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Postanesthetic Emergence Delirium in Children: Qualitative Differences between Sevoflurane vs Desflurane: A Randomized Clinical Trial

Elena Fernández Dueñas[1,2*], Pascual Sanabria Carretero[1,2], Francisco Reinoso-Barbero[1,2], Ana Fernández Dueñas[3], Leopoldo Martínez Martínez[4]

[1]Department of Pediatric Anesthesia-Critical Care-Pain Treatment, La Paz University Hospital, Madrid, Spain
[2]Idipaz Foundation, La Paz University Hospital, Madrid, Spain
[3]Directorate General of Public Health, Ministry of Health, Madrid, Spain
[4]Department of Pediatric Surgery, La Paz University Hospital, Madrid, Spain
Email: *efdezduenas@gmail.com

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Abstract

Background: Emergence Delirium (ED) is considered a usual complication in pediatric anesthesia. Aim: Analyze the quantitative and qualitative differences in ED in children receiving general anesthesia with sevoflurane or desflurane in day case surgery. Materials and Methods: Two hundred and two children, ASA I-II, who required outpatient elective day case surgery, were assigned to receive anesthesia with sevoflurane or desflurane. ED was assessed by a masked investigator using the Pediatric Anesthesia Emergence Delirium (PAED) scale at 5 and 15 minutes (min). Results: Mean time to wake up was shorter with desflurane compared with sevoflurane (6.0 versus 8.3 min, $p = 0.0001$). The overall incidence of ED was 21.3% and Postoperative Maladaptive Behavior Changes (POMBC) incidence was 22%; however, these were not related. Main factors found to be associated with ED were younger age, postoperative pain and preoperative anxiety. Although there were not statistically significant differences in ED incidence between sevoflurane (26.4%, 95% CI 17.3% - 35.4%) and desflurane anesthesia (16.3%, 95% CI 8.8% - 23.8%) ($p = 0.18$), scores of items 1 and 2 from PAED scale (eye contact and purposeful actions, items related to the patients' connection with their surroundings) were significantly higher in sevoflurane than in desflurane group ($p = 0.034$ and $p = 0.021$ respectively). Conclusion: Recovery after anesthetic maintenance with desflurane is faster and as safe as sevoflurane, including postoperative behavioral disorders. Although desflurane did not statistically decrease ED incidence as compared with sevoflurane, patients who were agitated with desflurane were qualitatively less disoriented and disconnected from their surroundings.

Keywords

Inhaled Agents, Sevoflurane, Desflurane, Emergence Agitation, Pediatric

1. Introduction

Emergence Delirium (ED) was defined by Sikich and Lerman as "a mental disturbance during recovery from general anesthesia and consists of hallucinations, delusions and confusion manifested by moaning, restlessness, involuntary physical activity, and thrashing about in bed" [1]. It is more frequent in children than in adults, generally has a limited duration and a spontaneous recovery. ED is considered a relevant complication in pediatric anesthesia, due to its high incidence, which may be as high as 80% [1] [2]. ED can cause serious complications in children and it is associated with prolonged length of stay in Post-Anesthesia Care Unit (PACU), extra nursing care and increase of parent's anxiety and dissatisfaction [3].

Some studies suggest that children suffering ED are at risk of developing Postoperative Maladaptive Behavior Changes (POMBC), such as enuresis, eating disorders, sleeping disorders and general anxiety [4] [5]. This is more frequent in children under 3 years of age [6], and can range from acute disturbances in the immediate postoperative period to milder changes that persist for days and even months afterwards. These disorders are not well studied, and their exact incidence is unknown. In a study published by Kotiniemi *et al.* [7], 47% of children undergoing outpatient surgery developed behavioral changes in the postoperative period and in 9% these persisted after one month. According to the work of Kain *et al.* [8], up to 50% of children undergoing outpatient surgery developed behavioral changes two weeks postoperatively. However, involvement of specific anesthetic agents in the development of POMBC has not yet been established.

