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SCIENTIFIC ARTICLE

Risk factors associated with anesthesia emergence delirium in children undergoing outpatient surgery



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KEYWORDS

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Abstract

Introduction: Anesthesia emergence delirium is a self-limiting clinical phenomenon very common in children. Although pathophysiology is still uncertain, some factors seem to be involved, such as rapid awakening in an unknown environment, agitation during anesthetic induction, preoperative anxiety, environmental disorders, use of preanesthetic medication, use of inhalational anesthetics, and postoperative pain.

Objective: To determine the prevalence and risk factors associated with anesthesia emergence delirium in children undergoing outpatient surgery.

Methods: A prospective observational study was carried out with 100 children aged 2–10 years, who underwent surgery on an outpatient basis. The study variables were: anesthesia emergence delirium and the associated risk factors (preoperative anxiety, child impulsive behavior, use of pre-anesthetic medication, traumatic induction, type of anesthesia, and postoperative pain). Multivariate Poisson's logistic regression was used to analyze the possible explanatory variables, where the prevalence ratios were estimated with the respective 95% confidence intervals, considering a significance level of 5%.

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Results: Delirium and pain were observed in 27% and 20% of children, respectively. Only postoperative pain after Poisson's regression, was shown to be associated with anesthesia emergence delirium, with a prevalence ratio of 3.91 ($p < 0.000$).

Conclusion: The present study showed 27% prevalence of anesthesia emergence delirium in the study population. The incidence of anesthesia emergence delirium was higher in children who had postoperative pain.

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PALAVRAS-CHAVE

Dor;
Criança;
Delírio

Fatores de risco associados a delírio no despertar da anestesia em crianças submetidas à cirurgia ambulatorial

Resumo

Introdução: Delírio ao despertar anestésico é um fenômeno clínico autolimitado muito comum em crianças. Apesar de fisiopatologia ainda incerta, alguns fatores parecem estar envolvidos, como despertar rápido em um ambiente desconhecido, agitação durante a indução anestésica, ansiedade pré-operatória, perturbações ambientais, uso de medicação pré-anestésica, uso de anestésicos inalatórios e dor pós-operatória.

Objetivo: Determinar a prevalência e os fatores de risco associados ao delírio ao despertar anestésico em crianças submetidas à cirurgia ambulatorial.

Métodos: Estudo observacional prospectivo, envolveu 100 crianças entre dois e 10 anos, submetidos à cirurgia em caráter ambulatorial. As variáveis de estudo foram: delírio ao despertar anestésico e os fatores de risco associados (ansiedade pré-operatória, comportamento impulsivo da criança, uso de medicação pré-anestésica, indução traumática, tipo de anestesia e dor pós-operatória). Foi feita a regressão multivariada de Poisson para análise das possíveis variáveis explanatórias, na qual foram estimadas as razões de prevalência com os respectivos intervalos de confiança de 95%, considerou-se o nível de significância de 5%.

Resultados: Delírio e dor foram observados em 27% e 20% das crianças respectivamente. Apenas a dor no pós-operatório, após a regressão de Poisson, mostrou ter uma associação com o delírio ao despertar anestésico, cuja razão de prevalência foi 3,91 ($p < 0,000$).

Conclusão: O presente estudo evidenciou uma prevalência de delírio ao despertar anestésico de 27% na população estudada. A incidência de delírio ao despertar anestésico foi maior em crianças que apresentaram dor no pós-operatório.

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Introduction

Anesthesia emergence delirium (AED) is a transient state of irritation and dissociation, which occurs after discontinuation of anesthesia in some patients and is not responsive to consolation. Also known as post-anesthetic delirium, it is characterized by mental confusion, irritability, disorientation, inconsolable crying, and prolonged post-anesthetic recovery time.¹⁻³

AED incidence varies widely according to its definition, patient's age, anesthetic technique used, surgical procedure, and use of adjunctive medication. The rates usually range from 10% to 50%, and it may affect up to 80% of patients.¹⁻⁵

