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ORIGINAL INVESTIGATION

The impact of emergence delirium on hospital length of stay for children who underwent tonsillectomy/ adenotonsillectomy: an observational retrospective study

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Abstract
Background: Emergence Delirium (ED) is a combination of disturbance of perception and psychomotor agitation that is common in pediatric patients after general anesthesia, especially at preschool age. Since the effect of ED on the length of stay has been studied in adults but infrequently in children, the aim of this study was to investigate the relationship between ED and length of stay in this population.
Methods: A single center, retrospective, observational study was carried out in children who underwent tonsillectomy or adenotonsillectomy. The Pediatric Anesthesia Emergence Delirium (PAED) scale was used to assess ED. In addition to the time to hospital discharge (time frame 24 hours), drugs used, comorbidities, early postoperative complications, and pain were investigated if potentially associated with the complication.
Results: Four hundred sixteen children aged from 1.5 to 10 years (183 female, 233 male) were included. ED occurred in 25.5% of patients (n = 106). Patients were divided into the ED group and the No-ED group. The discharge time was similar in both groups. No significant differences were observed in the frequency of postoperative complications. The use of fentanyl or dexmedetomidine did not affect ED occurrence. The frequency of pain was greater in the ED group, both in the recovery room and in the ward (p = 0.01).

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Conclusions: The occurrence of ED in children after tonsillectomy/adenotonsillectomy did not extend the length of stay.

Introduction

Despite improvements in anesthetic and surgical approaches, emergence delirium (ED) remains an important postoperative concern. This clinical condition is characterized by a combination of disturbance of perception and psychomotor agitation during early emergence from anesthesia. It is common in pediatric patients after general anesthesia (GA), especially at preschool age.[1-3] The reported prevalence in children differs among studies as it ranges from 10% to 80%.[4,5] This variability can be partially explained by the difficulty in definition and different tools used, and study design. These discrepancies also regard the clinical setting investigated. For instance, a higher incidence was reported in the setting of otorhinolaryngology (ENT).[6]

While in children ED is usually self-limiting with a benign course, it can increase the risk of self-harm and parental stress. Further, a special issue concerns the potential consequences of ED such as long-term outcomes in cognitive function, and psychological implications including but not limited to effects on food and sleeping disorders, or separation anxiety.[7-9]

Another aspect regards the correlation between ED and pain. Although their relationship is not clear, it seems that in children they are often present simultaneously. Somaini et al.,[10] for instance, found that in the early postoperative, ED and pain are associated in up to 65% of patients.

The effect of ED on the length of stay was studied in adults but infrequently in children. In a study, the authors found that ED and hypoactive emergence in adults were associated with increased costs and a greater frequency of perioperative complications. In turn, longer postanesthesia care unit (PACU) time and protracted length of stay were demonstrated.[11] In children, Pieters et al.[12] studied ED in different regimens of GA and showed that PACU time and length of stay were not influenced by the anesthesia strategy used.

On these premises, this study aimed at evaluating the occurrence of ED in pediatric patients undergoing tonsillectomy or adenotonsillectomy. The hypothesis that children with postoperative ED stay in the hospital longer than those without the complication was investigated.

Methods

This single center retrospective observational study involved children who underwent tonsillectomy or adenotonsillectomy surgery between November 2014 and September 2017. The investigation was conducted at the IRCCS Istituto Giannina Gaslini, Genova, Italy after approval by the institutional Ethics Committee (protocol number 048/2018).

This analysis included children aged 1.5—10.1 years with an American Society of Anasthesiologists (ASA) physical status $\leq$ III. Children with any type of neurological disability or psychiatric disorders or receiving therapy with psychotropic or antiepileptic drugs were excluded. Cases with missing or incomplete data in the medical record were not included in the analysis.

Endpoints

The primary endpoint of this study was to evaluate the occurrence of ED and its impact on length of stay in pediatric patients undergoing tonsillectomy or adenotonsillectomy. Since children who undergo tonsillectomy or adenotonsillectomy usually have a 24-hour hospital stay, the "discharge time" referred to this time frame.

