes (67,8%) e foi associada ao tempo de recuperação prolongado ($49,4 \pm 11,9$ *versus* $29,7 \pm 10,8$ min para crianças não-agitadas; $p < 0,001$). Os fatores positivamente associados ao delírio ao despertar incluíram idade mais jovem ($p = 0,01$, OR 3,3, IC95 1,2-8,6) e ansiedade moderada e grave pré-indução ($p < 0,001$, OR 5.6, IC95 2,3-13,0). As complicações do delírio ao despertar incluíram a remoção da linha intravenosa ($n = 1$) e sangramento do sítio cirúrgico ($n = 3$).
Conclusão: As crianças mais jovens que apresentam ansiedade séria no período pré-operatório possuem maior risco de desenvolver delírio pós-anestesia geral com sevoflurano. A incidência global de delírio foi de 19%.
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Introduction

The introduction of inhaled anesthetic agents with lower blood solubility (sevoflurane and desflurane) into clinical practice has permitted faster onset, more precise control and more rapid recovery from anesthesia.[1,2] Sevoflurane is most commonly used in pediatric anesthesia for inhalational induction and maintenance because of its decreased pungency, airway irritation and cardiovascular depression.[3] However, its use has been associated with a greater incidence of excitatory emergence in the post-operative period.[4]

Emergence delirium (ED) has been described by several authors as a clinical state during emergence from general anesthesia in which patients are awake but have an altered mental state manifesting as disorientation, inconsolability, confusion, and violent or harmful physical behavior.[4,5] These patients do not appear to recognize family members, display non-purposeful behavior and do not react appropriately to external stimuli.[6] Currently, there is no one accepted definition of ED and a number of scoring systems have been used to aid in the diagnosis.[6,7] A wide range of incidences from 10 to 80%[4] has been recorded in the literature and this may be in part due to differences in definitions used for diagnosis. Its underlying cause remains unknown. Age, preoperative anxiety, anesthetic technique or agents, surgical procedure, pain and the use or not of adjunctive medication have all been suggested to play a role in its development.[4,5,8,9] ED usually occurs early in the recovery period (the first 30 min) and is short-lived and self-limiting, lasting between 5 and 15 min.[4] However pharmacological intervention may be entertained, depending on the duration and severity of the event and may include analgesics, benzodiazepines and hypnotics such as fentanyl, propofol and midazolam.[4]

Restless recovery from anesthesia may cause injury to the patient, including the surgical site, and accidental removal of intravenous access, drains and surgical dressings. Extra nursing care may often be necessary.[10] This may then lead to delayed discharge from hospital, increased costs,

parental distress and overall dissatisfaction with the anesthetic care.[4] This study was therefore designed to assess the incidence of ED at the only dedicated pediatric hospital in Jamaica and identify possible contributing factors.

Materials and methods

The Bustamante Hospital for Children (BHC), Kingston, Jamaica is a 283-bed hospital, including a 5 bed Intensive Care Unit. It is the only specialist children's hospital in the English speaking Caribbean providing care to patients from birth to 12 years.

All American Society of Anesthesiologist (ASA) physical status I and II elective patients, between 3 and 10 years that presented for elective pediatric day-case surgery at the BHC between July 18 and November 23, 2011 and in whom sevoflurane was not contraindicated for induction and maintenance of anesthesia, were eligible to participate in the study. Informed written consent was obtained from the parent or guardian of the child. Other exclusion criteria were:

1. Pre-existing neurological dysfunction and agitation (e.g. Down's Syndrome, autism).
2. ENT surgeries associated with the feeling of ''suffocation'' such as adenoidectomies and tonsillectomies.
3. Ophthalmic procedures where postoperative eye patches would be applied, which could possibly contribute to patient disorientation during emergence.
4. Patients who are visually or hearing impaired that would possibly result in postoperative disorientation.
5. Major procedures such as cardiac and neurosurgical procedures.

Pre-operative assessment was done and preoperative medications administered were recorded.

Anxiety assessment was done on the ward by the research anesthetist just before transfer to the operating theater (OT) and then in the OT after separation from parents, prior to induction. The patient's anxiety level was assessed using the modified Yale Preoperative Anxiety Scale.[11] The mYPAS consists of 22 items in five categories (activity, emotional expressivity, state of arousal, vocalization, and use of parents). The highest behavioral level observed in each of the five mYPAS categories is the score for that category. The highest possible score that can be achieved (extreme agitation) is 22. The score has good inter- and intra-observer reliability, has been validated in the pediatric population and can be completed in less than a minute.[11] The scores were categorized into mild (5–10), moderate (11–15) and severe (16–22) anxiety.

