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SCIENTIFIC ARTICLE

Emergence delirium following sevoflurane anesthesia in adults: prospective observational study

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KEYWORDS
Emergence delirium;
Sevoflurane;
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Abstract
Background and objectives: Emergence delirium after general anesthesia with sevoflurane has not been frequently reported in adults compared to children. This study aimed to determine the incidence of emergence delirium in adult patients who had anesthesia with sevoflurane as the volatile agent and the probable risk factors associated with its occurrence.
Design & methods: A prospective observational study was conducted in adult patients who had non-neurological procedures and no existing neurological or psychiatric conditions, under general anesthesia. Demographic data such as age, gender, ethnicity and clinical data including ASA physical status, surgical status, intubation attempts, duration of surgery, intraoperative hypotension, drugs used, postoperative pain, rescue analgesia and presence of catheters were recorded. Emergence delirium intensity was measured using the Nursing Delirium Scale (NuDESC).
Results: The incidence of emergence delirium was 11.8%. The factors significantly associated with emergence delirium included elderly age (>65) ($p = 0.04$), emergency surgery ($p = 0.04$), African ethnicity ($p = 0.01$), longer duration of surgery ($p = 0.007$) and number of intubation attempts ($p = 0.001$). Factors such as gender, alcohol and illicit drug use, and surgical specialty did not influence the occurrence of emergence delirium.
Conclusions: The incidence of emergence delirium in adults after general anesthesia using sevoflurane is significant and has not been adequately reported. Modifiable risk factors need to be addressed to further reduce its incidence.
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PALAVRAS-CHAVE
Delirium do despertar;
Sevoflurano;
Pacientes adultos;
Cuidados pós-anestésicos

Delirium do despertar após anestesia com sevoflurano em adultos: estudo observacional prospectivo

Resumo
Justificativa e objetivos: O *delirium* do despertar após a anestesia geral com sevoflurano não tem sido relatado com frequência em adultos como nas crianças. Este estudo teve como objetivo determinar a incidência de *delirium* do despertar em pacientes adultos submetidos à anestesia com sevoflurano como agente volátil e os prováveis fatores de risco associados a sua ocorrência.
Desenho e métodos: Um estudo observacional prospectivo foi conduzido com pacientes adultos sem distúrbios neurológicos ou psiquiátricos que foram submetidos à anestesia geral para procedimentos não neurológicos. Dados demográficos como idade, sexo, etnia e dados clínicos, incluindo escore ASA, estado cirúrgico, tentativas de intubação, tempo de cirurgia, hipotensão intraoperatória, drogas utilizadas, dor pós-operatória, analgesia de resgate e presença de cateteres foram registrados. A intensidade do *delirium* do despertar foi medida usando a Escala de Triagem de *Delirium* em Enfermagem (*Nursing Delirium Scale* – NuDESC).
Resultados: A incidência de *delirium* do despertar foi de 11,8%. Os fatores significativamente associados ao *delirium* do despertar incluíram idade avançada (>65) ($p = 0,04$), cirurgia de emergência ($p = 0,04$), descendência africana ($p = 0,01$), tempo maior de cirurgia ($p = 0,007$) e número de tentativas de intubação ($p = 0,001$). Fatores como sexo, uso de álcool e drogas ilícitas e especialidade cirúrgica não influenciaram a ocorrência de *delirium* do despertar.
Conclusões: A incidência de *delirium* do despertar em adultos após a anestesia geral com sevoflurano é significativa e não tem sido relatada adequadamente. Fatores de risco modificáveis precisam ser abordados para reduzir ainda mais sua incidência.
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Introduction

Delirium is a disturbance of consciousness with inattention accompanied by a change in cognition or perceptual disturbance that develops over a short period (hours to days) and fluctuates over time.[1] The hallmark symptom of delirium is an impairment of consciousness, usually occurring in association with global impairments of cognitive functions.[1] Delirium may be associated with a wide range of conditions.[2–4]

Delirium during the postoperative period can be divided into Emergence Delirium (ED) and Postoperative Delirium (PD) based on its onset.[2] ED is also referred to as Emergence Agitation (EA) or post-anesthetic excitement in the literature, and is a well-documented phenomenon occurring in children and adults during the immediate postoperative period and lasting for 5–15 min.[2] ED is a clinical condition in which patients are 'awake' but experience alterations in disorientation and other mental status changes that range from confusion and lethargy to violent and harmful behavior.[2] A direct association with the administration of a general anesthetic is likely because it occurs during the emergence process and mimics the excitation 'Stage II' of ether anesthesia as described by Guedel.[3] ED has been categorized under the DSM-IV diagnostic criteria as a substance-induced delirium.[3]

