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Factors Contributing to Postanesthetic Emergence Agitation in Pediatric Anaesthesia

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ABSTRACT

Emergence Agitation that has been first described by Eckenhoff et al. in 1960's is a dissociated state of consciousness in which the child is inconsolable, irritable, uncooperative, typically thrashing, crying, moaning or incoherent. It is also a common problem in pediatric postanesthetic care unit with an incidence ranging from 10 to 80%. This literature review focused on presence of Emergence Agitation and contributing factors in children under general anaesthesia. It was conducted on Medline in PubMed area, Alta Vista Data bases, CINHAL and Google scholar in January 2013 for publications written in English with the following keywords: "Emergence Agitation, Etiology, Treatment, Pediatric Anaesthesia, Postanesthetic Care Unit, Children, inhaled anesthetics, intravenous anesthetics and Post Anesthetic Emergence Delirium". In this paper, we intend to review the factors contributing postanesthetic emergence agitation in children to improve our vision in this area.

Introduction

Nowadays, about four million children undergo anaesthesia annually and Emergence Agitation (EA) has been identified as a significant problem in children at Post Anaesthesia Care Unit (PACU).[1] 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] The incidence of EA in Children who received volatile anesthetic agents (sevoflurane and

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desflurane) has been reported from 24 to 66%, [3] increasing to 80% in preschool children.[4] EA is a postanesthetic problem that interferes with child's recovery and presents a challenging situation for the post-anaesthesia care provider in terms of assessment and management.[3] Although, several factors have been identified as etiologic factors of EA, there is no entire description for emergence agitation. Many different causes have been suggested, such as rapid awakening in an unfamiliar settings, painful events like surgical wounds, agitation on induction, airway obstructions, environmental disturbances, duration of anaesthesia, hyperthermia, hypothermia, type and site of operation, premedication, inhaled and intravenous anesthetics and the anesthetic technique.[1,5-7] Although EA is usually self-limited and occurs within the first 30-minutes of recovery in PACU, it can last up to 2 days and leads to physical damage, disconnected 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-anaesthesia care providers. In addition, the administration of sedative and analgesic drugs is associated with increased recovery time and PACU discharge delay.[8-10] Generally, treatment in all cases mentioned above is directed to the correction of causative agents. Although, numerous medications have been studied to prevent or reduce EA in children, no special preventive method has been shown to be highly superior. Understanding the risk factors for EA helps us to determine the best way to control this phenomenon in the PACU period. Because of the contradictory results of previous studies conducted to determine the related risk factors of EA and the former review article written about EA in children in 2011 reviewed this phenomenon as a whole, herein, we reviewed the contributing factors for EA and suggested interventions.

Materials and Methods

A literature review about the possible causes of postoperative agitation in preschool children was conducted on Medline in PubMed area, Alta Vista Data bases, CINHAL and Google scholar in January 2013 for publications written in English with the following keywords: "Emergence Agitation, Etiology, Treatment, Pediatric Anaesthesia, Postanesthetic Care Unit, Children, inhaled anesthetics, intravenous anesthetics and Post Anesthetic Emergence Delirium (PAED). All articles written in English, focused on presence of EA and contributing factors in children under general anaesthesia from January 2011 to January 2013 were included. Publications were excluded if the anaesthesia technique was not general.

Results

A total 12 related articles met the criteria of our search, 10 of them were randomized control trials, one case report and one article was case control. Table 1 shows the list of the papers evaluated and the summary of the repossessed data.

Discussion

This review reveals that Emergence Agitation (EA) still remains a significant postanesthetic problem that interferes with the child's recovery and challenges the PACU care provider in terms of assessment and treatment. Considering the potential risk factors is important to appropriately differentiate and treat agitation in the pediatric PACU. We also have found evidences that some of anesthetics may lead to decrease the incidence of postanesthetic EA.