Standard monitoring of electrocardiography (ECG), non-invasive blood pressure (NIBP) and oxygen saturation (SpO_2) was applied. A total fresh gas flow of three times the estimated minute volume of the patient (50% oxygen in nitrous oxide) with 8% sevoflurane was used with a Mapleson F circuit, flushed for 2 min prior to induction of anesthesia. The anesthetic mask was then applied at the end of a normal expiration. After the eyelash reflex was lost, and the patient was at an adequate depth of anesthesia, an intravenous catheter was inserted. Any complications at induction or under anesthesia including coughing, breath-holding, laryngospasm, bronchospasm, arrhythmias, hypotension, hypertension and abnormal movements were recorded. The airway technique chosen was at the discretion of the anesthetist. Children requiring endotracheal intubation received intermittent positive pressure ventilation, while those requiring a LMA or facemask were allowed to breathe spontaneously, except for those having umbilical and supra-umbilical herniorraphies. Anesthesia was then maintained with sevoflurane (concentration adjusted as needed by the attending anesthetist) in 50% oxygen with nitrous oxide. Any analgesics administered intra-operatively were also noted, such as pethidine, diclofenac, acetaminophen or local anesthetics.

The surgical procedure performed was documented, and categorized into one of the 3 groups based on the extent of the operation as well as the expected severity of post-operative pain, as outlined in Table 1. At the conclusion of the procedure, sevoflurane was discontinued and the patient was transferred to the Post-Anesthesia Care Unit (PACU) provided respiration was well established, saturation on room air was satisfactory, and there was cardiovascular stability. Length of anesthesia was defined as time from induction until time of discontinuation of sevoflurane. The emergence time was also noted, from time of discontinuation of sevoflurane to time of eye opening or purposeful limb movement (the first to appear). During recovery, a trained observer (PACU nurse or researcher) blinded to the pre-operative anxiety score, recorded all emergence behaviors using Cravero's 5-point agitation scale every 5 min (Table 2) until the patient was awake, calm and discharged.[7] The presence and duration of ED were documented. ED

Table 1 Description of surgical grade categories.

Grade	Description	Examples
1	Minor procedures with minimal or no expected postoperative pain	Examination under anesthesia (EUA), dental procedures e.g. extractions and plastic surgery procedures, such as removal of lumps
2	More extensive procedures, with mild to moderate expected postoperative pain	General surgical procedures such as inguinal, umbilical, or epigastric hernia repair
3	Most extensive procedures, with moderate to severe expected postoperative pain	Urologic and orthopedic surgeries

Table 2 Cravero's Agitation Scale.[7]

Scale	Description
1	Obtunded, not responsive to stimulation
2	Asleep, but responsive to movement or other stimulation
3	Awake and appropriately responsive
4	Crying and difficult to console
5	Wild thrashing behavior needing restraint

was defined as: agitation with non-purposeful movement, restlessness, or thrashing; incoherence; inconsolability and unresponsiveness to nursing and subsequent parental presence. Children were not considered to have ED if there was clinical evidence suggestive of pain such as localization and apparent inadequate analgesia. In such cases, analgesia was administered and the patient was reassessed. Vital signs (heart rate, SpO_2 and respiratory rate) were documented at 5 min intervals. All pharmacologic and non-pharmacologic interventions (decided on by the PACU nurse and anesthetist assigned to the list) and adverse events were also recorded. Recovery time was defined as the time from admission to the PACU until the patient was fully awake, appropriately responsive and cooperative, with a Grade 3 or less on the Cravero Agitation Scale. Discharge criteria were in accordance with routine practice and included an awake, oriented patient who had optimal analgesia and stable vital signs.

The sample size was calculated using a single proportion method. This calculation was based on a presumed 30% incidence (based on the literature review) and to detect a 10% difference between populations. A sample population of 145 was required to yield a power of 80% and a confidence interval of 95%. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 12.0 (IBM, Chicago, IL). Parametric data were presented as mean $\pm$ standard deviation (sd) and were compared using unpaired Student's *t*-tests. Chi-square and Fisher's exact tests were used to compare non-parametric data. *p* values of <0.05 were considered significant. Ethical approval was obtained from the UWI Faculty of Medical Sciences Ethics Committee and the local Health Authority.

Results

Demographics

A total of 145 patients were studied, 86 (59%) of whom were females. Their mean age was 6.3 $\pm$ 2.3 years, with both median and mode of 6.0 and IQR of 4 years (Fig. 1). Surgical procedures performed included inguinal herniorrhaphies, reduction and fixation of fractures, orchidopexies, cyst removal, examinations under anesthesia and dental extractions. Most (61%) procedures were general surgical procedures such as herniorrhaphies, classified as Grade 2 (Table 3). There were 115 ASA 1 patients (79%) and 30 ASA 2 patients (21%). Chronic illnesses were uncommon and included asthma, sickle cell disease trait (HbAS) and sinusitis.