ED may lead to serious consequences for a patient such as injury, increased pain, hemorrhage, self-extubation, removal of catheters or drains. It can also necessitate physically or pharmacologically restraining the patient, often requires additional nursing support and delays recovery time.[3–5] ED can be disturbing to the anesthesiologists as well as Post Anesthesia Care Unit (PACU) staff and can lead to increased hospital costs.[3,6,7]

Emergence Delirium in the PACU was also found to be a strong predictor of postoperative delirium long after surgery.[8] Postoperative delirium in itself may be associated with increased morbidity, mortality, duration of hospital stay, technical, consultant and nursing costs.[9] The incidence of ED varies widely with reports ranging from as low as 3% to as high as 21%.[3,4,9,10] Despite its common occurrence and serious sequelae, ED has not been frequently studied in adults, studies being done much more commonly in the pediatric population.[6–8] The precise etiology of ED after general anesthesia remains unknown[3]; however, many factors may predispose a patient to agitation, which is frequently initiated by uncomfortable stimuli.[11] Previous reports have found some risk factors that are associated with the development of ED. These include age, history of alcohol abuse, type of surgery, use of sevoflurane as the volatile agent, use of anticholinergic drugs, duration of surgery and presence of a urinary catheter.[3,4,11]

To our knowledge, there have not been many published studies from Caribbean, investigating the incidence and factors associated with emergence delirium in adult patients after sevoflurane anesthesia. With this background, this prospective study aimed to determine the incidence and identify modifiable risk factors in adult patients in the Caribbean, which could be considered in risk reduction strategies in day-to-day operating room practice.

Methodology

A prospective observational study was conducted over a 6 month period in the PACU at the Eric Williams Medical Sciences Complex, a tertiary care teaching hospital in Trinidad & Tobago. Approval of the study protocol was obtained from the Ethics Committee of the Faculty of Medical Sciences, The University of the West Indies, St. Augustine. The 5 bed PACU is located within the main 'Block-of-8' operating-rooms suite, where procedures in the specialties including general surgery, orthopedic, otorhinolaryngology (ENT), urology, plastic, thoracic and maxillofacial surgeries are performed. Each PACU nurse cares for 1–2 patients. An anesthesiologist is responsible for the discharge of patients.

Inclusion criteria for the study were patients aged 18 years and older, undergoing general anesthesia with sevoflurane as the volatile agent, and admitted to the PACU after extubation in the operating room. The study excluded those who have undergone a neurosurgical procedure, patients known to have pre-existing neurological disease, (such as a history of chronic dementia, psychosis, mental retardation, cerebrovascular accident with residual cognitive impairment), patients who had the procedure exclusively under local/regional anesthetic technique, patients admitted to the PACU with endotracheal tube in situ, and patient refusal to participate. Informed written consent was obtained by the anesthesiologist administering the general anesthetic prior to induction. Patients who met the inclusion criteria were assessed for delirium in the PACU. This was done using the Nurses Delirium Scale (Nu-DESC),[12] 10 min after entry into the PACU. The Nu-DESC score is based on the Confusion Rating Scale and has a sensitivity and specificity of 0.95 and 0.87 respectively for detecting delirium in the PACU when compared against the gold standard, the DSM-IV criteria.[13,14] The Nu-DESC consists of the following five criteria: disorientation, inappropriate behavior, inappropriate communication, illusions/hallucinations and psychomotor retardation. Each is graded from 0–2 with a maximum of score of 10 and a score of 2 or greater indicating presence of delirium. It is easy to use and has an average completion time of 1 min.[13] In this study, a NuDeSc score of 2 and above was considered positive for the diagnosis Emergence Delirium, while those patients who scored less than 2, were considered not to have ED. The patients were categorized into two groups for the purpose of analysis, based on the presence and absence of delirium.

The sample size was calculated using the ED incidence of 4.7%, as reported by Lepouse et al.[6] Although the calculated sample size required for this study was only 69 patients, all consented patients were included to increase the validity of the study.

Demographic factors including age, gender, and ethnicity were recorded. Preoperative data included alcohol use (>3 times per week), illicit drug use, history of diabetes and/or hypertension, American Society of Anesthesiologists (ASA) score, type of surgical procedure, and surgical status (elective or emergency). The intra-operative clinical data recorded were episodes of hypotension (systolic blood pressure <20% of the baseline or requiring use of vasopressors), type of airway used, number of attempts at endotracheal intubation, volatile agent used, use of nitrous oxide, total morphine dose used intra-operatively, use of non-depolarising neuromuscular blockers, use of atropine and the length of surgery. Postoperatively, presence of a urinary catheter, postoperative pain and need for analgesics in the PACU were recorded.