Table 1. Characteristics and results of the studied papers (Continued)

Source /Date	Study Design	Cases	Age of patients	Anesthetic Technique patient (No.)	Premedication	Induction	Maintenance	Type of surgery	Agitation scale	EA[c] incidence
Na et al. [11] (2013)	RCT[i]	84	Pre-school children	Sevoflurane Anesthesia Remifentanil group (42 pt. [a])		thiopental, rocuronium, and 1% Sevoflurane	1% sevoflurane, 60% nitrous oxide in oxygen, and a continuous infusion of remifentanil	Adenotonsilectomy	PAED[b] & four-point EA scale	remifentanil group= 6 (4.25–10.25)
				Sevoflurane Anesthesia Sevoflurane group (42 Pt.)		thiopental, rocuronium, and 8% sevoflurane	2–3% sevoflurane			sevoflurane group= 11 (7.75–14.0)
Li et al. [12] (2013)	RCT	80	Pre-school children	Sevoflurane Anesthesia sufentanil 0.15 µg/kg		Sevoflurane anesthesia	-	repair of unilateral inguinal hernia	-	sufentanil group=9.1+/-3.5 fentanyl group=12+/-3.8 95% confidence interval [1.27+/-0.53]; p=0.001
				Sevoflurane Anesthesia fentanyl 1.5µg/kg						

Table 1. Characteristics and results of the studied papers (Continued)

Source /Date	Study Design	Cases	Age of patients	Anesthetic Technique patient (No.)	Premedication	Induction	Maintenance	Type of surgery	Agitation scale	EA[c] incidence
Kim et al.[13] (2013)	RCT	222	18-72 months	Sevoflurane Anesthesia propofol 1 mg kg(-1) (Group P) at the end of Op. --- Sevoflurane Anesthesia fentanyl 1 µg kg(-1) (Group F) at the end of Op. --- Sevoflurane Anesthesia saline (Group S) at the end of Op.		Sevoflurane anaesthesia 8% + O2	Sevoflurane 2-2.5% + O2 50%	inguinal hernia repair	PAED	Group P< Group F < Group S
Chen et al.[14] (2013)	RCT	84	2-7 y/o	Sevoflurane Anesthesia dexmedetomidine 1 µg·kg(-1) iv plus a 1 µg·kg(-1)·hr(-1) infusion, --- Sevoflurane Anesthesia ketamine 1 mg·kg(-1) iv plus a 1 mg·kg(-1)·hr(-1) infusion, --- Sevoflurane Anesthesia Normal saline		sevoflurane anesthesia	sevoflurane	strabismus surgery	PAED	PAED scores for EA were lower in the dexmedetomidine (P < 0.001) and ketamine (P = 0.002) groups than in the placebo group

Table 1. Characteristics and results of the studied papers (Continued)

Source /Date	Study Design	Cases	Age of patients	Anesthetic Technique patient (No.)	Premedication	Induction	Maintenance	Type of surgery	Agitation scale	EA[c] incidence
Singh et al.[15] (2012)	RCT	75	4m-7y/o	Isoflurane group, Sevoflurane group Desflurane group		8% sevoflurane and 100% oxygen	O(2) + N2O and isoflurane, O2 N2O and sevoflurane O2 N2O and desflurane	Sub umbilical surgery	PAED	NS[d]
Meng et al.[16] (2012)	Case-Control	120	5-14y/o	Sevoflurane Anesthesia: Placebo group Sevoflurane Anesthesia: low dexmedetomidine concentration group Sevoflurane Anesthesia: high dexmedetomidine concentration group	intravenous injection 40 µg/kg midazolam	At first, and then dexmedetomidine was given intravenously as an initial loading dose of 0.5 µg kg or 1 µg/kg over a 10-min period	infusion of 0.2 µg/kg/h or 0.4 µg kg/h over the surgery	tonsillectomy	VAS[e] score	Dexmedetomidine appears to be safe and effective to reduce the incidence of early emergence agitation

Table 1. Characteristics and results of the studied papers (Continued)

Source /Date	Study Design	Cases	Age of patients	Anesthetic Technique patient (No.)	Premedication	Induction	Maintenance	Type of surgery	Agitation scale	EA[c] incidence
Dahmani et al.[17] (2012)	Case report	1	3y/o		-	sevoflurane 6% (in a mixture ofO2/N2O: 50%/ 50%)	spontaneously breathing with a 3% sevoflurane end-tidal concentration (in a mixture of O2/N2O:50% /50%)	bilateral myringotomy	PAED	PAED score=19
Jeong et al.[18] (2012)	RCT	60	2-8y/o	Desflurane Anesthesia: group C received normal saline --- Desflurane Anesthesia: group K1.0 received ketamine 1.0 mg/kg intravenously before entering the operating room --- Desflurane Anesthesia: group K0.5 received ketamine 0.5 mg/kg 10 min before the end of the surgery	Atropine 0.01 mg/kg was injected intramuscularly 30 min before the induction of anesthesia	Thiopental sodium 5 mg/kg and rocuronium 0.6 mg/kg	oxygen 1.5 L/min, nitrous oxide 1.5 L/min and desflurane at 4-6 vol%	brief ophthalmic surgery	EA and the modified Children's Hospital of Eastern Ontario Pain Scale	K[f]1.0<K0.5<C

