Incidence and Risk Factors of Emergence Agitation in Pediatric Patients after General Anesthesia

Ananchanok Saringcarinkul MD*,
Sithapan Manchupong MD*, Yodying Punjasawadwong MD*

** Department of Anesthesiology, Faculty of Medicine, Chiang Mai University, Chiang Mai*

Objective: *To study the incidence and evaluate factors associated with emergence agitation (EA) in pediatrics after general anesthesia.*

Material and Method: *A prospective observational study was conducted in 250 pediatric patients aged 2-9 years, who received general anesthesia for various operative procedures in Maharaj Nakorn Chiang Mai Hospital between October 2006 and September 2007. The incidence of EA was assessed. Difficult parental-separation behavior, pharmacologic and non-pharmacologic interventions, and adverse events were also recorded. Univariate and multivariate analysis were used to determine the factors associated with EA. A p-value of less than 0.05 was considered significant.*

Results: *One hundred and eight children (43.2%) had EA, with an average duration of 9.6 $\pm$ 6.8 minutes. EA associated with adverse events occurred in 32 agitated children (29.6%). From univariate analysis, factors associated with EA were difficult parental-separation behavior, preschool age (2-5 years), and general anesthesia with sevoflurane. However, difficult parental-separation behavior, and preschool age were the only factors significantly associated with EA in the multiple logistic regression analysis with OR = 3.021 (95% CI = 1.680, 5.431, p < 0.001) and OR = 1.857(95% CI = 1.075, 3.206, p = 0.026), respectively.*

Conclusion: *The present study indicated that the incidence of EA was high in PACU. Preschool children and difficult parental-separation behavior were the predictive factors of agitation on emergence. Therefore, anesthesia personnel responsible for pediatric anesthesia should have essential skills and knowledge to effectively care for children before, during, and after an operation, including implementing the methods that minimize incidence of EA.*

Keywords: *Emergence agitation, Difficult parental-separation, Children, Pediatric, Sevoflurane*

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Emergence agitation (EA, also called emergence delirium), and excited and disoriented behavior on awakening from general anesthesia can be challenging for the post-anesthesia care provider. Early epidemiologic studies demonstrated a 5.3% incidence of EA in all postoperative patients, with a more frequent incidence in children (12-13%)[1,2]. In children who received volatile anesthetics (sevoflurane and desflurane) as primary factors, the reported incidence of EA has ranged from 24-66%[3], increasing to 80% in preschool children[4].

Correspondence to: Saringcarinkul A, Department of Anesthesiology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand. Phone: 053-945-522, Fax 053-945-526. E-mail: asaringc@yahoo.com

Due to a different society and culture, the authors' aim of the present study was to firstly determine the incidence of EA, and secondly, measure the risk factors associated with EA in Thai pediatrics after general anesthesia.

Material and Method

After the Institutional Ethics Committee's approval and parental informed consents were done. Two hundred and fifty children (aged 2-9 years), with ASA physical status I-II undergoing elective surgery at Maharaj Nakorn Chiang Mai Hospital, Thailand between October 2006 and September 2007, were enrolled into the present study. Children scheduled for major cardiothoracic or major vascular surgery, or

neurosurgery, and children with a history of mental impairment and/or developmental delay were excluded.

Before anesthesia the investigator assessed parental-separation behavior (1 = asleep; 2 = good separation; 3 = awake anxious, easily reassured; 4 = crying, cannot be reassured). The anesthetic management depended on the judgment of an attending anesthesiologist. Demographic and all anesthetic data (perioperative medications, the duration of anesthesia, and time to awakening) were recorded by the anesthesiologists. During the post-anesthesia recovery, a post-anesthesia care unit (PACU) nurse who did not know the anesthetic technique recorded all emergence behavior. The presence or absence of EA was assessed by using a five-point scale[5] (Table 1). EA was considered when a child cried or had thrashing behavior that required restraint (emergence score of 4 or 5) for at least 3 min. However, children who complained of localized pain were not considered to have EA. All pharmacologic and non-pharmacologic interventions and adverse events were also recorded. If there were no problem, children would be discharged after a 2-hour stay in the PACU.

The authors divided the patients into two categories using the emergence agitation scale: non-agitated patients (levels 0-3) and agitated patients (levels 4-5). The duration of EA and consequences, and the number of children needed to control the situation were recorded. Appropriate treatment for EA was performed by using psychological support from the parents or nurse, analgesics and/or anxiolytics. All patients regained a normal cognitive status before their discharge from the PACU.