The assessment of delirium in PACU using NuDESC scale was done by different personnel who were unaware of the details of the anesthesia management of the patient. The assessment and recording the score were done by a limited small number of personnel who had specific training in the use of the NuDESC scale. This was done in order to minimize bias in recording the data.

The Statistical Package for Social Sciences (SPSS) version 21 software was used to analyze the data. Continuous variables were analyzed with independent *t*-test; Pearson's Chi-square and Fisher's exact test analyses were done to determine the associations between the various perioperative variables and the presence of ED. After the initial analyses, a multivariate logistic regression was done to further determine the factors significantly associated with Emergence Delirium. Statistical significance was fixed at $p < 0.05$ level.

Results

Four hundred and seventeen (417) patients were enrolled in the study. The gender distribution was equal. Majority of the patients presented for elective surgery and belonged to all ASA categories. Different types of airways such as endotracheal tubes and laryngeal mask airways were used for the procedures. Anesthesia was maintained on sevoflurane as the volatile agent for all the patients, the dose adjusted by the individual anesthesiologists. Neuromuscular blocking agents, nitrous oxide and atropine were used in some patients. The preoperative characteristics of the patients including the prevalence of comorbidities, substance use, as well as the intra-operative and postoperative factors which could have possibly influenced ED are listed in Table 1.

Using the Nu-DESC, emergence delirium was diagnosed in 49 patients, giving an overall incidence of 11.8% in this setting. The scores recorded for each element of the Nu-DESC is shown in Fig. 1. Disorientation, inappropriate communication and psychomotor retardation were noted in patients who had a score of 1. Other elements noted included inappropriate behavior and illusions/hallucinations. As shown in Fig. 1, a relatively higher degree of inappropriate behavior and inappropriate communication were observed in patients who scored 2. Overall, psychomotor retardation appeared to be the most commonly observed element in the NuDesc score while illusions/hallucinations were the least recorded element in the score.

Continuous variables such as age, duration of surgery and intra-operative morphine dose were compared between the two groups. This is shown in Table 2. Only duration of surgery was significantly longer in patients who had delirium.

The comparison of preoperative categorical variables is shown in Table 3, while the comparison of intra-operative and postoperative factors is shown in Table 4.

Patients were categorized into younger and older age groups ($\leq$64 and $\geq$65) and analyzed for the presence of delirium. Elderly age group patients did have a significantly

Table 1 Preoperative characteristics of patients and intra-and-postoperative factors.

Variable		Number (%)
Preoperative characteristics		
Gender	Male	225 (54.0)
	Female	192 (46.0)
Comorbidities	Hypertension	105 (25.2)
	Diabetes mellitus	88 (21.1)
Substance Use	Illicit drugs use	43 (10.3)
	Regular alcohol use	39 (9.4)
ASA Grade	ASA I	207 (49.6)
	ASA II	159 (38.1)
	ASA III	50 (12.1)
	ASA IV	1 (0.2)
Surgical status	Elective	340 (81.5)
	Emergency	77 (18.5)
Intraoperative factors		
Airway	Endotracheal tube	269 (64.5)
	Laryngeal mask airway	139 (33.3)
	Others[a]	9 (2.2)
Drugs used	Neuromuscular blocking agents	323 (77.5)
	Atropine	239 (57.3)
	Nitrous Oxide	42 (10.1)
Events	Hypotension	124 (29.7)
Postoperative factors		
Urinary catheter in situ		78 (18.7)
Requirement of analgesia in the Recovery Room		120 (28.8)

[a] Facemask, rigid bronchoscope, tracheostomy.

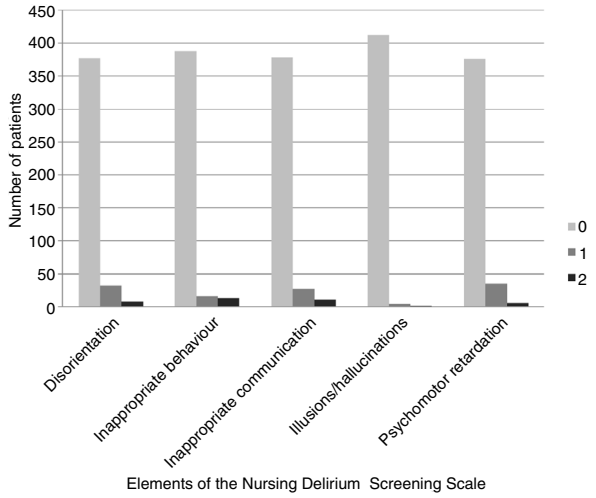

Figure 1 The scores recorded by the Nursing Delirium Screening Scale.

higher risk of developing ED compared to younger patients ($p = 0.04$).