As secondary endpoints, the incidence and severity of the adverse events in the immediate postoperative period and the incidence and degree of postoperative pain were evaluated.

Emergence delirium and pain assessment

In this retrospective investigation, the pediatric anesthesia emergence delirium (PAED) tool for evaluating ED was used.[13] During the postoperative monitoring in the PACU, the PAED scale was used 3 times, every 10 minutes, by a dedicated nurse. In the data collection, the PAED value taken into consideration was the highest obtained in the three evaluations. On the ward, the PAED tool was administered only once in the first hour after returning from the PACU.

The Face, Legs, Activity, Cry, Consolability scale (FLACC scale) or the Numeric Rating Scale (NRS) were used to evaluate the severity of postoperative pain.

General anesthesia

The anesthesia procedure was the same in all cases. Anesthesia was induced with O_2 (40%), N_2O (60%), and Sevoflurane through a face mask. Standard anesthesia monitoring was applied. Fentanyl (1—2 mcg.kg^{-1}) or dexmedetomidine (1—2 mcg.kg^{-1}), propofol (3 mg.Kg^{-1}), dexamethasone (0.3 mg.kg^{-1}) and rocuronium (0.6 mg.kg^{-1}) were administered intravenously (IV). Patients were supine throughout the procedure. Orotracheal intubation was performed with a cuffed tracheal tube. Mechanical ventilation was started with a small tidal volume (6 ml.kg^{-1}), a positive-end expiratory pressure setting of 4—5 cmH_2O, and a FiO_2 targeted to maintain a peripheral oxygen saturation (SpO_2) level > 95% and end-tidal carbon dioxide level of 35—40 mmHg. Anesthesia was maintained with 1 MAC Sevoflurane and opioids (fentanyl 1—2 mcg.kg^{-1} or remifentanil 0.25—0.30 mcg.kg^{-1}. min^{-1}). Heart rate (HR) and noninvasive blood pressure (NIBP) were recorded every 5 minutes. For preemptive analgesia, paracetamol (15 mg.kg^{-1} IV) was administered to all the patients immediately after orotracheal intubation.

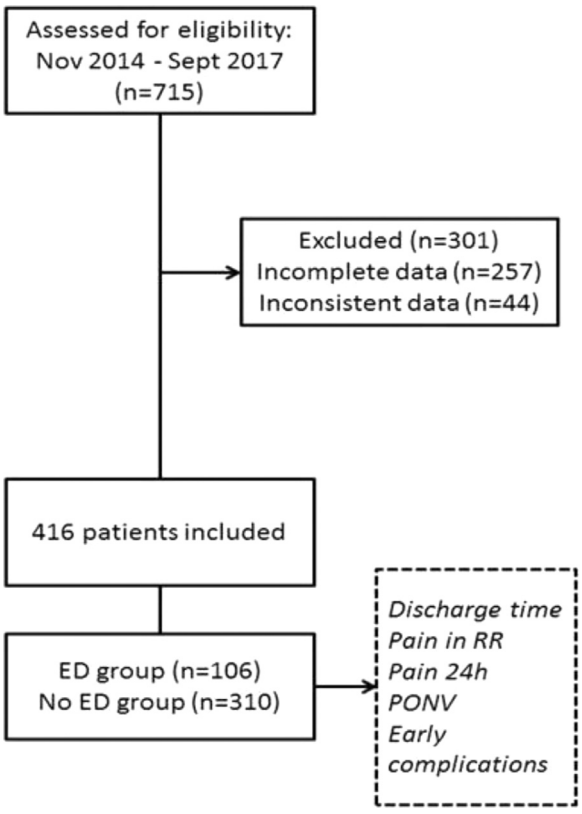

Figure 1 Study flow chart.

Postanesthesia care unit

At the end of the surgical procedure, patients were transferred to the PACU for 30-minute monitoring (HR, electrocardiogram, SpO_2, NIBP, pain evaluation). The occurrence of ED was recorded. The presence and the severity of cardiovascular complications including bradycardia, tachycardia, hypotension, hypertension, desaturation episodes, and laryngospasm were documented. The pain intensity was graded in the PACU and while the patient was in the ward (24 hours).