The reported incidence of EA ranged from 12% to 80% in the children[1-4]. By assuming a 65% incidence of EA in healthy 2- to 9-year-olds, the sample size of 210 patients was determined (expected proportion, 0.65; precision, 0.10; CI 95%). Discrete categorical data were presented as frequency (percent); continuous data were presented as mean $\pm$ SD. In univariate analysis, the tests used to compare groups were the Chi-squared test, Fisher's exact test (count less than 5), and two-sample t-test as required. A multivariate analysis was performed using a backward binary stepwise logistic regression to examine and determine risk factors of delirium. All data were analyzed with the Statistical Package for Social Science (SPSS for Windows, version 15.0). Results were expressed as odds ratio (OR) with 95% CI. A p-value of less than 0.05 was considered significant.

Results

Two hundred and fifty children were enrolled into the present study over a 1-year period. All of them were assessed and EA in the PACU occurred in 108 patients (Table 1). The demographics and characteristics of the subjects are shown in Table 2.

One hundred and eight children (43.2%) had EA (Table 4), with a mean duration of 9.61 $\pm$ 6.78 minutes. 66.7% of the agitated children were 2-5 years old. EA associated with adverse events occurred in 29.6% of the agitated group. Fourteen pulled out a surgical drain or an i.v. catheter (12.9%), ten injured themselves with increasing pain (9.3%), five had bleeding at the surgical wound (4.6%), and three cases injured the attending staff (2.8%). Agitated children were treated with either psychological support, medication or both. Only two agitated cases subsided without intervention (1.9%) (Table 3).

Among agitated children, 26.9% had received chloral hydrate for premedication, while only 16.2% obtained it in non-agitated children (p = 0.058). The percentage of patients who had been pre-medicated with benzodiazepines was comparable in both groups (40.7% in agitated and 45.8% in non-agitated patients, p = 0.505). The number of children aged 2-5 years was

Table 1. Emergence scale: Data are expressed as frequency and percent (n = 250)

Score[a]	Description	Frequency (%)
0	Localized or complained of pain	36 (14.4%)
1	Obtunded with no response to stimulation	15 (6.0%)
2	Asleep but responsive to movement or stimulation	51 (20.4%)
3	Awake and responsive	40 (16.0%)
4	Crying	56 (22.4%)
5	Thrashing behavior that required restraint	52 (20.8%)

[a] Children with an emergence score of 4 or 5 for at least 3 min were classified as agitated

Table 2. Demographic and characteristic data of the subjects

	Agitated (n = 108) (43.2%)	Non-agitated (n = 142) (56.8%)	Total (n = 250)	p-value[a]
Male sex	72 (66.7%)	78 (54.9%)	150 (60.0%)	0.081
Age 2-5yrs / 6-9yrs	72 (66.7%)/36 (33.3%)	65 (45.8%)/77 (54.2%)	137 (54.8%)/113 (45.2%)	0.002*
ASA I(%) / ASA II (%)	88 (81.5%)/20 (18.5%)	111 (78.2%)/31 (21.8%)	199 (79.6%)/51 (20.4%)	0.627
Had previous surgery	37 (34.3%)	67 (47.2%)	104 (41.6%)	0.054
Difficulty separating	48 (44.4%)	26 (18.3%)	74 (29.6%)	<0.001*
Benzodiazepine premed	44 (40.7%)	65 (45.8%)	109 (43.6%)	0.505
Chloral hydrate premed	29 (26.9%)	23 (16.2%)	52 (20.8%)	0.058

[a] p-value was obtained from Pearson Chi-square
* Statistically significant

Table 3. Pharmacologic and non-pharmacologic intervention in agitated children (n = 108)

Intervention	Frequency (%)
No intervention	2 (1.9%)
Psychological support	36 (33.3%)
Paracetamol	2 (1.9%)
Benzodiazepine	1 (0.9%)
Opioid	9 (8.3%)
Psychological support and opioid	51 (47.2%)
Psychological, opioid and benzodiazepine	7 (6.5%)

Table 4. Summary of anesthetic drugs, and anesthetic and awakening time in agitated and non-agitated children after general anesthesia

	Agitated (n = 108) (43.2%)	Non- agitated (n = 142) (56.8%)	Total (n = 250)	p-value[a]
Propofol	15 (13.9%)	31 (21.8%)	46 (18.4%)	0.150
Sevoflurane	74 (68.5%)	75 (52.8%)	149 (59.6%)	0.017*
Isoflurane	33 (30.6%)	56 (39.4%)	89 (35.6%)	0.187
NMB	69 (63.9%)	84 (59.2%)	153 (61.2%)	0.529
Succinylcholine	14 (13.0%)	30 (21.1%)	44 (17.6%)	0.131
Atracurium	67 (62.0%)	76 (53.5%)	143 (57.2%)	0.223
Anesthetic time[b]	85.1 ± 62.4 min	75.6 ± 53.7 min	79.7 ± 57.7 min	0.199□
Awakening time[b]	9.1 ± 17.0 min	8.1 ± 15.1 min	8.5 ± 16.1 min	0.656□