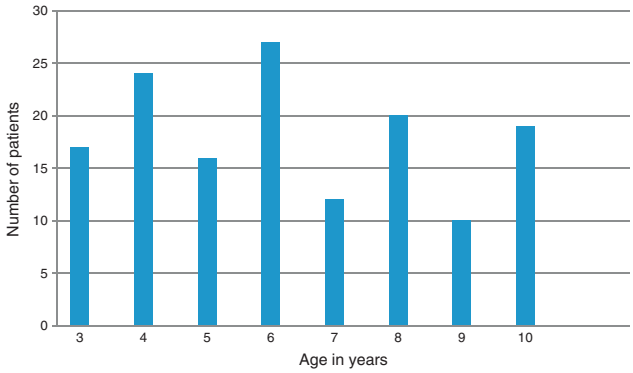

Figure 1 Distribution of age in years.

Pre-operative

Most patients (98%) in the study were not premedicated. Only one patient received midazolam and 2 patients received promethazine (Phenergan). The mYPAS scores on the ward were significantly lower than those just prior to induction of anesthesia. Mild anxiety (score of 5–10) was seen in 91% of patients preoperatively on the ward, compared to 65% prior to induction of anesthesia. Severe anxiety (mYPAS 16–22) was seen in only 2% of patients on the ward, which increased to 14% just prior to induction (Table 3).

Intra-operative course

The majority of patients (90%) had a laryngeal mask airway (LMA), 7 (5%) required endotracheal intubation and 8 (5%) had a face mask only. The most frequent

Table 3 Patient characteristics.

Characteristic	Frequency (%)
Sex	
Male	59(41%)
Female	86(59%)
Age	
3–6 years	84 (58%)
7–10 years	61(42%)
Procedure	
Grade 1	32(22%)
Grade 2	88(61%)
Grade 3	25 (17%)
ASA score	
I	115(79%)
II	30(21%)
Anxiety level on ward	
Mild	131(91%)
Moderate	11(7%)
Severe	3(2%)
Pre-induction anxiety	
Mild	94(65%)
Moderate	30(21%)
Severe	21(14%)

Table 4 Frequency of complications during anesthesia.

Complications	Frequency (%)
Breath holding	13(9%)
Coughing	18(6%)
Laryngospasm	4(3%)
Hypotension	3(2%)
Wheals	2(1%)
Emesis and abnormal movement	1(1%)

complication observed was breath holding, which occurred in 9% of patients, followed by coughing in 6% of patients (Table 4). The length of anesthesia ranged between 6 and 185 min (trimmed mean 40.0 ± 17.1, median 37 min, IQR 19 min). Time to emergence ranged from 1 to 50 min (mean 19.5 ± 11.7 min, median 19 min, IQR 20 min). For analgesia, rectal acetaminophen was administered to 86% of patients, intravenous pethidine (meperidine) was given to 96% and 72% received local infiltration with 0.25% bupivacaine.

Recovery period and ED

Recovery time ranged from 5 to 76 min (mean 33.5 ± 13.4 min). ED was seen in 28 (19.3%) patients and ranged from 1 to 37 min (mean 6.9 ± 7.8 min). Most cases of ED lasted 5 min or less (64%). Thirteen (46%) of the patients with ED required pharmacological treatment with pethidine (meperidine); and midazolam or ketamine was added in 5 of those patients. Episodes of ED were associated with a prolonged recovery time of 49.4 ± 11.9 min, compared with 29.7 ± 10.8 min for non-agitated children ($p < 0.001$). In the ED group, one child (4%) removed an IV line, 3 (11%) experienced increased bleeding at the surgical site and 1 (4%) removed a surgical dressing.

Factors associated with emergence agitation

There was a significant relationship between age and the development of ED: 26% of patients aged 3–6 years were found to be agitated, compared to 10% of patients aged 7–10 years ($p = 0.01$, OR 3.3, 95% CI 1.2–8.6). The mean age of the patients who developed ED was 4.8 ± 1.5 years compared to a mean age of 6.7 ± 2.3 years for those patients who did not ($p < 0.001$).

Patients who had moderate and severe anxiety just prior to induction were more likely to develop ED in the postoperative period ($p < 0.001$, OR 5.6, 95% CI 2.3–13.0). Only 10% of patients with mild anxiety developed ED, compared with 37% of patients with moderate or severe anxiety. This association was not seen with mYPAS scores done on the ward preoperatively.