Although male patients were more likely to develop ED (13.3%) than female patients (9.9%), this difference was not statistically significant ($p = 0.277$). Both diabetics and non-diabetics were found to have similar incidences of ED, 12.5% and 11.6% respectively ($p = 0.806$). ED was present in 12.5% in non-hypertensives compared to 9.5% in hypertensive patients ($p = 0.413$). The proportion of alcohol users in the study was only 9.4% compared to 90.6% non-users, although the incidences of ED were very similar between the 2 (12.8% and 11.6%, $p = 0.795$). Similarly, only 10.3% of patients admitted to use illicit drugs compared to 89.7% who did not; however the incidence of ED in patients who used illicit drugs was 11.6%, while it was 11.8% in the non-users ($p = 0.979$). The incidences of ED in the various ASA categories were also comparable: I (12.1%), II (10.7%), III (14.0%) and IV (0.0%), ($p = 0.903$).

Of the 124 patients who developed intra-operative hypotension, 14.5% were noted to have ED. In comparison, 10.6% were diagnosed with ED in intra-operatively normotensive patients ($p = 0.254$). The number of patients with an endotracheal tube (64.5%) almost doubled those who had a LMA (33.3%). The incidence of ED in those with an endotracheal tube (13.4%) was also higher that of the LMA patients (8.6%). No statistically significant difference in the incidence of ED was found between the groups ($p = 0.368$).

Nitrous oxide was used in 10.1% of patients, however, similar incidences of ED were observed in those it was used (9.5%) and in those it was not used (12.0%) ($p = 0.803$). Similarly, 12.8% of the patients who had Neuromuscular Blocking

Table 2 Age, surgical duration, morphine dose and emergence delirium.

Variable	Range	Overall ($n = 417$) Mean ± SD	Delirium absent ($n = 368$) Mean ± SD	Delirium present ($n = 49$) Mean ± SD	p-value[a]
Age (y)	18–93	48.3 ± 16.7	47.7 ± 16.5	52.6 ± 17.5	0.05
Surgical duration (min)	10–540	102.7 ± 78.9	98.9 ± 76.3	131.3 ± 92.5	0.007
Morphine dose (mg)Mean ± SD	0–30	5.7 ± 4.1	5.5 ± 4.0	6.6 ± 4.2	0.08

SD, Standard Deviation.
[a] p-value by independent t-test.

Table 3 Pre-operative factors and emergence delirium.

Factor	Total n (%)	Delirium absent n (%)	Delirium present n (%)	p-value[a]
Age				
≤64	342 (82.0)	307 (83.4)	35 (71.4)	
≥65	75 (18.0)	61 (16.6)	14 (28.6)	0.04
Ethnicity				
African descent	190 (45.6)	158 (83.2)	32 (16.8)	
Indian descent	174 (41.7)	160 (92.0)	14 (8.0)	
Other	53 (12.7)	50 (94.3)	3 (5.7)	0.01
Gender				
Male	225 (54.0)	195 (86.7)	30 (13.3)	
Female	192 (46.0)	173 (90.1)	19 (9.9)	0.277
Diabetes mellitus				
Yes	88 (21.1)	77 (87.5)	11 (12.5)	
No	329 (78.9)	291 (88.4)	38 (11.6)	0.806
Hypertension				
Yes	105 (25.2)	95 (90.5)	10 (9.5)	
No	312 (74.8)	273 (87.5)	39 (12.5)	0.413
Alcohol use				
Yes	39 (9.4)	34 (87.2)	5 (12.8)	
No	378 (90.6)	334 (88.4)	44 (11.6)	0.795
Illicit drug use				
Yes	43 (10.3)	38 (88.4)	5 (11.6)	
No	374 (89.7)	330 (88.2)	44 (11.8)	0.979
ASA score				
I	207 (49.6)	182 (87.9)	25 (12.1)	
II	159 (38.1)	142 (89.3)	17 (10.7)	
III	50 (12.0)	43 (86.0)	7 (14.0)	
IV	1 (0.2)	1 (100)	0 (0)	0.903
Surgical status				
Elective	341 (81.8)	62 (81.6)	306 (89.7)	
Emergency	76 (18.2)	14 (18.4)	35 (10.3)	0.04

[a] p-value using Fisher's Exact Test or Pearson Chi-Square Test.