[a] p-value was obtained from the Chi-square test
□p-value was obtained from the two-sample t-test
* Statistically significant
[b] Values expressed as mean ± SD

significantly higher in the agitated group than in the non-agitated group (67% and 46%) ($p < 0.002$). The incidence of difficult parental-separation behavior was significantly less frequent in non-agitated children than in agitated children (18.3% and 44.4%) ($p < 0.001$) (Table 2). The agitated cases were anesthetized with sevoflurane more often than the non-agitated patients (68.5% and 52.8%) ($p = 0.017$) (Table 4). The incidence of delirium in children who had EYE/ENT surgery was 57.1%, while the incidences in orthopedic, endoscopy,

Table 5. Multivariate analysis of risk factors for emergence agitation

Factor	Odds ratio	95% CI	p-value[a]
Age 2-5 yrs old	1.857	1.075-3.206	0.026*
Difficult separation from parents	3.021	1.680-5.431	<0.001*
Sevoflurane	1.643	0.947-2.850	0.078

[a] p-value was derived from backward binary stepwise logistic regression
* Statistically significant

urology, and general surgery cases were 43.3, 31.0, 47.0, and 33.3%, respectively. However, the number of agitated children was not significantly higher than that of non-agitated children in EYE/ENT surgery (p = 0.067).

The univariate analysis between agitation and non-agitation groups presented an incidence of EA that was significantly related to three variables (age 2-5 years, difficult parental-separation behavior, and anesthesia with sevoflurane) (Table 2, 4).

Multivariate analysis by backward binary stepwise logistic regression found that of the three variables used in the present study, two were significant in postanesthetic agitation. Children with difficult parental-separation behavior had 3 times the risk of developing delirium (OR = 3.021, 95% CI = 1.680, 5.431, p < 0.001). Preschool children (age 2-5 yrs) had increased risk of EA (OR = 1.857, 95% CI = 1.075, 3.206, p = 0.026), while children anesthetized with sevoflurane were not at risk of agitation (OR = 1.643, 95% CI = 0.947, 2.850, p = 0.078) (Table 5).

Discussion

The incidence of EA in the present study was 43.2%, with an average duration of 9.6 $\pm$ 6.8 minutes. EA associated with adverse events occurred in 29.6% of agitated children. Difficult parental- separation behavior was significantly associated with a higher incidence of agitation. Preschool age increased the risk of EA. However, general anesthesia with sevoflurane was not found as a predictive risk factor from multivariate analysis.

Several previous studies investigated the incidence and risk factors of agitation on emergence. The reported incidence of EA after general anesthesia was 12-80%[1-4]. This problem was a frequent phenomenon in children who demanded increased nursing care in the PACU, and had delayed reunion with their parents, which may lead to adverse sequelae in some cases[3]. To minimize this problem after general anesthesia, the authors defined the risks and treatment methods when they occurred. A high percentage of EA was found in the present study (43.2%). Due to the variation in protocols and in the definition of EA, it was difficult to make comparisons with other studies.

Some variables such as age, anxiety of the child, type of surgery and pain after operation were related and may predict the occurrence of EA[6,7]. A relationship between anxieties in children who underwent surgery was linked to emergence delirium, as reported in the study of Kalin ZN[8]. In contrast to the previous study, the authors found that children with difficult parental-separation behavior had the risk of developing EA.

The present study showed the increased incidence of EA in preschool children which was in accordance with some previous reports[9,10]. These children may be psychologically less mature than school-aged children and less able to cope with sudden awakening in a strange environment[9].

Studies associating sevoflurane with excessive EA continue to appear in the anesthetic literature[10-12]. The underlying mechanism of sevoflurane-induced agitation remains unclear. Rapid recovery of consciousness was proposed as one possible mechanism[13]. Wells LT et al[14] mentioned that rapid return to consciousness did not automatically lead to agitation or disorientation. Both sevoflurane and propofol allow rapid awakening from general anesthesia, but only propofol anesthesia allows a rapid, smooth, and pleasant emergence. The present study found that sevoflurane anesthesia in children undergoing surgery did not pose the risk of EA, which was in accordance with the study of Lerman J et al[15].

Some early reports suggested that EA was encountered more frequently in young people who underwent tonsillectomy or head and neck surgery[2,16]. Voepel-Lewis T et al[3] demonstrated that an otorhinolaryngology procedure had an independent risk of EA. The authors found a high incidence of EA in EYE-ENT procedures, but it was not a predicted risk factor.

Prevention was ethically indicated, and opioids have long been considered the only consistent and reliable therapy for EA[9]. Previous studies recommended 1-2 microgram/kg i.v. fentanyl before the end of the anesthetic[17]. The present study found that 14.4% of agitated children could localize or complain of pain. While 8.3% of agitated children received opioids only, 47.2% needed both psychological support from the parents and opioids. This data showed that the total number of opioid injections was higher than the frequency of localized pain. To avoid this problem, a special measurement to assess pain score in young children was needed.