Table 1. Characteristics and results of the studied papers (Continued)

Source /Date	Study Design	Cases	Age of patients	Anesthetic Technique patient (No.)	Premedication	Induction	Maintenance	Type of surgery	Agitation scale	EA[c] incidence
Choi et al.[19] (2011)	RCT	40 40	2-12y/o	Sevoflurane Anesthesia: N2O group (Group N; n = 40, sevoflurane and 70% N2O) Sevoflurane Anesthesia: remifentanil group (Group R; n = 40, sevoflurane with remifentanil infusion at the rate of 0.17 µg/kg/min)	Glycopyrrolate 0.005 mg/kg IM	thiopental 5 mg/kg, rocuronium 0.6 mg/kg and 3-4vol% sevoflurane in oxygen 5 L/min (FIO2 1.0)	group N received sevoflurane and 70% N2O for maintenance of anesthesia (FIO2 0.3) Group R received sevoflurane with remifentanil infusion at the rate of 0.17 µg/kg/min (FIO2 0.3: O2 0.6 L/min, medical air 4.4 L/min)	tonsillectomy/ adenoidectomy	4-point scale	NS
Zand et al.[20] (2011)	RCT	167	2-7y/o	1.Sevoflurane Anesthesia with parental presence without premedication 2. Sevoflurane Anesthesia 3.Halothane Anesthesia with parental presence 4. Sevoflurane Anesthesia with oral midazolam premedication	- oral midazolam premedication - oral midazolam premedication	sevoflurane (or halothane) and 60% nitrous oxide in oxygen at a flow rate of 10 L/min.	Sevoflurane was started at 1% and gradually increased up to 70% at intervals of every three breaths. Halothane was started at 0.5% and increased to 4% with increments of 0.5% after every three breaths.	for short (less than 0.5 hour) outpatient surgeries	emergence agitation scale	Postoperative agitation was significantly less in patients who received halothane anesthesia with oral midazolam premedication

Table 1. Characteristics and results of the studied papers (Continued)

Source /Date	Study Design	Cases	Age of patients	Anesthetic Technique patient (No.)	Premedication	Induction	Maintenance	Type of surgery	Agitation scale	EA[c] incidence
LI et al. [21] (2011)	RCT	105	3–11 y/o	Sevoflurane Anesthesia: normal saline (control group), ---------- Sufentanil 0.2 µg/kg (S2) ---------- Fentanyl 2 µg/kg (F2) 1 minute after loss of the eyelash reflex	-	sevoflurane	sevoflurane	adenotonsilectomy	PAED scales	The incidence of severe agitation was significantly lower in S2 and F2 groups vs. the control group
Lee et al. [22] (2011)	RCT	56 ---------- 56 ---------- 56		Sevoflurane Anaesthesia: ET-A group (n = 56, endotracheal tube and extubation whilst awake) ---------- Sevoflurane Anaesthesia: ET-D group (n=56, endotracheal tube and deep extu- bation) ---------- Sevoflurane Anaesthesia: LMA-D group (n = 56, experienced LMA and deep removal)		8% sevoflurane in nitrous oxide/oxygen (3/1 l/min) mixture via a face mask 2 µg/kg fentanyl for analgesia and 0.1 mg/kg ondansetron to prevent nausea and vomiting	sevoflurane with air/oxygen (1/1 l/min) mixture in a semiclosed circle system	Subumbilical Surgery	-	LMA-D[g] patients compared with patients in the ET-A[h] Group (21.4% Vs. 41.1%)

Abbreviations: [a] Pt (Patient), [b] PAED (Post anesthetic Emergence Delirium), [c] EA (Emergence Agitation), [d] NS (No Significant), [e] VAS (visual analog scale), [f] K (Ketamine), [g] Laryngeal Mask Airway – Deep (LMA-D), [h] Endotracheal- Awake, [I] Randomized Clinical Trial.

