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Incidence of Emergence Agitation in Children Receiving General Anesthesia: Risk Assessment and Prophylactic Effect of Propofol

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Original Article

ABSTRACT

Background: *Postoperative emergence agitation (EA) occurs in up to 80% of children undergoing general anesthesia(GA). Propofol was proposed as a safe and effective agent to reduce, prevent and eliminate Postoperative emergence agitation.*

Objective: *To assess the incidence of postoperative EA and the effect of Propofol as prophylactic agent*

Patients & Methods*: A randomized controlled clinical trial conducted at the Central Teaching Hospital of Pediatrics, during a period of 16 months included 100 pediatric patients less than 16 years of age and were scheduled for different surgeries under general anesthesia . Patients equally assigned into two groups to receive either 1 mg/kg Propofol intravenously at 7 minutes before recovery (Propofol group) or receiving 5 ml normal saline (saline group) as control.. All standard procedures and protocols of anesthesia were applied.*

Results*: The mean PAED score was significantly lower in Propofol group, (8.3 ± 2.4) compared to control group (12.8 ± 3.7) at 5 postoperative minutes, and continue to reduce at the next time; 10 and 15 minutes, (P<0.05). The overall incidence of EA in Propofol group was (14%) vs. (74%), in controls, the relative risk (RR) for the incidence of EA at 5 minutes and 10 minutes was; 0.52 and 0.38, respectively, indicated a protective , prophylactic effect of Propofol (P<0.001).*

Conclusions: *Propofol was safe and effective agent for prophylaxis and prevention of postoperative emergence agitation. Age is the main risk factor for postoperative agitation,*

Keywords: *General anesthesia, Inhalational anesthesia, Propofol, Emergence agitation, Incidence, risk factors*

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1. INTRODUCTION

Post-anesthesia agitation (PA) also known as emergence delirium (ED), emergence excitation and emergence agitation (EA), is a status occurs after emergence from general anesthesia accompanied by psychomotor agitation and disorders. It has been described as a mental disorder during recovery from general anesthesia consisting of hallucinations, uncontrollable weeping, confusion, restlessness and involuntary physical movements. It is more common in children, and is generally a self-limited phenomenon (1,2). However, it is considered an important complication due to its high incidence, it occurs in almost 10 to 80% of children undergoing general anesthesia , particularly, inhalational ones (3,4). During agitation, pediatric patients can injure themselves or others. In addition to having self-harm, EA leads to prolong the time of stay in the post-anesthetic recovery unit (5,6). It has no defined etiology, but related factors and diagnostic criteria have been described. There are differences in the literature regarding the incidence of EA, and the etiology is not clear (7) . Factors related to the patient, the surgical procedure, the anesthetic, and the concomitant medication used could influence. The psychological implications of EA in children are also unknown; some studies suggest that these children are at greater risk of developing negative behaviors in the postoperative period (3,8,9).

Anesthesia in children safety and complications

During the past decades, there have been great developments in anesthesia devices and drugs, so that general anesthesia can be used safely in children of all ages, any surgery can be performed under general anesthesia without any problems or serious complications. In children, complete sedation does not lead to long-term complications or effects on the nervous system or intellectual ability(10,11). Therefore, anesthetic procedures are very safe in children, but there are always risks with any medication. Minor side effects of anesthesia, such as a sore throat, nausea, and vomiting, can be common. Serious complications from anesthesia are rare(12,13). At present, the complications of anesthetic procedures in children are exceptional , although as always in pediatrics, all procedures and all treatments have risks (14). In the case of general anesthesia, the possible complications are: Sore throat , mouth or teeth lesions due to the intubation procedure. drowsiness , confusion or nervousness upon waking are also not uncommon. Nausea or vomiting on waking, difficult breathing upon awakening, aspiration leading to pneumonia (rare), and very rarely, heart problems , stroke

or other life-threatening complications(12,15). Scientists have investigated the effects of anesthetics on the developing brain but no evidence that administered anesthetic agent be associated with these problems in children (16,17). Furthermore, over the past decades, pediatric anesthesiologists have made significant progress in ensuring the safety of young children undergoing general anesthesia (16) . According to the U.S. Food and Drug Administration (FDA) indications in 2016, alert has been issued for the anesthetic drugs that can be involved in anesthesia for children, these drugs are Desflurane, Etomidate , Halothane , Isoflurane, Ketamine, Lorazepam , Methohexital, Midazolam , Pentobarbital , Propofol and Sevoflurane (18).

1.1. Inhalational anesthesia

The inception of inhalation anesthesia dates back to 1846, when William Thomas Morton performed the first anesthesia with diethyl ether(19). The most commonly used types of inhalation anesthesia currently are Isoflurane, Sevoflurane, and desflurane. Widespread use of nitrous oxide (N2O) continues with these anesthetic gases, due to the synergistic and secondary effect of the gas on these agents. However, the current trend is towards a gradual decline in its use because it is involved in environmental pollution and has no major side effects. In general, inhalation anesthesia is used in most current anesthetic procedures. In pediatrics, they are widely used as sole agents, as they meet all the requirements for optimal anesthesia.(20–22).