Differences in ED characteristics between desflurane and sevoflurane anesthesia in children have still not been fully elucidated due to unvalidated scales to measure ED and different definitions, surgical procedures and treatments of pain [9] [10] [11] [12]. The use of the only validated scale Pediatric Anesthesia Emergence Delirium Scale (PAED) [1], allows the standardization of ED comparative studies between both halogenated agents. Locatelli *et al.* [3] using PAED scale observed remarkable differences in ED duration between sevoflurane and desflurane. However, as far as we know, no authors have investigated specifically the qualitative differences of ED caused by sevoflurane and desflurane.

The aim of this study was to evaluate the differences of ED in children receiving sevoflurane and desflurane in day case surgery, both the quantitative (incidence) and the qualitative differences in the type of delirium, and its relationship with intraoperative and postoperative complications, specifically with postoperative behavioral changes or other known risk factors.

2. Materials and Methods

After approval by our Hospital Ethics Committee and Spanish Medicines Agency (AEMPS) and parental written informed consent, a prospective randomized controlled trial was conducted between December 2015 and March 2017 (EUDRACT: 2015-002399-25). We enrolled 202 patients, aged between 1 month and 18 years old, American Society of Anesthesiologists (ASA) physical status I or II, undergoing general pediatric elective day case surgery under general anesthesia. Exclusion criteria included ASA III and IV children, patients with cognitive impairment, emergency surgery, children with an upper respiratory tract infection in the preceding two weeks, obstructive sleep apnea, and maladaptive behavior changes including attention-deficit hyperactivity disorder.

In the preoperative holding area, an observer blinded to randomization evaluated anxiety using the modified Yale Preoperative Anxiety Scale (m-YPAS). Both patients and parents received m-YPAS. Patients with a score above 30 in m-YPAS were premedicated with intranasal or sublingual midazolam 0.3 $mg \cdot kg^{-1}$ (up to 10 mg) 20 to 30 minutes (min) before surgery. At the operating room anesthesia was induced by mask with incremental increases in inspired sevoflurane (2% - 6%) in 100% O_2. After intravenous (iv) cannulation, fentanyl 1 $mcg \cdot kg^{-1}$ was administered. A subgroup of patients received additionally a single bolus of propofol 1.5 $mg \cdot kg^{-1}$ if the anesthesiologist in charge was not comfortable with the jaw relaxation in order to facilitate airway management.

Then a Laryngeal Mask Airway (LMA) was inserted and children were assigned to receive 1 MAC of sevoflurane (sevoflurane group) or of desflurane (desflurane group) for maintenance of anesthesia level as measured by BIS around 40-50. Randomization sequence was created by a research assistant not involved in the study, in blocks of four, using a computer-generated random allocation sequence. Group allocation was concealed in sequentially opaque sealed envelopes given by the research assistant. Sevoflurane or desflurane was administered by the principal investigator with 40% O_2. An anesthetic gas extractor was used to keep ambient level of gases exposure below the recommended limits, following our hospital's methodology [13].

Local infiltration anesthesia or a peripheral nerve block (including, penile, ilioinguinal and iliohypogastric nerve block) was performed in all patients prior to the surgical incision. Furthermore, all children received intravenous dose of ondansetron 0.1 $mg \cdot kg^{-1}$. Supplementary boluses of fentanyl 0.5 - 1 $mcg \cdot kg^{-1}$ were administered if heart rate increased more than 20% of pre-incision baseline heart rate or mean arterial pressure. Patients who were administered other kind of medications, different from this protocol, were excluded from the study. Standard monitoring was used intraoperatively.

Child's behavior was evaluated during pre-induction in the operating room within the first minute of the anesthetic induction. Behavior was classified in three groups: "calmed and cooperative", "anxious and tearful", and "agitated or non-cooperative".

After surgery ended, anesthetic gas was discontinued and LMA was removed when the patient was alert enough to make purposeful movements. Emergence time was defined as time for displaying regular respiratory pattern, facial grimacing, and purposeful movement after stopping desflurane or sevoflurane administration. The patient was then transferred to the PACU, which is next to the operating room.

The PACU nurse, who was blind to the anesthetic agent used and was appropriately trained on the PAED Scale, the Face, Legs, Activity, Cry, Consolability (FLACC) Scale and the Faces Pain Scale (FPS), evaluated ED, pain and possible complications when the patient was considered fully awake (opening eyes, vocalizing, moving purposefully or spontaneously).