Agents (NMBA) experienced ED, compared to 8.5% in patients who were not given NMBAs ($p = 0.268$). Patients who received atropine had an increasing trend of experiencing ED than those who did not (14.2% vs. 8.4%), but the difference was not statistically significant ($p = 0.069$).

In PACU, most patients (81.3%) did not have a urinary catheter in situ; the incidence of ED (11.2%) was comparable in those with a catheter (14.1%) ($p = 0.474$). Of those that required rescue analgesia in the PACU, 15% developed ED in comparison to 10.4% who did not require analgesia ($p = 0.190$). Although the proportion of patients scheduled for emergency surgery was smaller, the incidence of ED in emergency surgical patients was significantly higher ($p = 0.04$).

The presence of ED in patients belonging to each surgical specialty was analyzed. Table 5 depicts the distribution of

Table 4 Intra-operative and postoperative factors and emergence delirium.

Factor	Total *n* (%)	Delirium absent *n* (%)	Delirium present *n* (%)	*p*-value[a]
Intra-operative hypotension				
Yes	124 (29.7)	106 (85.5)	18 (14.5)	
No	293 (70.3)	262 (89.4)	31 (10.6)	0.254
Airway type				
LMA	139 (33.3)	127 (91.4)	12 (8.6)	
ETT	269 (64.5)	233 (86.6)	36 (13.4)	
Other	9 (2.2)	8 (88.9)	1 (11.1)	0.368
Nitrous oxide use				
Yes	42 (10.1)	38 (90.5)	4 (9.5)	
No	375 (89.9)	330 (88.0)	45 (12.0)	0.803
Number of intubation attempts				
None	141 (33.8)	129 (91.5)	12 (8.5)	
1	227 (54.4)	197 (86.8)	30 (13.2)	
2	40 (9.6)	35 (87.5)	5 (12.5)	
3	7 (1.7)	7 (100)	0 (0)	
>3	2 (0.5)	0 (0)	2 (100)	0.001
Non-depolarising neuromuscular blockers				
Yes	323 (77.5)	282 (87.3)	41 (12.7)	
No	94 (22.5)	86 (91.5)	8 (8.5)	0.268
Atropine use				
Yes	239 (57.3)	205 (85.8)	34 (14.2)	
No	178 (42.7)	163 (91.6)	15 (8.4)	0.069
Urinary catheter in PACU				
Yes	78 (18.7)	67 (85.9)	11 (14.1)	
No	339 (81.3)	301 (88.8)	38 (11.2)	0.474
PACU analgesia				
Yes	120 (28.8)	102 (85.0)	18 (15.0)	
No	297 (71.2)	266 (89.6)	31 (10.4)	0.190

LMA, laryngeal mask airway; ETT, type of airway.
[a] *p*-value using Fisher's Exact Test or Pearson Chi-Square Test.

Table 5 Type of surgery and emergence delirium.

	Type of surgery						
	General (*n* = 207)	Orthopedic (*n* = 74)	ENT (*n* = 3)	Maxillofacial (*n* = 16)	Plastic (*n* = 7)	Thoracic (*n* = 68)	Urology (*n* = 42)
Overall (%)	49.6	17.7	0.7	3.8	7.0	16.3	10.1
Delirium absent (%)	88.4	90.5	100	93.8	100	82.4	88.1
Delirium present (%)	11.6	9.5	0	6.3	0	17.6	11.9

Pearson Chi-Square value (4.459); df (6); *p*-value (0.615).

the patients in each specialty and the comparison. Thoracic surgery had the highest incidence of ED (17.6%), followed by General Surgery and Urology, although there was no statistically significant difference between the groups.

Most patients either had an LMA or needed only 1 intubation attempt. The incidence of ED increased to 100%, when patients had more than 3 attempts at intubation.

After initially analyzing individual factors for association with ED, a stepwise multivariate logistic regression analyses were done to determine the factors significantly associated with ED. The adjusted odds ratios, 95% Confidence Intervals and the *p*-values of the significant factors associated with ED are depicted in Table 6.

The demographic factors significantly associated with ED were age and ethnicity, while emergency surgical status and longer surgical duration were the clinical factors significantly associated with ED. All other factors including gender, the number of attempts at intubation, the type of airway

Table 6 Multivariate analyses of the factors associated with emergence delirium.