1.1.1. Sevoflurane

Sevoflurane (fluoromethyl 2,2,2-trifluoro-1 (trifluoromethyl) ethyl ether) is a colorless, volatile and non-flammable liquid. It is stable at room temperature with a boiling point of 58.6°C and a vapor pressure of 157 mmHg. Moderate steam pressure allows the use of a standard variable side vaporizer(23–25). The minimum alveolar concentration (MAC), that is, the alveolar concentration necessary to prevent a locomotor response in 50% of anesthetized patients to a harmful stimulus such as a skin incision during a surgical procedure, is 2.05% 21. Thus, its effectiveness is much lower than other inhalational drugs such as halothane and isoflurane, which is three times more powerful than Desflurane. The absence of airway irritation, and a rapid increase in the concentration of alveolar anesthesia make sevoflurane an excellent choice for induction in both pediatric and adult patients. In the

same way, its lower solubility in the blood favors a rapid decrease in the alveolar concentration of the drug when it is discontinued and wakes up faster compared to isoflurane. In general, postoperative complications from sevoflurane are rare. Among the negative reactions. Postoperative nausea, vomiting, cough, and excitement (the latter is classified as a "very common adverse reaction") (23–25).

1.1.2. Desflurane

Desflurane (2- (dimethoxy) -1,1,1,2-tetrafluoroethane) belongs to the group of fluorinated methyl ethyl ether. It has the same structure as Isoflurane except for replacing the chlorine atom with the fluorine atom, which gives it physical properties very different from the other halogenated ones. It is a useful drug for maintenance of anesthesia, and has a safe cardiovascular form, similar to isoflurane and sevoflurane. Desflurane is potentially irritating and can cause salivation, respiratory arrest, coughing, and laryngospasm if used during anesthesia induction. This means that it is not recommended as an inflammatory agent in pediatric patients(26,27).

1.2. Propofol

Propofol is diisopropylphenol, licensed intravenous short-acting anesthetic agents used for induction, maintenance of GA in both adults and pediatric patients and for sedation in the context of intensive care units (e.g., patients undergoing mechanical ventilation and tracheal intubation), or diagnostic procedures (e.g., endoscopy and interventional radiology). Clinically, Propofol used indicated for induction and in maintenance of general anesthesia (28–30) and it is authorized in children from 1 month of age and older. Its use is not recommended in patients <1 month. Also it is used in sedation in intensive care units but its use is contraindicated in patients <16 years of age. It can also be used as an antiemetic in very low doses (31,32) . Although its mechanism of action is not perfectly established, its effect on the brain GABA is postulated (32,33). Side effects of Propofol are rare ,however, Cardiorespiratory depression, amnesia, myoclonus , pain in the administration site, allergic reactions in individuals sensitive to its components have reported (34). Many previous studies indicated the use of Propofol as prophylactic against emergence agitation incidence in children receiving general anesthesia when administered at the completion of the operation and discontinuation of maintenance anesthesia(35–40).

1.3. Post-anesthesia emergence agitation:

Post-anesthesia emergence agitation(EA) was first described in the early 1960s by Eckenhoff et al. EA refers to the wide variety of behavioral disorders that occur in many patients after awakening from general anesthesia. It is an acute phenomenon, which begins on awakening from anesthesia and continues throughout the initial recovery period. It is generally self-limited and usually lasts less than 30 minutes. It is an alteration of consciousness or attention to the environment that surrounds the patient, and is characterized by a large number of presentations, which include crying, excitement, delirium, moaning, disorientation, and inconsistencies (1–7). It occurs more frequently in pediatric patients. In international literature, the terms "postanesthetic excitement", "postoperative agitation" and "postoperative delirium" are frequently interchanged. It is difficult to tell the difference, especially in children, and it can create confusion. However, no unified definition has been adopted due to its heterogeneity and complexity of presentation; including alterations in perception , attention and cognition; These alterations develop in a short period of time, are not explained by a previous neurological disease, and there is evidence that they are caused by intoxication, an adverse effect of a drug, or a medical pathology. However, postoperative agitation is not often suggestive for significant behavioral changes like delirium. Agitation can have many origins and predisposing factors such as preoperative anxiety , pain or separation from parents in pediatric patients (1–7) . The mechanism responsible for EA and the increased incidence in preschool-age pediatric patients is unclear.