Complications were defined as adverse events if not related to the preoperative surgical condition.[14,15] Specific complications were classified as: Bradycardia: reduction of HR below 20% compared to baseline (detected at anesthesia induction); Tachycardia: increase in HR rate above 20% compared to baseline (detected at anesthesia induction); Hypotension: reduction of systolic blood pressure below 20% compared to baseline (detected at anesthesia induction); Hypertension: increase in mean arterial pressure above 20% compared to baseline (detected at anesthesia induction); Desaturation: SpO_2 reduction below 90% of the baseline value for more than 15 seconds; Emergence delirium: assessed within 30 minutes after awakening (score $\geq$ 10 at the PAED scale evaluation). Pain: score $\geq$ 4 for both FLACC or NRS scale.

Statistical analysis

Descriptive statistics were generated for the whole cohort and data were expressed as mean and standard deviation (SD), median and range for continuous variables, and as absolute or relative frequencies for categorical variables. The distribution of the data was analyzed by employing the Kolmogorov-Smirnov test. Differences between groups were evaluated with Student's *t*-test for continuous variables and with $\chi 2$ or Fisher's exact test for categorical variables. Pearson correlation coefficient was used.

A p-value < 0.05 was considered statistically significant, and all p-values were based upon two-tailed tests. Statistical analysis was performed using SPSS for Windows (SPSS Inc, Chicago, Illinois USA).

Results

In this retrospective analysis, 715 patients were assessed for eligibility. Three hundred and one were excluded for incomplete data (n = 257) or inconsistent data (n = 44). Finally, 416 children aged from 1.5 to 10.1 years (183 female, 233 male) were included (Fig. 1). Patients' characteristics are reported in Table 1. ED occurred in 25.5 % of patients (n = 106).

All patients included in the analysis were divided into two groups: the ED group and the No-ED one. There were no significant differences between the groups in terms of gender and ASA (American Society of Anesthesiologists) physical

Table 1 Patient characteristics and intraoperative data.

		All n = 416	Delirium n = 106	No Delirium n = 310	*p*-value
Gender, F/M	n	183/233	46/60	137/173	0.91
Age at surgery, years	Mean ± SD	4.6 ± 1.4	4.3 ± 1.3	4.7 ± 1.4	**0.01**
	Median (range)	4.3 (1.5–10.1)	4.3 (1.7–8.1)	4.9 (1.5–10.1)	
Weight, kg	Mean ± SD	18.1 ± 4.6	16.9 ± 4.3	18.4 ± 4.7	**0.004**
	Median (range)	17 (9.5–40)	17 (9.5–36)	18 (11–36)	
Clinical features					
ASA I		209 (50.2)	47 (44.3)	162 (52.3)	0.31
ASA II		202 (48.6)	57 (53.8)	145 (46.9)	
ASA III		5 (1.2)	2 (1.9)	3 (1)	
OSAS n (%)		130 (31.3)	42 (39.6)	88 (28.4)	**0.04**

ASA, American Society of Anesthesiologists physical status; OSAS, Obstructive Sleep Apnea Syndrome.