It is believed that this phenomenon occurs most commonly in children from 2 to 5 years old, who undergo

relatively painful surgical procedures under general inhaled anesthesia.⁶ Regarding the associated factors, many have been suggested as possible triggers of AED, such as rapid awakening in an unknown environment, agitation during anesthetic induction, preoperative anxiety, airway obstruction, environmental disorders, use of pre-anesthetic medication, anesthetic technique, type of anesthetic used (inhaled, venous), and postoperative pain.^{5,7,8}

Although self-limited and of short duration, the occurrence of AED predisposes the child to traumatic injuries in the early postoperative period and produces intense anxiety in parents and, therefore, it is a cause of concern for anesthesiologists and pediatric surgeons.⁶⁻¹⁰

In view of the above, the purpose of this study was to determine the prevalence and risk factors associated with AED in children undergoing outpatient surgery.

Methods

A prospective, observational cohort study that involved 100 patients between 2 and 10 years of age, undergoing surgery in the outpatient block of the Institute of Integral Medicine Professor Fernando Figueira (IMIP), Recife, Pernambuco, Brazil, from 2013 to 2015. The study was previously approved by the Institutional Research Ethics Committee, and patients were only included after written informed consent and children's statement of assent was given by those responsible.

Children who underwent ambulatory anesthesia were included. Children with neurological disease, musculoskeletal disease, and taken neuroleptic drugs preoperatively were excluded. All children received inhaled anesthesia with sevoflurane and nitrous oxide and were kept under face mask or laryngeal mask, at the discretion of the anesthetist.

The Epi-Info 3.5.1 Statcalc software was used for sample size calculation based on relevant literature data; considering a prevalence of 18.18% DPO with $\pm 8/10\%$ range and 95% confidence interval, we found a sample size of 100 children.¹¹

In addition to the demographic variables (sex and age), data on children's impulsive behavior; use of pre-anesthetic medication; preoperative anxiety; traumatic induction; type of induction and maintenance of anesthesia; type of surgery; duration of anesthesia; use of propofol, opioids, and analgesics; occurrence of AED and postoperative pain were collected.

Anxiety was defined according to the modified Yale Preoperative Anxiety Scale (EAPY-m),¹² consisting of five domains that contemplate the child's relationships with the environment (activity and state of apparent awakening), vocalization, emotional expressiveness, and interaction with parents.¹³ In total EAPY-m score calculation, a partial score based on the observed score divided by the number of categories in that domain is assigned to each domain. The score of each domain is added to the others and multiplied by 20 and considered positive if the achieved values are greater than 30.

As for AED, the Pediatric Anesthesia Emergence Delirium (PAED) was used,¹⁴ a validated scale for the Portuguese language and reliable to measure this phenomenon. This scale consists of five items and considers whether the child makes contact with the caregiver's eyes, whether they have deliberate and decisive actions, whether they are aware of their surrounding environment, whether they are restless and inconsolable. AED was considered as values greater than 10 in the PAED scale.

Pain was measured using the Hanallah scale, which quantifies changes in systolic blood pressure before and after the procedure, crying, movement, agitation, and verbalization of children. Postoperative pain was considered as values higher than 6 on the Hanallah scale.¹⁵

Impulsive behavior was defined from the observation of parents, who defined the children as aggressive or not. Traumatic separation was defined as the occurrence of inconsolable crying on the part of the child, need of force to be withdrawn from the parents' lap, and traumatic induction, such as need of force to apply the mask for anesthetic induction.

Statistical analysis

Data analysis was performed using the Stata package version 12.1. For most numerical variables, mean and its respective standard deviations were used. For the age variable, since there was no normal distribution (Shapiro–Wilk test), median and range (min–max) were used as a measure of central tendency. For analysis purposes, the age variable was categorized in infants (below 2 full years), preschool (from 2 to 5 full years), and school (over 5–10 full years). Fisher's exact test was used for this variable (one of the expected values was less than 5). Odds ratio (OR) was calculated for the various outcomes, as well as its 95% confidence interval.

Poisson regression was performed: first, all variables considered important (preoperative anxiety, aggressive behavior, traumatic separation, traumatic induction, pain, and categorized age) were placed in the model and sequentially removed; second, only variables with significance level of 20% were maintained. At the end, only those variables that remained significantly associated with the outcome were selected and the 5% level was considered.

