Original Article

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Postanesthetic Emergence Agitation in Pediatric Patients under General Anesthesia

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Abstract

Objective: Postanesthetic emergence agitation is a common problem in pediatric postanesthetic care unit with an incidence ranging from 10 to 80%. This study was done to determine the prevalence of emergence agitation and associated risk factors in pediatric patients who underwent general anesthesia.

Methods: This cross-sectional descriptive and analytic study was performed on 747 pediatric patients aged 3-7 years that underwent general anesthesia for various elective surgeries at Bou-Ali Sina Hospital in Sari, Iran between January 2010 and January 2011. A non-probability quota sampling technique was used. The presence of emergence agitation was recorded using Pediatric Anesthesia Emergence Delirium Scale. The factors linked with Emergence Agitation were recorded in a questionnaire. The data were analyzed using SPSS software 16 and independent sample t-test, χ^2 and binary logistic regression. *P*-values less than 0.05 were considered as significant.

Findings: One hundred thirty-four (17.9%) children had emergence agitation. The most frequent surgical procedures were ENT surgical procedures 315 (42.2%), abdominal surgery 177 (23.7%), orthopedic surgery 137 (18.3%), urology 97 (13%) and ophthalmic surgery 24 (3.2%). Otorhinolaryngological surgical procedures (P=0.001), pain (P<0.05) and induction behavior of children (P<0.005) were associated with higher rates of post anesthetic emergence agitation (P=0.001).

Conclusion: This study identified the multiple independent risk factors which are associated with emergence agitation in children. To minimize the incidence of postanesthetic emergence agitation, these risk factors should be considered in the routine care by care providers in postanesthetic care unit.

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Introduction

Emergence agitation (EA) was described at first by Eckenhoff et al in the early 1960s. EA has been described as a dissociated state of consciousness in which the child is inconsolable, irritable, uncooperative, typically thrashing, crying, moaning or incoherent[1]. Nowadays, about 4 million children undergo general anesthesia annually and EA has been identified as a significant problem in children at Postanesthetic Care Unit (PACU) with an incidence ranging from 10 to 80%[2]. EA as a postanesthetic problem interferes with child's recovery and presents a challenging situation for post-anesthesia care provider in terms of assessment and

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management[3]. Although, several factors have been identified as etiologies of EA, there is no entire description for emergence agitation. Many different causes have been suggested, such as rapid awakening in an unfamiliar environment, painful events like surgical wounds, agitation on induction, airway obstructions, environmental disturbances, the duration of anesthesia, hyperthermia, hypothermia, type and site of operation, premedication, inhaled and intravenous anesthetics and the anesthetic technique[2,4-6]. Although EA is usually self-limited and occurs within the first 30-minutes of recovery in PACU, but it can last up to 2 days and lead to physical damage, disconnection of intravenous catheters, removing of dressing or drainage tube and monitoring devices. On the other hand, controlling the agitated child needs more nursing care and more post-anesthesia care providers. In addition, administration of sedative and analgesics is associated with increased recovery time and delayed PACU discharge[7-10]. Generally, treatment in all cases mentioned above is directed to the correction of causative agents[11]. Although, numerous medications have been studied to prevent or reduce EA in children, no special preventive method has been shown to be highly superior. So, this cross-sectional descriptive and analytic study had been undertaken to determine the prevalence of EA, evaluate the risk factors associated with and predictive of it, and describe the outcomes related to EA in children aged 3 to 7 years that underwent general anesthesia for elective surgical procedures.

Subjects and Methods

With the approval from the HSR Ethics Committee of Mazandaran University of Medical Sciences and parental informed consent, this cross-sectional descriptive analytic study was performed on 747 children aged 3-7 years with ASA physical status I-II who underwent elective surgery at Bou-Ali Sina Hospital in Sari, northern Iran, between January 2010 and January 2011. A nonprobability, quota sampling technique was used. The children enabled to localize the pain, undergoing regional anesthetic technique, recovery time less than 10 minutes, and history of neurological or cardiovascular disorders were excluded. All perioperative routine care was performed under supervision of an anesthesiologist or other physicians and care providers. The data were recorded in a questionnaire including four separated parts; the first part included the demographic characteristics and the three remaining parts included the behavioral criteria of EA and related factors in pre-anesthetic, during anesthesia, and post- anesthetic period in PACU.