Na et al. (2013) in a study to investigate the effect of sevoflurane anaesthesia in combination with remifentanil during the induction and maintenance of anaesthesia found that PAED score in remifentanil group was significantly lower than sevoflurane group (P=0.007) and the proportion of patients with PAED scores ≥10 and four point scale scores ≥3 were significantly lower in the remifentanil group than in the sevoflurane group.[11]Comparing the effect of sufentanil and fentanyl by Li et al. on emergence agitation in preschool children who underwent repair of unilateral inguinal hernia following sevoflurane anaesthesia have showed that 0.15μg/kg sufentanil compared with a single dose of 1.5μg/kg fentanyl could significantly decrease the incidence of emergence agitation without delaying the recovery time.[12]

Similarly, in a study by Lee et al., to investigate the effect of sufentanil to reduce emergence agitation after sevoflurane anaesthesia in children undergoing adenotonsilectomy compared with fentanyl, they had concluded that administration of sufentanil at 0.2 μg/kg after induction of anaesthesia could reduce emergence agitation more without delaying the recovery time or causing significant hypotension in children compared with fentanyl.[21]

It has been shown that propofol comparing with fentanyl to prevent of EA after sevoflurane anaesthesia in children was more effective and associated with lower PAED score.[13]

Intraoperative administration of ketamine and dexmedetomidine has also decreased the incidence of EA and PAED score in pediatric patients under sevoflurane anaesthesia.[14]

The incidence of EA has been reported higher with sevoflurane compared with desflurane and isoflurane. However, among the three anesthetic agents no correlation was found between the incidence of EA and duration of anaesthesia or age.[15] Evaluating the efficacy and safety of dexmedetomidine for emergence agitation after tonsillectomy under sevoflurane anaesthesia in children appeared that dexmedetomidine could be safe and effective to reduce the incidence of early emergence agitation in children after tonsillectomy. Initial loading dose of 1.0 μg/ kg followed by a maintenance infusion of 0.4 μg/kg/hrs was a better choice for children who received sevoflurane anaestesia.[16]

Allowing one of the parents to enter the PACU and holding the child was associated with reduced risk factor of EA and/ or to treat it.[17]

Similarly, the results of Zand et al.'s study to compare the effects of midazolam premedication and parental presence during sevoflurane and halothane anaesthesia induction on the incidence of postoperative agitation in pediatric patients revealed that the presence of a parent at induction of sevoflurane anaesthesia was as effective as midazolam premedication in decreasing the incidence of postoperative agitation. Midazolam premedication effective to decrease postoperative EA associated with halothane was used as the anesthetic agent.[20]

The results of the study with the different dosages of ketamine with desflurane anaesthesia by Jeong et al. for brief ophthalmic surgery demonstrated that both the incidence of EA and pain scales were at least in K1.0 group compared with the K0.5 and placebo groups.[18]

Investigating the effect of remifentanil as an alternative to N2O by Choi et al. in 2011 on EA and the presence of postoperative pain in preschool children under general anaesthesia with sevoflurane for tonsillectomy/ adenoidectomy surgery indicated that severity post-operative pain in remifentanil group was more that the N2O group (P=0.012). There were no significant differences between the two groups in incidence of EA.[19]

Lee et al. in their study to compare the effect of laryngeal mask airway (LMA) and the removal of the LMA in a deeply anaesthetized state with endotracheal tube (ET) and extubation when the

patient was awake or deeply anaesthetized on the incidence of emergence agitation in preschool children after sevoflurane anaesthesia for subumbilical surgery concluded that using an LMA and deep removal could decrease post-operative emergence agitation more than endotracheal tube and awake extubation after sevoflurane anaesthesia in pediatric patients.[22]

Conclusions

This review has identified that short time to awakening, sevoflurane anaesthesia, otorhinolaryngology procedures, preschool children age and difficult parental-separation behavior were the risk factors of EA. On the other hand the combination of remifentanil, sufentanil, propofol, ketamine and dexmedetomidine with sevoflurane anaesthesia and using an LMA and deep removal of ET reduce the incidence of EA.

Conflict of Interest

None declared.

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