Variable	Odds Ratio	95% Confidence Intervals		Significance
		Lower bound	Higher bound	
Age (older)	1.03	1.01	1.05	$p = 0.01$
Gender	1.58	0.80	3.10	$p = 0.187$
Ethnicity (African)	3.69	1.02	13.12	$p = 0.04$
Intubation attempts	1.31	0.52	3.30	$p = 0.56$
Type of airway (ETT)	0.93	0.22	3.96	$p = 0.92$
Intra-operative hypotension	1.19	0.60	2.40	$p = 0.62$
NMBA use	0.65	0.20	2.10	$p = 0.47$
Atropine use	1.51	0.68	3.36	$p = 0.31$
Rescue analgesia in PACU	1.57	0.79	3.13	$p = 0.19$
Surgical status (Emergency)	2.31	1.13	4.74	$p = 0.02$
Surgical duration (longer)	1.04	1.01	1.07	$p = 0.02$

NMBA, neuromuscular blocking agents.

used, presence of intra-operative hypotension and the need for analgesia in PACU were not significantly associated with ED as denoted by the logistic regression analyses.

Discussion

The incidence of ED in adult surgical patients after general anesthesia using sevoflurane as the volatile agent in a Caribbean tertiary care teaching hospital is significant and comparable to the previously published reports from other regions. Internationally published studies show a widely varying incidence of ED ranging from 3% to 20%.[3,4,9,10] This wide variation may be perhaps due to the fact that a precise definition and timeline for ED does not exist so far. In addition, there are also wide variations in the protocols to diagnose and measure ED, which may render a direct comparison difficult.[15] The present study did find some factors to be attributable to ED. These factors are ethnicity, older age, emergency surgical status and the length of surgery.

Ethnicity has not been identified in the previous literature to have a significant association with the incidence of ED. In Trinidad and Tobago, people of African and Asian Indian descent comprise the majority of the population, each contributing to almost 45%, while Caucasians, Middle Easterners, Chinese and mixed races contribute to the rest. The enrolled patients in the present study clearly reflected the nation's demographic pattern, with equal proportions of patients belonging to the African and Indian ethnicities, followed by other ethnicities. However, African ethnic patients had higher odds ratio of developing ED (Table 6). This may be explained in part by the anatomical differences related to stature and size of the patients. African descent patients are usually phenotypically larger than their Indian ethnic counterparts and require larger LMAs, endotracheal tubes, nasogastric tubes, urinary catheters and higher doses of anesthetic drugs based on weight. Lepouse et al. has suggested that awakening from anesthesia with foreign devices in situ may be linked to ED.[6] Furthermore, cultural differences may also be influential for the manifestation of ED, including varying perceptions and attitudes toward surgery, pain and strange environments.

Despite their smaller numbers, emergency surgical patients had a higher incidence of ED compared to elective patients. This is in contrast to the finding of Lepouse et al. where emergency surgical status had no influence on the occurrence of ED.[6] Elective operations afford patients enough time to become both mentally and physically prepared for surgery. Fears regarding the surgical procedure, postoperative pain and the recovery period can also be addressed. In an emergent situation, this luxury of time may not be available to the patient and the healthcare provider. Often, patients only learn of the need for surgery within a few hours (or a few days) of the procedure. Patients in the height of their anxiety, imagining over the prospect of surgery, may not fully comprehend all the information conveyed by the healthcare provider, thus predisposing them for more anxiety. In addition, emergency patients may also have physiological derangements which are seldom seen in elective situations. These may include (but not limited to) electrolyte and metabolic disturbances, decreased oxygen carrying capacity, altered gas exchange etc., which, due to the involvement of the central nervous system, may also be hypothetically attributable to the increased incidence of ED.

Another risk factor identified in this study for ED, is the longer duration of surgery. More than two hours of surgical duration was positively associated with the incidence of ED. This finding corroborates with the results of many other studies, who also reported that longer the surgery, higher the risk of ED.[6,16,17] Longer surgical procedures may predispose patients to have foreign bodies (e.g., airways) in situ for a longer period of time, relatively more consumption of anesthetic drugs, larger fluid shifts, blood loss, electrolyte imbalance, hypothermia etc., which may be again attributable to the development of ED.

Almost two-thirds of patients in the present study had general anesthesia with an endotracheal tube placement, and in patients who had more than three attempts at intubation, the incidence of ED was 100%. This can be easily explained by the fact that multiple attempts do predispose for trauma resulting in upper airway edema. Notwithstanding this, in the present study, the number of attempts for endotracheal intubation was not significantly associated with ED, according the logistic regression analyses. When

there are multiple attempts at intubation, most patients in our setting do receive dexamethasone invariably.

Sanders et al. reported that ED tends to affect younger individuals.[17] Radtke et al. also found age to be a significant factor for ED, with younger patients (<40 years) and older patients (>64 years) having a higher incidence of ED compared to middle aged patients.[16] In the present study, although the mean ages for patients with and without ED were comparable, the elderly age was significantly associated with ED (Table 4).