At pre-anesthetic period, the child's behavior during separation from his parents and at the time of induction of general anesthesia was graded as calm/cooperating, slightly anxious/fearful, or restless/uncooperative and recorded at presence of an anesthesiologist. The presence or absence of behavior was recorded by yes/no into the questionnaire. Perioperative medications, induction and maintenance of anesthetic agents, duration of anesthesia, time of awakening (namely, time from anesthetic off to time of initial arousal) were recorded. During PACU, all routine monitoring was performed and all emergence behaviors were observed and recorded by a trained nurse using the reliable and valid Pediatric Anesthesia Emergence Delirium (PAED) scales (Table 1)[12]. Then the answers of each item were converted into scores and summed together and considered as PAED score; the higher the score, the more agitated child. A cutoff ≥12 was considered as presence of EA[13].

Differentiating EA from the symptoms of postoperative pain was done using FLACC behavioral scales with five categories including Face, Legs, Activity, Cry and Consolability[14]. Each of the five categories was scored from 0-2, resulting in a total between 0 and 10. The results of FLACC scale were interpreted as follows: 0 = Relaxed and Comfortable; 1-3 = Mild discomfort; 4-6 = Moderate pain; 7-10 = Severe pain or discomfort or both.

Also, all the pharmacologic and non-pharmacologic interventions, undesired side effects and time of discharge from recovery, and physical disturbances were recorded. The patients have been discharged according to PACU discharge criteria with routine practice and at the discretion of the PACU nurse.

Also, the questionnaire has been shown to have

Table 1: Pediatric Anesthesia Emergence Delirium (PAED) scales

Point	Description of Items	Scoring				
		not at all	just a little	quite a bit	very much	extremely
1	**The child makes eye contact with the caregiver**	4	3	2	1	0
2	**The child's actions are purposeful**	4	3	2	1	0
3	**The child is aware of his/her surroundings**	4	3	2	1	0
4	**The child is restless**	0	1	2	3	4
5	**The child is inconsolable**	0	1	2	3	4

validity in a variety of studies and populations[13,14], and reliability of the questionnaire has been approved via a pilot study and Cronbach's Alpha equal to 0.76 was obtained.

Data were analyzed using SPSS software 16 and independent sample t-test, χ^2 and binary logistic regression. *P*-values less than 0.05 were considered as significant.

Findings

Seven hundred forty- seven children aged 3-7 years with ASA class I-II were enrolled over a one year period. One hundred thirty four children (17.9%) had EA. From total, 479 (64.1%) were males and 268 (35.9%) females. The mean age of the patients was 4.89±1.42 years. From 134 patients with EA, 89 (11.9%) were males and 40 (6.0%) females (*P*>0.05). The previous history of surgery and medical diseases were seen in 22 (2.9%) and 8 (1.1%) patients, respectively (*P*>0.05).

The mean duration of anesthesia was 34.40±28.46 minutes. The incidence of EA was higher in operative procedures less than one hour duration (*P*=0.022). The mean of awakening time from anesthesia in EA and non-EA patients was 6.20±2.98 and 4.85±4.06, respectively. A significant relationship was observed between mean of awakening time from anesthesia and incidence of EA (t=3.601 df=742, *P*<0.05).

The most frequent surgical procedures were ENT 315 (42.2%), abdominal surgery 177 (23.7%), orthopedic surgery 137 (18.3%), urologic surgery, 97 (13%) and ophthalmic surgery 24 (3.2%), respectively. Otorhino-laryngological surgical procedures were associated with higher rates of EA (*P*<0.05) (Table 2). The most sites operated on were the head and neck areas (45.6%), trunk (22.4%), extremities (18.1%) and pelvic area (13.9%). There was significant statistical relationship between the site of operation, and frequency of EA (*P*<0.05). This relationship was higher in the head and neck surgery (*P*<0.05) [OR: 0.34, CI95% (0.23-0.50)]

Temper tantrum was seen in 620 children (83.1%) and 99 (13.3%) of them experienced EA (*P*=0.003). From 191 children (25.6%) with history of anxiety, 36 (4.8%) had EA (*P*> 0.05). Among the 94 (12.6%) of children with different degrees of pain at PACU, 61 (8.2%) had presented EA (*P*<0.05). Also, the incidence of EA was higher in children with FLACC scored 1-3 (*P*<0.05).

There was no relationship between behavioral separation of the patients and EA (*P*>0.055), but their induction behavior had significant relationship with EA in PACU (*P*<0.005) (Table 3).