Pain was assessed with FLACC scale in non-cooperative children and with FPS scale in cooperative children. It was classified as "no pain" (0 points in FLACC or FPS scale), "mild pain" (1 - 2 in FLACC or FPS scale), "moderate pain" (3 - 5 in FLACC scale or 3 - 4 in FPS scale), and "severe pain" (6 - 10 in FLACC scale or 5 - 6 in FPS scale). If the patient presented moderate-severe pain, the nurse in PACU administered 10 mg·kg^{-1} (up to 500 mg) paracetamol.

ED severity was defined as the higher PAED scale score presented during the first 5 min or during the 5 - 15 min after awakening. A PAED score of 0 was assigned if the child was falling asleep again. A PAED score of ≥10 was defined as an "ED event" occurring. If a patient presented a PAED score of ≥16 in any moment, the nurse administered 0.1 mg·kg^{-1} midazolam, and from there after no more patient's data were included during their stay in PACU.

Patients were discharged from PACU when they met the modified Aldrete score of ≥9 as per institutional guidelines.

A telephone follow-up questionnaire was conducted 15 days after surgery to evaluate POMBC using the Post Hospitalization Behavior Questionnaire (PHBQ) scale [14]. For patients with POMBC, a second telephone follow-up was performed 30 days after surgery. PHBQ scale consists of 27 items that are generally classified into six categories of anxiety: "general anxiety", "separation anxiety", "sleep anxiety", "eating disturbances", "aggression against authority" and "apathy/withdrawal" [4] [15]. In our study, this scale was classified into four categories to facilitate the completion of the questionnaire: "loss of appetite", "sleep disturbances", "nocturnal enuresis" and "changes in behavior".

3. Statistical Analysis

The sample size was calculated based on the assumption of an estimated global ED incidence of 30% (following literature review) in a population of 250 patients. With an α-error of 0.05, and a precision of 5%, considering an attrition rate of 5%, a total sample of 200 patients was required.

Continuous data (age, weight, surgical time, emergence time, duration of PACU stay, severity of ED) were presented as mean ± Standard Deviation (SD) and were analyzed using Kruskal-Wallis and Wilcoxon tests. Categorical data (incidence of ED, gender, preoperative anxiety, quality of induction, postoperative pain, intraoperative and postoperative complications, POMBC) were expressed as frequency, percentage and 95% Confidence Interval (95% CI), and were analyzed using Chi-square and Fisher exact tests.

A multivariate logistic regression analysis was conducted to identify independent risk factors for ED. The relationship between ED and preoperative anxiety was analyzed using another logistic regression analysis. Risk factors are expressed as Odds Ratio (OR) with 95% CI.

In all analyses, a *P*-value of < 0.05 was considered statistically significant. Statistical analysis was performed using R Statistics Package (R-Core Team 2014).

4. Results

We enrolled 202 patients, although two patients declined to participate and 17 patients were excluded after allocation from data analysis as they deviated from protocol. Overall, 183 patients, 91 in the sevoflurane group and 92 in the desflurane group, completed the study (CONSORT diagram; **Figure 1**). The two groups were similar with respect to age, weight, sex, type and duration of surgery, needs of preoperative midazolam and intraoperative propofol (**Table 1**). Emergence time was significantly shorter with desflurane than with sevoflurane although there were no differences between both groups in duration of PACU stay (**Table 1**).