In conclusion, the authors' findings indicated that the incidence of EA was high in PACU. Preschool children and difficult parental-separation behavior were the predictive factors of agitation on emergence. Therefore, anesthesia personnel who are responsible for pediatric anesthesia should have essential skills and knowledge to effectively care for children before, during, and after an operation, including implementing the methods that minimize incidence of EA.

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อุบัติการณ์และปัจจัยการเกิดภาวะกระวนกระวายหลังฟื้นจากยาสลบในผู้ป่วยเด็กที่ได้รับการระงับความรู้สึกแบบทั่วไป

อานันท์ชนก ศฤงคารินกุล, สิทธาพันธ์ มั่นชูพงศ์, ยอดยิ่ง ปัญจสวัสดิวงศ์

วัตถุประสงค์: *เพื่อศึกษาหาอุบัติการณ์การเกิดภาวะกระวนกระวาย หลังฟื้นจากยาสลบในผู้ป่วยเด็กที่ได้รับการระงับความรู้สึกแบบทั่วไป*

วัสดุและวิธีการ: *เป็นการศึกษาเชิงพรรณนาแบบไปข้างหน้าโดยเก็บข้อมูลจากเด็ก 250 คนอายุระหว่าง 2-9 ปี ที่ได้รับการระงับความรู้สึกแบบทั่วไป เพื่อการผ่าตัดต่าง ๆ ในโรงพยาบาลมหาราชนครเชียงใหม่ ตั้งแต่ เดือนตุลาคม พ.ศ. 2549 ถึง เดือนกันยายน พ.ศ. 2550 อุบัติการณ์การเกิดภาวะกระวนกระวายหลังฟื้นจากยาสลบ จะถูกประเมินพฤติกรรมของเด็กที่แยกจากผู้ปกครองได้ยาก การรักษาด้วยยาหรือแก้ไขด้วยวิธีอื่น ๆ และเหตุการณ์ที่ไม่พึงประสงค์จากภาวะกระวนกระวายที่เกิดขึ้นถูกบันทึกข้อมูลไว้ ใช้การวิเคราะห์แบบ univariate และ multivariate เพื่อหาปัจจัยที่สัมพันธ์กับการเกิดภาวะกระวนกระวายหลังฟื้นจากยาสลบโดยถือค่า $p < 0.05$ มีนัยสำคัญทางสถิติ*

ผลการศึกษา: *เด็ก 108 คน (ร้อยละ43.2) เกิดภาวะกระวนกระวายหลังฟื้นจากยาสลบ มีระยะเวลาเฉลี่ย 9.6 $\pm$ 6.8 นาที ภาวะกระวนกระวายที่สัมพันธ์กับเหตุการณ์ที่ไม่พึงประสงค์เกิดในเด็ก 32 คน (ร้อยละ29.6) การวิเคราะห์แบบ univariate พบว่า ปัจจัยที่สัมพันธ์กับภาวะกระวนกระวายหลังฟื้นจากยาสลบ คือ พฤติกรรมของเด็กที่แยกจากผู้ปกครองได้ยาก เด็กวัยก่อนเรียน (2-5 ปี) และการดมยาสลบด้วย sevoflurane อย่างไรก็ตามมีเพียงพฤติกรรมของเด็กที่แยกจากผู้ปกครองได้ยาก และเด็กวัยก่อนเรียนที่สัมพันธ์กับภาวะกระวนกระวายหลังฟื้นจากยาสลบจากการวิเคราะห์แบบ multiple logistic regression ด้วยค่า OR = 3.021 (95% CI = 1.680, 5.431, $p < 0.001$) และ OR = 1.857 (95% CI = 1.075, 3.206, $p = 0.026$) ตามลำดับ*

สรุป: *จากการศึกษานี้แสดงถึงอุบัติการณ์ภาวะกระวนกระวายหลังฟื้นจากยาสลบที่สูงในหอพักฟื้น เด็กวัยก่อนเรียนและเด็กที่มีพฤติกรรมแยกจากผู้ปกครองได้ยาก เป็นปัจจัยเสี่ยงต่อการเกิดภาวะกระวนกระวาย หลังฟื้นจากยาสลบ ดังนั้นบุคลากรทางวิสัญญีผู้รับผิดชอบ ควรมีความรู้ และความชำนาญในการดูแลผู้ป่วยเด็ก อย่างมีประสิทธิภาพทั้งในช่วงก่อน ระหว่าง และหลังการผ่าตัด รวมถึงการหาวิธีการที่ช่วยลดอุบัติการณ์ ภาวะกระวนกระวายหลังฟื้นจากยาสลบ*