Table 2: The relationship between type of surgical operation and presence of EA

Surgical operations	Presence of EA [n(%)]		*P.* Value
	Yes	No	
ENT (n=315)	11.4 (85)	230 (30.8)	<0.001
Ophthalmology (n=24)	5 (0.7)	19 (2.5)	0.7
Urology (n=97)	16 (2.1)	81 (10.8)	0.7
Orthopedics (n=137)	11(1.5)	126 (16.9)	0.001
Abdominal (n=177)	17 (2.3)	160 (21.4)	0.001

EA: Emergence agitation

Table 3: Relationship between children's behavior in separation and induction times and EA

Behavior	EA	Calm & cooperate n (%)	slightly anxious & fearful: n (%)	Restless & un-cooperative: n (%)	*P.* Value
Separation's Behavior	Yes	7 (0.9)	104 (13.9)	23 (3.1)	0.1
	No	27 (3.6)	520 (69.6)	66 (8.8)	
Induction's Behavior	Yes	96 (12.9)	33 (4.4)	5 (0.7)	0.001
	No	535 (71.8)	70 (9.4)	6 (0.8)	

EA: emergence agitation

Table 4 shows the relationship between the anesthetic agents and the presence of EA. As shown in the Table, isoflurane and atracurium had the highest relationship with incidence of EA (P<0.05). The relationship was also significant with sufentanil and ketamine (P<0.05). The logistic regression analysis of the factors that had a significant effect on the incidence of EA, revealed that two factors; pain and children's induction behavior were associated with the increased incidence of EA from anesthesia (Table 5).

Discussion

Postoperative emergence agitation, also known as emergence delirium in international literature is a well-known clinical phenomenon with an incidence ranging 10-80%[15]. Recognizing the risk factors for EA is very important to minimize the contributing factors and managing EA appropriately.

We investigated multiple risk factors associated with EA such as the patient and surgical related factors, as well as anesthesia related risk factors such as rapid emergence and type of anesthetics. The incidence of EA in our study was 17.9% based on PAED score of ≥12. Most of EA occurred within the first 30 minutes of recovery at PACU. This finding is compatible with results obtained from previous studies[2,10].

The present study showed that the children aged 4-6 years had a higher incidence of EA compared to children aged 7 years. It may be due to less psychological and physiological immaturity of young-aged children compared to school-aged children being less able to cope with rapid awakening in an unknown environment[16]. Similar results have been reported by Aono et al in 1977[17].

The association between preoperative anxiety and postoperative agitation has been reported in previous studies[18,19]. Similarly, we found thatchildren with agitation during the induction of anesthesia had a higher risk of developing EA. Some early reports have suggested that

Table 4: The association between anesthetic agents and presence of emergence agitation

Anesthetic agents	Emergence Agitation			
	Yes [n (%)]	No [n (%)]	Total [n (%)]	*P.* Value
Atropine	9 (1.2)	13 (1.7)	22 (2.9)	0.004
Midazolam	126 (16.9)	575 (77.0)	701 (93.8)	0.9
Fentanil	77 (10.3)	313 (41.9)	390 (52.2)	0.2
Sufentanil	19 (2.5)	49 (6.6)	68 (9.1)	0.02
Alfentanil	3 (0.4)	22 (2.9)	25 (3.3)	0.4
Pethidine	7 (0.9)	47 (6.3)	54 (7.2)	0.3
Thiopental	91 (12.2)	352 (47.1)	443 (59.3)	0.02
Propofol	26 (3.5)	119 (15.9)	145 (19.4)	1
Ketamine	44 (5.9)	250 (33.5)	294 (39.4)	0.09
Halothane	5 (0.7)	6 (0.8)	11 (1.5)	0.02
Sevoflurane	19 (2.5)	105 (14.1)	124 (16.6)	0.4
Isoflurane	73 (9.8)	193 (25.8)	266 (35.6)	<0.001
Atracurium	92 (12.3)	304 (40.7)	396 (53.0)	<0.001
Succinylcholine	17 (2.3)	98 (13.2)	115 (15.5)	0.3

Table 5: Factors predictive of emergence agitation (Step 1a)

Variables	Wald statistic	*P*. Value
Temper tantrum	3.080	0.08
Induction behavior	10.724	0.001
ENT (1)	.195	0.7
Ortho(1)	.027	0.9
Abdomen (1)	1.930	0.2
H&N	1.374	0.2
Trunk	.729	0.4
Extremities	.354	0.5
Atropine (1)	.538	0.5
Sufentanil	.177	0.7
STP	.003	0.9
halothane	1.357	0.2
Isoflurane	3.460	0.06
Atracurium	.487	0.5
Pain	87.85	<0.001
Constant	0.76	0.4

Variable(s) entered on step 1: pain

otorhinolaryngological surgical procedures appeared to exhibit an increased incidence of agitation[3,20]. When Eckenhoff et al first described the EA in 1961, attributed the increased incidence among otolaryngologic procedures to the "sense of suffocation" [1]. After that, in 2003, Voepel-Lewis in a prospective study has shown that the otolaryngologic procedures are independent risk factors for EA[3]. In our study, EA was associated with ENT, abdominal and orthopedic surgical procedures. Also, surgical procedures performed on the head and neck was associated with higher risk of EA. So, not only the type of surgical procedure, but also the surgical site may play a role in the incidence of EA.