There were no differences between both groups in intraoperative and postoperative complications, including postoperative pain (**Table 2**). In the follow-up

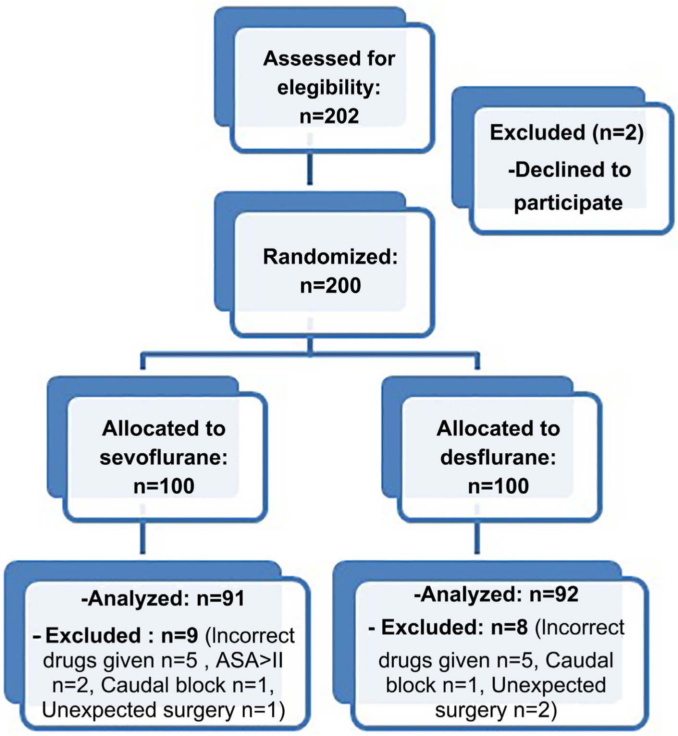

Figure 1. CONSORT flow chart.

Table 1. Patient demographics and perioperative characteristics.

Study Group		Sevoflurane[a] (n = 91)	Desflurane[a] (n = 92)	*p*-value
Age (year)		5.1 ± 3.6	6.2 ± 4.4	0.1695
Weight (kg)		21.8 ± 13.1	25.3 ± 15.6	0.103
Gender (male/female)		71/20	72/20	1.0
Surgical time (min)		28 ± 18.7	25.5 ± 15.2	0.328
Type of surgery	**Phimosis**	19	19	0.728
	Herniorrhaphy	17	21	
	Orchidopexy	16	17	
	Hydrocelectomy	6	12	
	Others	33	23	
Emergence time (min)		8.3 ± 4.6	6.0 ± 3.7	0.0001
Preoperative anxiety		34	36	0.805
Preoperative midazolam		33	38	0.484
Quality of induction	**Calmed**	69	69	0.373
	Anxious	14	12	
	Non-cooperative	8	11	
Intraoperative Propofol		38	38	0.950
Duration PACU stay (min)		48.4 ± 21.9	43.3 ± 22.4	0.292

Abbreviations: PACU: Post-Anesthesia Care Unit; POMBC: Postoperative maladaptive behavior changes. [a]Data are expressed as means ± SD or numbers, as appropriate.

Table 2. Intraoperative and postoperative complications.

STUDY GROUP		Sevoflurane[a] (n = 91)	Desflurane[a] (n = 92)	*p*-value
Intraoperative complications				
Laryngospasm		0	1	0.256
Severe bronchospasm		0	2	
Mild bronchospasm		3	4	
Stridor		5	7	
Coughing		5	5	
Early postoperative complications				
Vomiting, at PACU		6	4	0.504
Postoperative pain	No pain	52	56	0.437
	Mild pain	18	21	
	Moderate pain	14	10	
	Severe pain	7	5	
Bleeding or hematoma		3	4	0.710

Continued

Late postoperative complications			
Vomiting after discharge	4	4	0.987
Surgical wound infection	1	2	0.566
Postoperative Maladaptive Behavior Changes (POMBC)	17	18	0.872

[a]Values are number of patients (n). "Severe bronchospasm" required removal of laryngeal mask airway and endotracheal intubation to secure airway. "Mild bronchospasm" reverted with pharmacological treatment. $p > 0.05$ in all groups using Chi-square test.

questionnaire conducted 15 days after surgery, 7 from 183 patients could not be reached. A POMBC incidence of 20% (35 from 176 patients) was observed joining both groups. Of these, 15 patients (8.5%) experienced behavior changes (including hyperactivity, parental separation anxiety and apathy), 12 patients (6.8%) sleeping disorders (including night awakenings and nightmares), 5 patients (2.8%) eating disorders and 3 patients (1.7%) nocturnal enuresis. On day 30 after surgery all children had recovered from POMBC. A regression model was performed to study whether the following parameters were risk factors of POMBC: ED, age, sex, preoperative anxiety, quality of induction, anesthetic agents (sevoflurane, desflurane), postoperative pain and complications. None of these were related with behavior changes ($p > 0.05$). In fact, there were no differences between sevoflurane and desflurane regarding POMBC (**Table 2**).