There was no association between gender ($p = 1.0$), length of anesthesia ($p = 0.167$), emergence time ($p = 0.220$), grade of surgical procedure ($p = 0.686$), chronic illness ($p = 0.105$), dose of opioid analgesia given intra-operatively ($p = 0.938$), or use of wound infiltration ($p = 0.613$) (Table 5).

Table 5 Factors associated with emergence delirium.

Factor	With ED	Without ED	*p*-Value
Pre-induction anxiety level			
Mild	9 (9.6%)	85 (90.4%)	*<0.001*
Moderate	9 (30%)	21(70%)	
Severe	10(47.6%)	11(52.4%)	
Surgical grade			
1	5(26.3%)	14(73.7%)	0.686
2	17(16.8%)	84(83.2%)	
3	6(24%)	19(76%)	
Length of anesthesia	50.9 min	43.4 min	0.167
Time to emergence	20.1 min	17.1 min	0.220
Time to recovery	49.4 min	29.7 min	*<0.001*
Total pethidine dose	1.2 mg/kg	1.2 mg/kg	0.938

The italics highlight the statistically significant findings.

Discussion

This study documented an ED incidence of 19.3% in the pediatric surgical population (3–10 years) undergoing general anesthesia with sevoflurane at the BHC, Jamaica with younger age and pre-operative anxiety after parental separation being significant indicators. Reports from the international literature show incidences of ED ranging between 10 and 80%[4] in children who received sevoflurane anesthesia; however, variations in protocols and in the definition of ED in these studies make absolute comparison of results difficult. A study of children ages 3–7 years who had sevoflurane anesthesia and that also used a similar definition as in this study reported an incidence of 18%.[8]

Other studies have also been in keeping with our finding of higher incidences in younger children. Patients aged 3–5 years undergoing sevoflurane anesthesia had an incidence of ED of 40%, compared to 11.5% in those 6–10 years and an overall incidence of 26.7%.[12] In a study carried out in Thailand[13] the incidence of ED was significantly higher in the 2–5 year age group than the 6–9 year group (66.7% versus 45.8%, $p = 0.002$). After categorizing our patients into different age groups, we found that 26% of children aged 3–6 years experienced ED, compared to 10% in those who were 7–10 years.

The perioperative period is often extremely distressing for children and we observed a definite increase in anxiety following parental separation. The relationship between preoperative anxiety and ED seen was also observed in other studies. The odds of having marked symptoms of ED increased by approximately 10% when the mYPAS increased by 10 points.[14] Preoperative anxiety was found to be higher in children who developed severe ED that required pharmacologic treatment ($p = 0.032$).[15] ED occurred more frequently in children who exhibited difficult parental-separation behavior than in those who did not (44.4% versus 18.3%).[13]

Although pain has been implicated as contributing to the development of ED, a clear relationship has not been established. The administration of ketorolac or fentanyl has been shown to reduce the agitation associated with sevoflurane anesthesia in patients undergoing ENT surgery, suggesting

that adequate analgesia may reduce the incidence of ED.[4] The incidence of ED found in this study among patients 3–6 years is comparable to studies involving painless procedures (MRI) or using adequate regional anesthesia.[12,15–17] However, pain is difficult to differentiate from true ED as the signs are very similar, especially in younger patients.[18] We attempted to exclude the presence of localized pain when making the diagnosis of ED.

The time to recovery was delayed in those patients who developed ED, similar to other studies.[8,12,15,16,19] The prolonged recovery time most likely resulted from additional sedative pharmacologic treatment and other supportive therapies necessary to manage this phenomenon. The observed prolonged recovery process and delayed discharge could also have been influenced by complications resulting from the period of agitation such as increased bleeding, dislodged intravenous lines and drains.[8]

Limitations of this study included a lack of standardization of the concentration of sevoflurane used, doses and timing of adjunctive medications and these could have impacted on the incidence of ED. There may also have been observer bias, as the observers, although blinded to the levels of pre-operative anxiety, were not blinded to the anesthetic technique and surgical procedure.

Conclusions

Our findings indicate that sevoflurane associated ED occurs in children at the BHC at similar rates and durations to those observed in other studies. We identified younger age (3–6 years) and moderate to severe preoperative anxiety after parental separation, as positive predictors of ED. At the BHC, as in other hospitals in Jamaica, early parental separation continues to be practiced. A change in this policy may have a significant impact on the incidence of ED in our setting. The mYPAS score could be a valuable tool for identifying children who are at risk for developing ED.

Conflicts of interest

The authors declare no conflicts of interest.

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