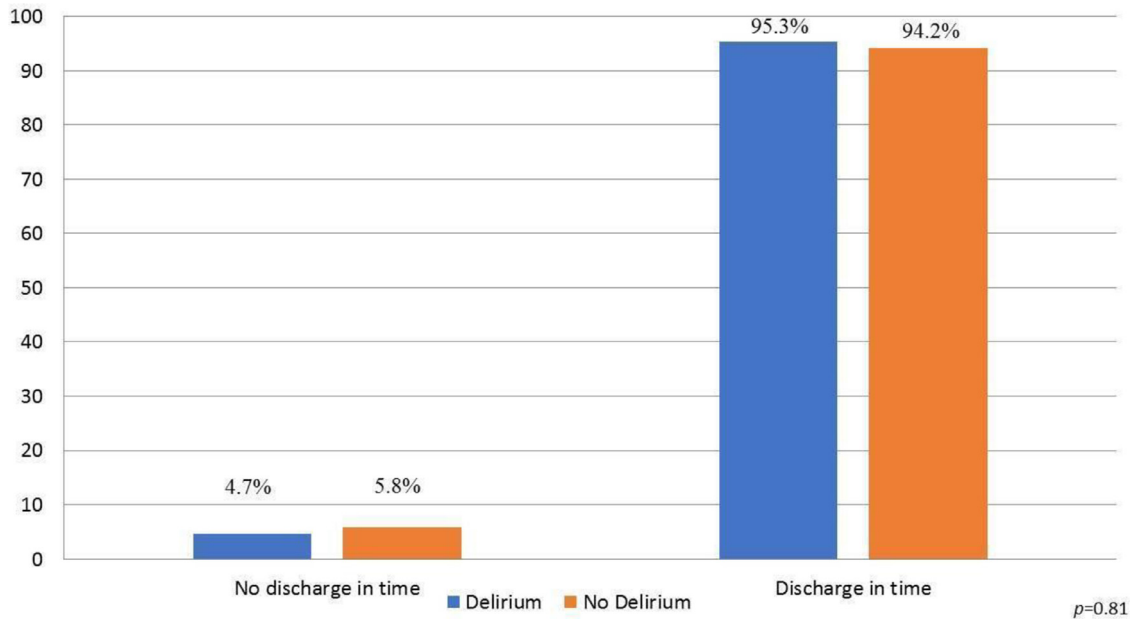

Figure 2 Duration of hospitalization in ED patients.

status, while the children without ED were statistically older and weighed more at the time of surgery (Table 1).

With regard to the primary outcome, the duration of hospitalization was not statistically different between the two groups. The discharge time occurred in 95.3% of ED group and 94.2% in those who were not affected by the complication ($p = 0.81$) (Fig. 2).

Concerning clinical data, about 40% of patients who experienced ED suffered from obstructive sleep apnea syndrome (OSAS) whereas in the No-ED group only 28.4% presented OSAS ($p = 0.04$) (Table 1).

These OSAS/no-OSAS subgroups were further analyzed. It was found that dexmedetomidine was administered in almost 70% (200/286; 69.9%) in no-OSAS patients, versus 53.8% (70/130) in OSAS patients ($p = 0.002$).

Duration of surgery was similar in the two groups while awakening time in children with ED was significantly less than in those without ED (25 ± 10.1 vs. 27.4 ± 10.8, $p = 0.05$). Increased length of stay at the PACU was observed in the No-ED group ($p < 0.05$) (Table 2).

About the drug used, the difference in the incidence of ED between the patients that used fentanyl or dexmedetomidine was not significant ($p = 0.72$).

The rate of complications in both groups was similar. Compared to those without pain, the number of children manifesting ED and pain was higher in the PACU ($p = 0.01$) and in the first 24 postoperative hours ($p = 0.01$).

No significant differences were found on postoperative nausea and vomiting (PONV) (Table 3).

Discussion

In the adult population, ED is a well-known complication that influences length of stay, mobility, and mortality during the perioperative period. On the other hand, in children, while several studies investigated the effects of ED on length of stay in the PACU, there is not enough evidence to determine the role of the complication on the duration of hospitalization.[16] Probably, many gaps that exist on the phenomenon are related to the lack of complete knowledge on the mechanisms of emergence from GA.[17] In our retrospective analysis, conducted in a setting of children who underwent tonsillectomy/adenotonsillectomy, ED did not affect length of stay.

Although the results of the present study found no relationship between ED and length of stay, the analysis showed interesting data. Recent studies highlighted the link between postoperative disturbances in consciousness and attention, and preoperative OSAS.[18] In our retrospective investigation, ED was significantly recorded in OSAS children ($p < 0.05$). Because according to the current recommendation, OSAS children are usually extubated while fully awake,[19] this need could lead to distress manifested by excessive agitation.

Table 2 Surgery data and recovery room stay.