We performed a multivariate logistic regression analysis to evaluate the risk factors associated with the occurrence of ED. A significant association was found between the occurrence of ED with age and postoperative pain (**Table 3**). Other variables that were tested but were not found significant were gender, administration of a bolus of propofol, inhalational agent, midazolam premedication, quality of induction and intraoperative complications (**Table 3**). Preoperative anxiety was also found to be a risk factor associated with ED. Patients that received only sevoflurane, sevoflurane + midazolam, sevoflurane + propofol and sevoflurane + midazolam + propofol, were compared to their equivalent subgroup in the desflurane arm but none of these ED incidence differences were statistically significant.

The total incidence of ED was 21.3% (39 from 183, 95% CI 15.3% - 27.3%) at any time during their stay at PACU. Incidence and severity of ED were reduced over time, decreasing by half 15 min after arriving to PACU: at 5 min the incidence was 18% (33 from 183, 95% CI 12% - 24%) whereas at 15 min these was 8% (15 from 183, 95% CI 4% - 12%), ED was recurrent or prolonged in 9 patients. In 9 patients (5%) pharmacological treatment was required to control extreme agitation (PAED score ≥ 16) with midazolam 0.1 $mg \cdot kg^{-1}$. There were no statistical differences in ED incidence between sevoflurane and desflurane groups, nor in the ED severity at 5 min or at 15 min, or on the need of additional midazolam for ED management between both agents (**Table 4**). However, scores

Table 3. Predictors of ED.

Variable		OR (95% CI)	*p*-value
Age[a]		0.80 (0.68 – 0.94)	0.008
Preoperative Anxiety[b]		2.96 (1.41 - 6.69)	0.048
Propofol[a]		0.36 (0.13 - 1.03)	0.058
Postoperative pain[a]		-	-
	Mild	4.14 (1.31 - 13.09)	0.016
	Moderate	15.21 (4.71 - 49.08)	<0.001
	Severe	55.78 (9.48 - 328.38)	<0.001
Constant[a]		0.281 (-)	0.015

[a]Predictors and constant obtained by a multivariate logistic regression analysis. AUC ROC = 0.872 (0.800 - 0.945). [b]Predictor obtained by a logistic regression analysis.

Table 4. Perioperative outcomes.

Study Group	Sevoflurane[a] (n = 91)	Desflurane[a] (n = 92)	*p*-value
ED incidence	24/91 (26.4%)	15/92 (16.3%)	0.185
PAED Score (5 min)	4.2 ± 5.5	3.7 ± 4.4	0.468
PAED Score (15 min)	2.8 ± 4.1	2.01 ± 3.6	0.150
Patients needing midazolam for ED management	5/9 (56%)	4/9 (44%)	0.637

Abbreviations: PAED: Pediatric Anesthesia Emergence Delirium. ED: Emergence Delirium. [a]Data are expressed as means ± SD or numbers (%), as appropriate.

of items 1 and 2 from PAED scale (eye contact and purposeful actions) were significantly higher in sevoflurane than in desflurane group (p = 0.034 and p = 0.021 respectively). Scores of item 3 (awareness of the surroundings) were also higher in sevoflurane group, although this difference was not statistically significant (p = 0.068). There were no differences in items 4 and 5 (restlessness and inconsolability) between the two groups (p = 0.777 and p = 0.366 respectively) (**Figure 2**).

5. Discussion

In the present study, our data confirm the findings of previous studies on emergence time, that showed it is shorter using desflurane than sevoflurane for anesthesia maintenance [16] [17].