Results

One hundred patients between 2 and 10 years of age were invited to participate in the study. Of these, none refused and there were no losses after starting data collection.

Clinical and socio-demographic characteristics of patients are shown in Table 1. The sample studied had a mean age (\pm SD) of 4.1 years and 66% were male. Regarding type of surgery, hernia repair was predominant, followed by genitourinary procedures. About half of the children were classified by their parents as having aggressive behavior and 41% were anxious.

Induction and maintenance of anesthesia were performed through inhalation valve, by appropriate coupling of the facial mask with gradual increase of sevoflurane until reaching minimum anesthetic concentration (MAC) values between 2% and 3%, using such levels for anesthetic

Table 1 Demographic characteristic of children undergoing outpatient surgery at IMIP.

Variables	<i>n</i> = 100
Age-years-median (min–max)	4.1 (2–5)
Male- <i>n</i> (%)	66 (66)
Type of procedure- <i>n</i> (%)	
Herniorrhaphy	38 (38)
Genitourinary	32 (32)
Herniorrhaphy associated with genitourinary procedure	7 (7)
Correction of branchial cleft or thyroglossal cyst	23 (23)
Impulsive behavior- <i>n</i> (%)	50 (50)
Pre-anesthetic medication- <i>n</i> (%)	3 (3)
EAPY-m-mean (SD)	35.3 (4.01)
Anxiety- <i>n</i> (%)	41 (41)

SD, standard deviation; EAPY-m, Modified Yale Preoperative Anxiety Scale; *n*, numbers.

Table 2 Descriptive data of postoperative results.

Variables	n = 100
Hanallah scale-mean (SD)	2.3 (2.53)
Pain n (%)	20 (20)
PAED-mean (SD)	6.17 (4.3)
Delirium n (%)	27 (27)

SD, standard deviation; Hanallah scale, pain rating scale; PAED, Pediatric Anesthesia Emergence Delirium.

maintenance; 50% nitrous oxide (N₂O) was added during induction and maintenance of anesthesia.

Only 3% of children received preanesthetic medication. Peripheral blockade was used to control postoperative pain in 82% of children and in only 4% of them complementary opioid was used. In 97% of the sample, early analgesia was performed with dipyrone; the remaining 3% were excluded due to allergic contraindications. In 53% of cases, those responsible for the children were present in the anesthesia recovery unit on awakening.

Table 2 shows that the frequency of pain and delirium was 20% and 27%, respectively, and the mean Hanallah and PAED scores were 2.3 (2.53 SD) and 6.17 (4.3), respectively.

Bivariate analysis (Table 3) showed no association of AED with any of the clinical and socio-demographic variables studied in Table 1. Likewise, we found no association between AED and preoperative anxiety ($p=0.781$), traumatic separation ($p=0.135$), use of force at induction ($p=0.259$), and preschool age ($p=0.921$). However, a significant association was found between AED and impulsive behavior ($p=0.043$) and postoperative pain ($p=0.001$). However, after multivariate analysis of risk factors using the Poisson model, we identified only one explanatory variable: postoperative pain, whose odds ratio was 3.91 (2.15–7.11; $p<0.001$).

Discussion

AED and pain were seen in 27% and 20% of children, respectively. There was no association of delirium with preoperative anxiety, traumatic separation, use of force at induction, and preschool age. In bivariate analysis, impulsive behavior and pain were associated with AED; however in multivariate analysis using the Poisson regression model

only one variable remained statistically significant: postoperative pain.

Emergence delirium (ED) is a well-documented clinical phenomenon, mainly in children, studied since the 1960s.^{16,17} It is still considered a mysterious complication that occurs after pediatric anesthesia and, although the pharmacology of fast acting volatile agents such as sevoflurane and desflurane, is highly suspect in this complication genesis, no strong evidence has been published to support this hypothesis. In fact, it is believed that multiple factors are related to this event, such as rapid return to consciousness in unfamiliar environment, agitation during anesthetic induction, preoperative anxiety, environmental disorders, use of pre-anesthetic medication, use of inhaled anesthetics, postoperative pain, and preschool age.^{14,18–20}

Data obtained in this study suggest that postoperative pain favors the incidence of ED. In fact, most literature evidence points to a strong association between these two factors.^{21–23} The reason for this association, as well as the pathophysiology of AED, remains to be elucidated. One possible explanation would be that any condition capable of interfering with brain conduction would make the brain vulnerable, impair brain activity and favor the emergence of neurological manifestations after surgery. A recent systematic review suggests that future well-conducted studies should be conducted to ensure that pain is a contributory or confounding factor in AED diagnosis.²⁴ In our study, specifically, two validated scales were used in an attempt to make an adequate differential diagnosis between these two conditions, in addition to the multivariate analysis, in order to control the confounding factors.