Postoperative pain appears to be an aggravating factor, and its behavioral manifestations may be confused with emergence agitation diagnosis[11]. Several studies have discussed that pain during impaired consciousness leads to severe EA in some children[21,22]. However, a clear relationship has not been established[3]. In differentiating postoperative pain from EA, we used both FLACC and PAED tools to facilitate the decision making in involved children. We found that although EA decreased after adequate pain control, it was not eliminated completely. This suggests that EA can be presented despite adequate pain control. The authors believe that FLACC may be less reliable in children who experienced EA than in those who experienced pain only. Nevertheless, clinical experience and the review of the literature have suggested that when caring for children in PACU, it may not be necessary to differentiate EA from pain, especially because the treatment is similar for both of them[23].

Midazolam was the most common premedication used in the present study. We have found no increased EA with midazolam. Some authors have observed a reduction in preoperative anxiety and easier to separate children from parents. Also, they observed a reduction in agitation when midazolam was used as premedication followed by sevoflurane as anesthetic[24]. However, some authors have reported that emergence time was prolonged when midazolam was used[25]. Among the inhaled anesthetic agents used in this study, isoflurane was associated with 9.8% of EA compared with sevoflurane (2.5%) and halothane (0.7%). EEG changes caused by the effects of isoflurane and sevoflurane on the central nervous system have also been suggested as a possible causative agent of agitation[26,27].

Propofol has been demonstrated to be effective as an adjunct to sevoflurane inhalational general anesthesia in reducing the incidence of EA[28,29]. We have also found no relationship between Propofol and increased EA.

Among the intravenous anesthetics used in the present study, ketamine has been shown not to be associated with increasing risk of EA. Dissimilar

result was reported by Eckenhoff et al with ketamine during emergence from anesthesia[1]. Conversely, Dalens et al showed that the administration of 0.25 mg/kg of ketamine at the end of the MRI in children reduced agitation with no delay in discharge[30].

Sufentanil is a potent opioid which is usually used as a standard treatment of EA because it relieves pain without influencing PACU length of stay[31]. Our finding has shown a controversy related to sufentanil effect on EA. We found a positive association between sufentanil used as opioid and the incidence of EA. The authors suggest that the co-administration of sufentanil and isoflurane may cause this controversy.

There are controversies about the effect of duration of anesthesia on the incidence of EA[32-34]. The higher incidence of EA has been observed in short-duration surgery[35-37] as well as in the long-duration[35]. We detected that short anesthetic procedures were associated with higher incidence of EA. It was suggested that EA may be attributed to shorter-duration surgeries due to rapid washout of anesthetics from the body, causing rapid emergence before analgesics have enough time to act and reach their peak effect[38].

Atracurium was another anesthetic agent that we detected related to the incidence of EA in our patients. We have found no studies discussing the effect of atracurium on EA. Although, laudanosine as main metabolite of atracurium can play a role in EA because of its CNS excitation effect[39]. The authors suggest that it cannot be the causative phenomenon, because laudanosine can be activated in neuromuscular junction at its non-clinical high concentration. On the other hand, the short duration of most surgical procedures could not be associated with such phenomenon.

Conclusion

This study has identified that multiple independent risk factors such as post-operative pain, short time awaking, anesthetic drugs including sufentanil, isoflurane, atracurium, and also ENT surgeries, as well as site of operation were the risk factors of EA in children aged 3-7 years. Although EA in this sample was relatively of short duration, pharmacologic intervention was required in 6.7% of cases, and EA was associated with a prolonged PACU stay without significant adverse effect only in 2% of all cases.

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Authors' Contribution

M. Mohkamkar, F. Farhoudi: Data collection and Acquisition of data
AR. Alam Sahbpour, SA Mousavi: Critical revision of Manuscript
S. Khani and S. Shahmohammadi: Concept/design, Data analysis and Manuscript preparation
All authors approved of the final version of the article.

Conflict of Interest: None

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