An overall ED incidence of 21.3% was observed in this study, which is also similar to other studies that use PAED scale to measure ED. There is a great variability in the incidence reported in the literature due to different causes: unharmonized diagnostic method, unclear physio-pathological mechanisms, unknown influence of anesthetic agents and insufficient identification of risk factors. Many factors have been suggested to play a potential role in the initiation of

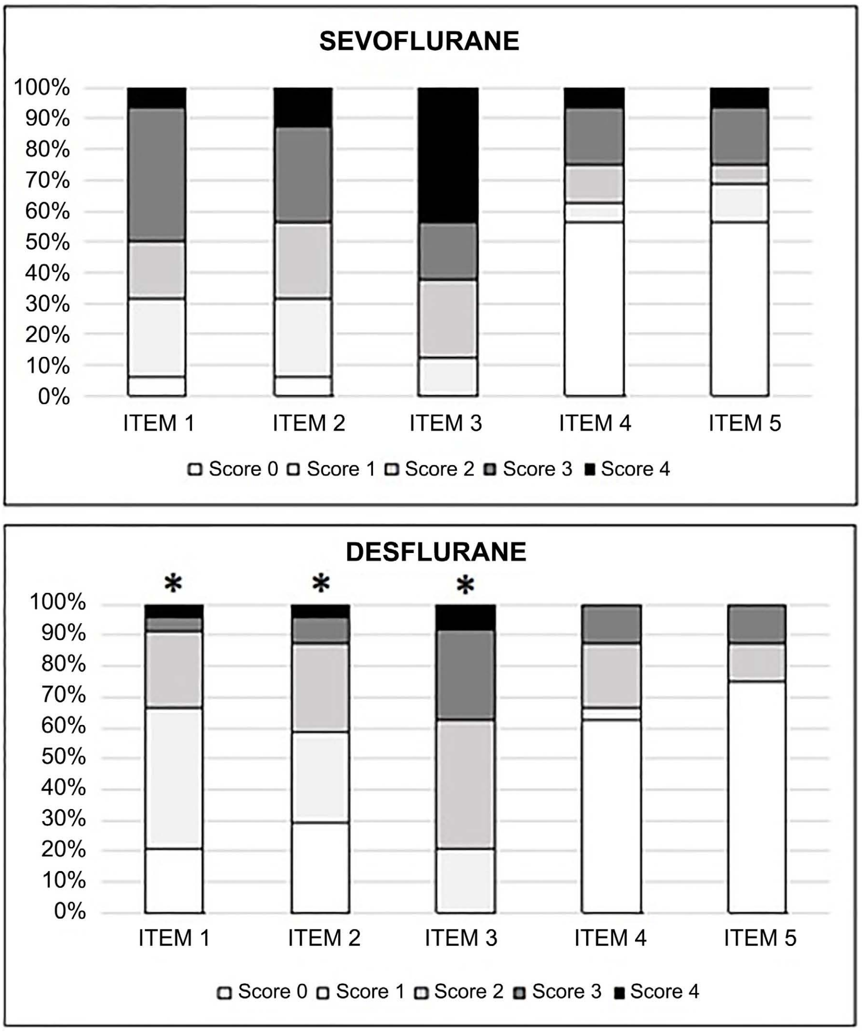

Figure 2. Patients (%) per score of each PAED scale item in sevoflurane and desflurane groups (*$p < 0.07$ compared with sevoflurane).

ED, including factors related to anesthesia, surgery, the patient and adjunct medication [18]. The pharmacology of the fast-acting volatile agents sevoflurane and desflurane is highly suspected to be implicated in the genesis of ED, however there is no strong evidence in the literature to support this theory. Recently, interictal epileptiform discharges during anesthesia induction have been suggested to be related to the development of ED in children. This would be most likely associated with a hyperexcitable neuronal response to general anesthesia [19].

The time of appearance of ED is primarily in the first minutes of the postoperative period, where it is both more prevalent and more intense. In our study, ED incidence at 5 min of PACU stay was 18% (95% CI 12% - 24%) with a severity of 3.9 ± 5, whereas at 15 min ED incidence was reduced by more than half, and its severity was reduced by a third. These findings are similar to other studies concerning time of onset of ED [3] [20].