In line with it, a recent study found a lower incidence of agitation with intraoperative intravenous ketorolac in minor ENT surgeries, in which the analgesic drug peak effect occurred after awakening.²⁵ Likewise, a study with two groups of patients undergoing inhaled anesthesia with sevoflurane for non-surgical procedures showed that the use of dexmedetomidine intraoperatively reduced the incidence of AED by more than 40%.²⁶ However, in contrast, another study reported a high incidence of agitation upon awakening in patients undergoing general anesthesia under caudal block that determined effective analgesia, which raised the theory that even when postoperative pain is efficiently treated or absent, postoperative agitation may occur.²⁷

Table 3 Distribution of patients according to variables of interest and occurrence of AED.

Variables	AED		Bivariate analysis	
	Yes n (%)	No n (%)	Odds ratio (95% CI)	p
Preoperative anxiety (n = 41)	13 (48.15)	28 (38.36)	1.25 (0.76–2.04)	0.781 ^a
Impulsive behavior (n = 50)	18 (66.67)	32 (43.84)	1.52 (1.04–2.21)	0.043 ^a
Traumatic separation	10 (37.04)	30 (41.10)	0.88 (0.44–1.73)	0.135 ^a
Use of force at induction	18 (66.6)	44 (61.1)	1.19 (0.59–2.38)	0.259 ^a
Pain	14 (51.85)	6 (8.22)	4.3 (2.41–7.67)	<0.001 ^a
Preschool age	14 (51.85)	41(6.16)	0.73 (0.44–1.2)	0.921 ^b

AED, anesthesia emergence delirium.

^a Qui-quadrado.

^b Fisher exact test.

Regarding rapid awakening volatile agents, it is believed that since its introduction AED disorders have become more frequent, with percentages that may range from 18% to 20%.^{24,28-30} In our study, we could not evaluate the association between sevoflurane and AED because all patients received this volatile anesthetic agent for induction and maintenance of anesthesia.

Moreover, we found no association between AED, preoperative anxiety, and preschool age, which contradicts the literature data, which believe that this phenomenon is more frequent in highly anxious and younger children (between 2 and 5 years of age).^{4,28,31} The explanation for the higher frequency of AED in preschoolers would be that this particular group of children has exacerbated emotional lability when faced with a stressful situation in a strange environment. Furthermore, areas of the hippocampus are still physiologically immature and favor cerebral instability.²⁷

Regarding preoperative anxiety, it is believed that high scores are predictive of adverse neurological events following anesthesia, such as agitation upon awakening and behavioral changes. Research with 791 children showed that the risk for agitation upon awakening increases by 10% for each 10-point increase in the children's preoperative anxiety evaluation score.³² Likewise, it is believed that children with impulsive behavior, less sociable, and whose parents are more anxious belong to another risk group and are more likely to develop AED.³³ However, in our study, specifically, these two associations were not proven.

In fact, in bivariate analysis, we observed a positive association between impulsive behavior and AED, but after multivariate analysis this could not be proven, which suggests that this phenomenon needs to be further investigated.³⁴

AED is a frequent complication and requires new and well-conducted studies to more accurately establish the related risk factors. However, in our study, postoperative pain arises with a phenomenon related to AED and, therefore, it seems reasonable to believe that strategies for AED prevention and therapy should particularly include pain control.

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This study (entry number: 3.576) was approved by the Human Research Ethics Committee of the Instituto de Medicina Integral Prof. Fernando Fig (IMIP) on November 14, 2012, under the number 3130-12.

Conflicts of interest

The authors declare no conflicts of interest.

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