There have been conflicting reports on the influence of gender on ED. While Sanders et al. reported a higher predisposition in male patients, Lepouse et al. did not find a significant association.[6,17] The present study also did not find a significant association between gender and presence of ED.

Sanders et al. also suggested that ED was more common in otherwise healthy patients.[17] Patients with co-morbidities and a higher ASA grade should therefore be at risk of developing ED. In fact, Lepouse et al. showed ASA grade to be influential on the incidence of ED.[6] The present study did not find co-morbidities such as diabetes mellitus and hypertension as well as ASA grades to be impacting on ED, which is similar to the conclusion drawn by Radtke et al.[16]

The detrimental effects on alcohol and illicit drug use on the brain are well recognized. However, Radtke et al. found no significant association between alcohol abuse and ED.[16] Similarly, the present study also did not find a significant influence of and illicit drug usage on the development of ED.

Intra-operative hypotension may predispose a patient to cerebral hypoperfusion. However, the effect of intra-operative hypotension on ED is not well documented in the literature. Again, presence of intra-operative hypotension did not influence ED in the present study. It may be possible that the duration of intra-operative hypotension might have been the key factor, which was not specifically recorded in the present study.

Previous studies have suggested that the type of surgical procedure predisposes a patient to developing ED. Oral cavity and ENT procedures were identified by Yu et al. as being significantly associated with ED.[5] Lepouse et al. identified higher incidence of ED in breast and abdominal surgery.[6] Radtke et al. reported a higher incidence in patients undergoing musculoskeletal surgery, than those having oral, ENT or intra-abdominal procedures.[16] In the present study, thoracic surgery patients had the highest incidence of ED, although there was no statistically significant difference between the specialties. This may be due to smaller number of patients in the individual specialties.

The use of nitrous oxide and Neuromuscular Blocking Agents (NMBA) were not significant factors in the occurrence of ED. These findings are very similar to Radtke et al., who also found no significant association between ED and nitrous oxide or NMBA use.[16]

Several authors have reported anticholinergic drugs such as atropine to be deliriogenic,[17–19] whereas the current study could not find any impact.

The dose of intra-operative morphine did not have an impact on the incidence of ED in the present study, similar to Radtke et al.[16]

Yu et al. identified the presence of a urinary catheter as being a risk factor for ED.[5] Lepouse et al. also suggested that various catheters may startle patients on awakening from general anesthesia.[6] The present study however, did not find a significant relationship of ED with the presence of catheters in the postoperative period.

Pain may be a confounding factor when assessing ED in the PACU.[8] Inadequately treated postoperative pain has been well recognized to be associated with ED. In fact, Radtke et al., did report that postoperative pain was strongly associated with ED.[16] Patients who had a pain score of 6–10 in the Numerical Rating Scale (NRS), were twice as likely to develop ED as those with a score of 0–5. Davis et al. demonstrated that when fentanyl was given to children IV or intra-nasally for moderately painful procedures, the incidence of ED reduced.[20] The present study although did not specifically assess pain scores, it did not find a significant relationship between ED and the need for rescue analgesics in the PACU. Other authors have suggested that ED may still occur even when postoperative pain is adequately treated.[21–23] In pediatric patients, even in the absence of postoperative pain ED may still be present, indicating that ED may be a clinical phenomenon separate from pain.[7]

There are some limitations to the present study. Many other factors such as premedication with benzodiazepines have been shown to be associated with the development of ED.[24] Some studies have shown a beneficial effect of benzodiazepines in children.[25] This was not included in our study since it is an observational study and premedication is seldom used in our setting.

Although preoperative anxiety has been suggested as a risk factor for ED, this was not assessed in the present study. Other limitations include patient-introduced errors by providing false information during the history taking. For example, many patients deny illicit drug use due to the social stigma. Also, in the present study, the number of patients enrolled within individual specialty was small, which could have influenced the results. The ideal time frame for assessing ED is unknown.[6] This study chose to assess ED when the patient has been declared 'ready for discharge' by the anesthesiologist; which is usually by 10 min after admission to the PACU. However, based on the patient's clinical condition, the type and nature of the surgery and the course of intra-operative events, the time interval between admission to the PACU and discharge may vary widely between patients. Therefore, some patients might have fallen out of the optimum window for ED detection. Another major limitation of the study is that we did not assess and record the postoperative pain scores of patients in PACU.