1.3.1. Risk factors different risk factors postulated to be involved in the development of EA, these can be categorized as :

Patient's related factors :

Age, maturation status, character of the child and preoperative anxiety). Higher risk to develop EA in preschool-age than older children and the risk reduced with advancing age. Preoperative anxiety can prolong the induction of anesthesia, and predispose to alterations in the child's behavior. Some experts attribute EA to the unique neurodevelopmental characteristics of this age group and the effects of the new inhalation anesthetics on them (1,9).

***Surgery related factors*:** (such as type of procedure, or postoperative pain). Certain surgical procedures, such as otorhinolaryngology, ophthalmology and thyroidectomies, have been associated with a higher incidence of EA (41)

***Anesthesia related factors*:**

Some authors associate EA with the alterations in the electroencephalogram (EEG) characteristic of sevoflurane.(35,42) with some medications administered perioperatively. Inhalation agents have a higher risk of developing PA than intravenous anesthetics. The duration and depth of anesthesia also been postulated as a risk factor. Alterations in metabolism have been found in some parts of the brain of children anesthetized with sevoflurane compared to Propofol (43) .

***Quick wake up* :**

It has also been postulated that the recovery of consciousness of the new inhalation agents when so rapid, postoperative analgesia does not have time to be effective, and agitation could be a response to pain(8,44). The rapid recovery of consciousness in an environment unfamiliar to the child could also be related . Moreover, they have not found differences in the incidence of EA when abruptly suspended Sevoflurane against when it is reduced gradually and controlled (45)

2. PATIENTS and METHODS

After acceptance by the Ethics and Clinical Research Committee in our hospital and health directorate, we carried out a comparative, randomized single-center clinical trial was performed in the operating rooms of the surgical area of our hospital during a period of 16 months (from April 2018 to August 2019). To achieve greater homogeneity, both the anesthetic technique and the data collection were carried out by the authors.,

Inclusion criteria

1. Pediatric patients at age of 3- 12 years.
2. ASA I or II physical state.
3. Scheduled different surgical procedures under general anesthesia.
4. At least 6-hour fasts for solid foods or regular formulas, 4 hours for breast milk, and 2 hours for water.
5. Subjects whose parents and / or legal representatives agree to participate in the study by signing the informed consent.

The exclusion criteria: Patient with one or more of the following was excluded

1. Surgeries or concomitant pathology not fit for general anesthesia.
2. Recent or ongoing respiratory tract infection.
3. Treated for behavioral disorders
4. Neurological diseases or psychomotor disorders.
5. Obstructive Sleep Apnea Syndrome .
6. Need for mechanical ventilation after the procedure.
7. Emergency surgeries.
8. ASA physical state ≥ 3.
9. Non-compliance with the protocol during the study

Anesthetic procedure and protocol

Patients are scheduled for surgical intervention under GA from the waiting list, after going through the anesthesia consultation , all required investigations were requested and a basic physical examination is performed. Once parents gave their written consent to participate in the study, the patients were included. All procedures were performed according to the usual standard clinical practice protocols of the general anesthesia and resuscitation. All the children were evaluated by the anesthesiologists (authors). Anxiolytic pharmacological premedication was administered. The degree of preoperative anxiety that the child presented was evaluated using the modified Yale Preoperative Anxiety Scale . The child's behavior during parental separation and anesthetic induction was noted by the anesthesiologists. Intraoperative monitoring was according to the standard recommendations. Subsequently, inhalation induction was performed, using the tidal volume technique in progressive increments every 10 seconds . Once sufficient anesthetic depth had been achieved and after the excitation phase had ceased , a peripheral venous line was channeled. Subsequently, the maintenance of anesthesia was performed. After completing the surgical procedure, the corresponding the corresponding inhalation agent was suspended, without increasing the flow of fresh gas, and the laryngeal mask was removed when the child moved consciously or when he or she opened the eyes, according to the usual technique. The child was later transferred to the post anesthesia recovery room when had coordinated spontaneous movements, stable SpO 2 without oxygen therapy, and good respiratory mechanics.

Assignment of patients into the two arms of the study:

The 100 patients were equally assigned into two groups , 50 patients in each

Propofol group*:* Included patients who received Propofol of (1 mg/kg) at the end of inhalational anesthesia (7 minutes before end of surgery) as prophylactic to prevent EA.

Saline (control) group**:** Included patients who received intravenous normal saline(5ml).