We found that ED decreases more with desflurane than with sevoflurane although this difference was not statistically significant. In the literature, the results of ED incidence with sevoflurane and desflurane anesthesia in children are scarce and contradictory. The meta-analysis conducted by He *et al.* [16] on the effects of anesthesia with both agents in pediatric population, which includes five studies on ED, reported that desflurane produces a slightly greater ED than sevoflurane. However, none of the studies included in this meta-analysis [16] used the validated PAED scale, current gold standard for measuring ED. Instead, these studies used simple scales and included small series of patients undergoing ENT (ear, nose, throat) and neurosurgical procedures, both known to increase ED incidence [21]. Another meta-analysis conducted by Lim *et al.* [17], which included only three studies that used PAED scale, obtained conflicting findings. However, like our study, it concluded that there were no differences regarding ED incidence between both agents. No differences were also found in the meta-analysis from Costi *et al.* [12], that included seven studies of which only one used PAED scale.

In our study, the main risk factor of ED was age, regardless of anesthetic agent used. As age increased 1 year, probability of experiencing ED was reduced by 20% in a very significant way ($p = 0.008$), the inflection point being 5 years old ($p = 0.00015$). Age less than or equal to 5 years old significantly increased the probability of ED, and this was more intense when it happened. This is in line with previous studies [22]. Increase in ED incidence in preschool children may be due to an exacerbation of their emotional lability in stressful situations and to their central nervous system immaturity. In addition, development of cholinergic function and of the hippocampus may also have a role in the susceptibility of pre-school children to develop agitation [23].

Preoperative anxiety is a known factor associated with ED [4]. In our study, although all children who were believed to be anxious were premedicated with midazolam, preoperative anxiety increased almost 3 times the risk of developing ED (OR = 2.96, $p = 0.0033$) independently of the anesthetic agent used for anesthesia maintenance. This reinforces the importance of psychological preparation of children to reduce preoperative anxiety. Other measures should be routinely conducted, such as allowing parental presence at induction of anesthesia, providing detailed information to parents and children about the perioperative procedure in lay language and allowing presence of clowns or video games in the preoperative area. It should be noted, that after completion of our study, we now allow parental presence at induction of anesthesia in all procedures with positive results in reducing the incidence and intensity ED [24]. Concerning midazolam premedication, its effect on preventing ED has been studied by many authors with conflicting results. Like in our study, Costi *et al.* [12] in their Cochrane meta-analyses and Dahmani *et al.* [25] in their meta-analyses found that midazolam administered as premedication or at the beginning of surgery did not have a role in preventing ED. More recent studies concerning the time of administration of midazolam, either at the beginning or at the end of surgery, also did not find a difference in reduction of incidence of ED [26].

Interestingly the risk of suffering ED decreased by 64% with the administration of a bolus of propofol ($p = 0.058$). This effect was independent of age, and it improved the predictive capacity of the multivariate model. Although this was not statistically significant in our study, we believe that with a bigger sample size a statistically significant decrease in risk would have been observed. Dahmani *et al.* [25] showed that propofol prevents ED if it is administered during or at the end of the surgical procedure. In our study, the protective effect of propofol administered during anesthetic induction lasted until the immediate postoperative period. This was probably due to the type of surgeries included in our study which were of short duration, and thus the effect of propofol would still last after awakening of the patient.

Postoperative pain was also found to be an ED risk factor in both groups. The probability of ED increased more than 4 times when pain was "mild", and up to 15 and 56 times when pain was "moderate" and "severe" respectively ($p < 0.001$). Since child's behavior may be similar in ED and pain, and given that PAED and FLACC scales share some of its items, both pain and ED may be mislabeled and overestimated. Given that pain could be a possible confounding factor, in order to appropriately evaluate ED, postoperative pain must be completely controlled with adequate analgesia, as done in our study. We performed local infiltration anesthesia or a peripheral nerve block in all patients, in addition to administering an intraoperative bolus of fentanyl on request. However, it might still be possible that pain plays a role in ED in some children as it is easy, even for a trained observer, to diagnose pain and ED even in the absence of nociceptive stimulation or pain [3] [27].