		All n = 416	Delirium n = 106	No Delirium n = 310	*p*-value
Duration of surgery, min	Mean ± SD	19.8 ± 7.2	19.6 ± 6.6	19.8 ± 7.4	0.74
	Median	20 (4–50)	20 (8–50)	18 (4–50)	
RR time, min	Mean ± SD	26.8 ± 10.7	25 ± 10.1	27.4 ± 10.8	**0.05**
	Median	(5–65)	(9–62)	(5–65)	

RR, recovery room.

Table 3 Comparison of postoperative complications between two groups.

	Delirium[a] n = 106	No Delirium[a] n = 310	*p*-value
Bradycardia	8 (7.5)	20 (6.5)	0.66
Tachycardia	10 (9.4)	25 (8.1)	0.68
Hypotension	8 (7.5)	20 (6.5)	0.66
Hypertension	4 (3.8)	9 (2.9)	0.75
Desaturation	17 (16)	47 (15.2)	0.88
Laryngospasm	22 (20.8)	45 (14.5)	0.17
Desaturation in RR	6 (5.7)	19 (6.1)	1
Bradycardia in RR	4 (3.8)	20 (6.5)	0.47
Pain RR	10 (9.4)	9 (2.9)	**0.01**
Pain 24 h	26 (24.5)	43 (13.8)	**0.01**
PONV	7 (6.6)	36 (11.6)	0.19

RR, recovery room; PONV, postoperative nausea and vomiting.
[a] Data expressed as number and percent [n (%)].

We also searched for other possible causes underlying the higher incidence of ED in that subgroup. Of note, there was a correlation with the drugs used, as dexmedetomidine was more often administered to no-OSAS patients (p = 0.002). Since the purpose of a retrospective analysis is to find correlations between various elements investigated in order to translate the results into clinical practice for improving outcomes, this finding seems to be prospectively very important.[20] Further investigations are needed to better dissect the multiple aspects of this phenomenon.

Another important finding concerns the study of the correlation between drugs used and the development of ED. Although in the literature many studies highlighted the potential benefits of dexmedetomidine for preventing ED without delaying emergence from anesthesia, in our retrospective analysis there was no significant difference in the incidence of ED between patients who received fentanyl or dexmedetomidine.[21-23] Even in this case it would be advisable to conduct detailed analysis on larger sample numbers.

The occurrence of ED was not associated to important complications, except pain. The incidence of pain was higher in children who experienced ED compared to those included in the No-ED group. While several investigations demonstrated that preemptive analgesia can reduce the incidence of ED, we found ED in patients with pain despite the use of paracetamol immediately after orotracheal intubation.[24] Probably, pain can play a role in induction of ED, although it may not be the sole cause for explaining this multifactorial phenomenon. For instance, research proved that this complication can manifest despite adequate pain control.[25] Regardless of the precise pathogenic link between ED and pain, the diagnosis of ED in a child with pain remains a great challenge despite the use of PAED. Of note, some of the pain behaviors overlap with those recognized by the PAED tool.[26] This is another gap necessarily to be addressed by research.

Study limitations

This analysis has several limitations. First, because this is a retrospective study, the available data were extracted from medical charts. Moreover, because the analysis encompassed a small cohort of patients in a specific clinical setting, it is not possible to obtain firm conclusions on the phenomenon. Thus, the lack of statistical significance of difference in the primary outcome might be due to insufficient power.

An important limitation is the lack of important data on risk factors for ED such as preoperative anxiety, patient preexisting behavior, and patient and parent interaction with healthcare providers. However, this study was not designed to characterize the risk factors of ED but to assess the impact of the complication on hospital length of stay.

Conclusions

The occurrence of ED can have important clinical implications. In addition to the clinical aspects, ED could increase hospital length of stay and costs. Hospitalization time, indeed, is a hot topic in order to reduce health service costs in pediatrics too. In this study, ED was not associated with prolonged postoperative hospitalization in pediatrics, although the phenomenon was linked to OSAS and an increased occurrence of postoperative pain. Moreover, the small simple size analyzed is a weakness and other large investigations are needed for investigating this paramount point.

Conflicts of interest

The authors declare no conflicts of interest.

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