Nevertheless, in conclusion, the study could reasonably determine the incidence of Emergence Delirium in adults after sevoflurane general anesthesia in our setting which was around 12%. Elderly age, African ethnicity, emergency surgery, and longer duration of surgery were found to be significantly associated with the incidence of ED. It is therefore important for clinicians to recognize those patients who may be at risk of developing ED, and other modifiable factors, so that appropriate measures can be taken to reduce ED and thus patient morbidity and improve patient satisfaction.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Fricchione GL, Nejad SH, Esses JA, et al. Postoperative delirium. Am J Psychiatry. 2008;165:803–12.
2. Burns A, Gallagley A, Byrne J. Delirium. J Neurol Neurosurg Psychiatry. 2004;75:362–7.
3. Scott GM, Gold JI. Emergence delirium: a re-emerging interest. Sem Anesth Perioperat Pain Med. 2006;25:100–4.
4. Silverstein JH, Timberger M, Reich DL, et al. Central nervous system dysfunction after non-cardiac surgery and anesthesia in the elderly. Anesthesiology. 2007;106:622–8.
5. Yu D, Chai W, Sun X, et al. Emergence agitation in adults: risk factors in 2000 patients. Can J Anesth. 2010;57:843–8.
6. Lepouse C, Lautner CA, Liu L, et al. Emergence delirium in adults in the post-anesthesia care unit. Br J Anaesth. 2006;96:747–53.
7. Duffen A, Williams A. Should sevoflurane be used for maintenance of anesthesia in children? Br J Hosp Med (Lond). 2011;72:598.
8. Vlajkovic GP, Sindjelic RP. Emergence delirium in children: many questions, few answers. Anesth Analg. 2007;104:84–91.
9. Hudek K. Emergence delirium: a nursing perspective. AORN J. 2009;89:509–16.
10. Sharma PT, Sieber FE, Zakriya KJ, et al. Recovery room delirium predicts postoperative delirium after hip-fracture repair. Anesth Analg. 2005;101:1215–20.
11. Rose DK. Recovery room problems or problems in the PACU. Can J Anesth. 1996;43:116–28.
12. O'Brien D. Acute postoperative delirium: definitions, incidence, recognition and interventions. J Perianesth Nurs. 2002;17:384–92.
13. Williams MA, Ward SE, Campbell EB. Confusion: testing versus observation. J Gerentol Nurs. 1988;14:25–30.
14. Radkte FM, Franck M, Schneider M, et al. Comparison of three scores to screen for delirium in the recovery room. Br J Anaesth. 2008;101:338–43.
15. Gooden R, Tennant I, James B, et al. The incidence of emergence delirium and risk factors following sevoflurane use in pediatric patients for day case surgery, Kingston, Jamaica. Rev Bras Anestesiol. 2014;64:413–8.
16. Radtke FM, Franck M, Hagemann L, et al. Risk factors for inadequate emergence after anesthesia: emergence delirium and hypoactive delirium. Miner Anestesiol. 2010;76:394–403.
17. Sanders RD, Pandharipande PP, Davidson AJ, et al. Anticipating and managing postoperative delirium and cognitive decline in adults. BMJ. 2011;343:d4331.
18. Parikh SS, Chung F. Postoperative delirium in the elderly. Anesth Analg. 1995;80:1223–32.
19. Fong HK, Sands LP, Leung JM. The role of postoperative analgesia in delirium and cognitive decline in elderly patients: a systematic review. Anesth Analg. 2006;102:1255–66.
20. Davis PJ, Greenberg JA, Gendelman M, et al. Recovery characteristics of sevoflurane and halothane in preschool-aged children undergoing bilateral myringotomy and pressure equalization tube insertion. Anesth Analg. 1999;88:34–8.
21. Weldon BC, Bell M, Craddock T. The effect of caudal analgesia on emergence agitation in children after sevoflurane versus halothane anesthesia. Anesth Analg. 2004;98:321–6.
22. Cravero J, Surgernor S, Whalen K. Emergence agitation in paediatric patients after sevoflurane anesthesia and no surgery: a comparison with halothane. Paediatr Anaesth. 2000;10:419–24.
23. Uezono S, Goto T, Teruik K. Emergence agitation after sevoflurane versus propofol in pediatric patients. Anesth Analg. 2000;91:563–6.
24. Kudoh A, Takase H, Takahira Y, et al. Postoperative confusion increases in the elderly long-term benzodiazepine users. Anesth Analg. 2004;99:1674–8.
25. Cho EJ, Yoon SZ, Cho JE, et al. Comparison of the effects of 0.03 and 0.05 mg/kg midazolam with placebo on prevention of emergence agitation in children having strabismus surgery. Anesthesiology. 2014;120:1354–61.