We are unaware of other studies that compare the characteristics of ED between both agents in terms of PAED scale items. Our study found that differences in ED were due to scores in items 1 and 2 (eye contact and purposeful actions), which were higher with sevoflurane than with desflurane. There were no differences in item 3 (awareness of the surrounding) ($p = 0.068$), however we believe that with a bigger sample size we would have also found differences in this item. These items (1 - 3) are related to the patients' connection with their surroundings. We observed no differences between both agents in scores of items 4 (restlessness) and 5 (inconsolability). Therefore, patients agitated with sevoflurane were definitively more disoriented and disconnected from the environment than those agitated with desflurane. This is a very important qualitative aspect because lack of eye contact with their children can provoke more stress in high-monitoring parents [28]. These aspects, disorientation and surrounding disconnection, are actually those that make very difficult to calm the agitated patient after sevoflurane anesthesia. This affects patient's comfortability and requires a more intense care of the patient in order to avoid displacements of catheters or venous lines and, in some instances, treatment with a sedative drug is needed. In fact, some authors have considered items 1 - 3 more specifically associated to a clinical impression of delirium than items 4 - 5 [3]. In essence, these items can be resources and time consuming. In our study, patients in both groups took the same time (45 min) to be discharged from PACU. However, other studies have shown that desflurane allowed to discharge patients from PACU more rapidly than after sevoflurane anesthesia when using a clinical score such as Steward's recovery score [29].

The change of a single fluorinated molecule, produces not only pharmacokinetic differences (such as half-life, absorption rate and distribution) but also important pharmacodynamic differences: desflurane is a more pungent airway irritant, more vasodilator than sevoflurane, and has different actions on central nervous system [30]. No epileptiform movements have been described with desflurane, equi-MAC of both anesthetics do not produce similar EEG-derived indices (desflurane BIS/CAM ratio is lower than sevoflurane's) and its analgesic properties are different [31] [32]. Desflurane administered at equipotent 1.0 MAC produces significantly lower Surgical Pleth Index (SPI) values than sevoflurane [33]. Therefore, it is not surprising that the effect on ED is also different.

It should be noted that desflurane, like other inhalation agents, has a potential effect on global climate change given its known greenhouse effect [34] [35]. This could be counteracted with the use of scavenging devices such as carbon filters, placed through hoses in the exhaled gas outlet from the anesthesia breathing circuits or in the waste gas outlet of the anesthesia machine. Technologies are currently being developed and refined to capture and destroy scavenged agents, thereby further reducing their atmospheric release [36]. The possibility of rescuing them again is also actually being considered, extracting them from these carbon filters where they remain trapped, in order to be reused, achieving recycling in the form of a circular economy (CONTRAfluran™) [37]. Furthermore, we should always consider to use low oxygen/air flows, appropriate for the delivery system used [38].

In our study, regardless of anesthetic agent used, up to 20% of children experienced POMBC during the first two weeks after surgery. This is in line with previous studies that also used PHBQ to assess POMBC after day case surgery [39]. POMBC appears to be a limited phenomenon, as 30 days after surgery all children had recovered from POMBC. However, it is unclear whether these young patients could develop phobias, post-traumatic stress disorders and/or other long-term behavioral changes. We did not find association between the occurrence of ED and POMBC, suggesting that POMBC etiology is multifactorial. Other factors, such as previous healthcare experiences, were not analyzed in our study and may have influenced POMBC development. Future research may determine whether ED has long-term sequela in children, as currently there is no evidence on this.

6. Conclusion

In order to reduce ED and its consequences in children**,** it is advisable to identify patients at risk and take preventive measures, such as reducing preoperative anxiety, controlling postoperative pain and providing a single bolus of propofol intraoperatively. Selecting desflurane for anesthetic maintenance allows a faster recovery and is as safe as sevoflurane, including postoperative behavioral disorders. Although desflurane did not statistically decrease ED incidence as compared with sevoflurane, patients who were agitated with desflurane were qualitatively less disoriented and disconnected from their surroundings.

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Conflicts of Interest

F. Reinoso-Barbero has collaborated with Baxter as instructor in courses of Clinical Management of Desflurane in Children. This collaboration started after the finalization of this clinical trial.

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