Assessment for Emergence agitation:

Assessment of postoperative EA in all patients was performed using the Pediatrics Anesthesia Emergence Delirium (PAED) scale (**Table 1**) (46) which is scored and reported at 5 , 10 and 15 minutes of stay in the recovery room. According to the literatures, it is considered EA when the score on the PAED scale was ≥ 10. If the child was asleep at the time of measurement, it was considered as "not agitated" and it was given a score of 0

Table 1. Pediatrics Anesthesia Emergence Delirium (PAED) scale (46)

Items	Scoring				
	Not at all	Just a little	Quite a bi	Very much	Extremely
The child establishes contact with the caregiver	4	3	2	1	0
The child's actions are for a purpose	4	3	2	1	0
The child is alert to his environment	4	3	2	1	0
The child is restless	0	1	2	3	4
The child is inconsolable	0	1	2	3	4

Statistical methodology:

According to standard equations of sample size calculation , the required sample was calculated using the Open Epi® online software (47) , with a precision of 5% with α = 5% and estimating a loss of 5%, a sample of at least 88 patients would be required in both groups and approximated to 100 patients assigned into two studied groups with 50 patients in each . The descriptive calculations for each of the qualitative variables were the percentage and number of samples of each of the classes within a given variable. For the quantitative variables, the mean ± standard deviation was calculated. When the predictor variable was qualitative, contingency analyzes were used using the Chi-Square statistic. To compare quantitative variables, repeated measure ANOVA test was applied to compare the change in

PAED score at subsequent measurements time (5, 10 and 15 minutes). To compare PAED scores in-between both groups, Students' t test used. Significance of differences or correlations made under assumption of two tailed P. value (significance level) of ≤ 0.05. To assess the risk of incidence of EA in both studied groups, relative risk (RR) was calculated. Pearson's and Spearman's tests used to estimate the correlation of PAED score at the end of follow up time and other variables.

3. RESULTS

One hundred patients were enrolled in this clinical trial , represented the two arms of the study , Propofol and saline groups with 50 patients in each . A descriptive analysis of the patients, with the distributions of age, sex, weight, BMI, residence, and physical state (ASA class) are shown in (**Table 2**). All included patients in both groups were ASA I-II. However, both groups were almost matched for their baseline characteristics, in all comparisons, P. value > 0.05, not significant.

In Propofol group, the mean total anesthesia time , mean operation time and mean time of stay in recovery room were relatively longer compared to saline group, with no significant differences, (P>0.05). Mean wake up time was slightly shorter in Propofol than saline group; 7.2 min vs. 7.4 minutes, respectively, (P>0.05), furthermore, difference between both groups was neither significant in the presence of pain during stay in recovery room nor the analgesic medication use in recovery room, (**Table 3**).

The mean PAED score was significantly lower in Propofol group, (8.3 ± 2.4) compared to that in control group (12.8 ± 3.7) at 5 minutes postoperative, and continue to reduce at the next time; 10 and 15 minutes, and the difference between both groups still significant, (P<0.05). Furthermore, in both groups , PAED score reduced significantly with progressing time, (P<0.001) (**Table 4 and Figure 1**).

According to standard cutoff point of the PAED score used to diagnose EA, it had been found that the overall incidence of EA in Propofol group was significantly lower than saline group, 7 patients (14%) vs. 37 patients (74%), respectively, (P<0.001), (**Figure 2**). Moreover, when incidence of EA assessed at 5, 10 and 15 minutes, it was lower in all the

three points of time, the relative risk for the incidence of EA at 5, 10 and 15 minutes was below one; 0.52 and 0.38 and zero, respectively, which indicated a protective , prophylactic effect of Propofol to prevent EA, (**Table 5**).

Further analysis was performed to assess the effect of other variables on the PAED score and incidence of EA; bivariate correlation analysis was performed between PAED score as scale dependent variable from one side against other variables as independent covariates on the other side, results revealed that younger age was the main risk factor to develop EA, (P<0.05). Other variables did not show significant correlation, despite the effect of age, PAED score and incidence of EA were much lower in Propofol group indicated the prophylactic effect of administration of Propofol independently of other variables (**Table 6**).

Table 2. Baseline characteristics of the studied groups

Variable		Propofol group (n = 50)	Saline group (n = 50)	P. value
Age (years)	*Mean ± SD*	6.8 ± 2.7	7.1 ± 2.3	0.551
	Range	3 - 12	3 -12	
Weight (kg)	*Mean ± SD*	22.7 ± 3.6	23.2 ± 2.9	0.446
	Range	10 - 52	9 - 54	
BMI (kg/m^2)	*Mean ± SD*	16.9 ± 3.3	16.5 ± 3.4	0.756
	Range	13 - 26	14 - 27	
Sex	Male n (%)	32 (64%)	33 (66%)	1.00
	Female n (%)	18 (36%)	17 (34%)	
Residence	Urban n (%)	41 (82%)	43 (86%)	0.785
	Rural n (%)	9 (18%)	7 (14%)	
Physical state	ASA I-II n (%)	50 (100%)	50 (100%)	-

SD : standard error of mean, ns: not significant

Table 3. Clinical data of the studied groups

Variable		Propofol group (n = 50)	Saline group (n = 50)	P. value
Total anesthesia time (min)	Mean ± SD	42.3 ± 8.4	41.1 ± 9.3	0.472 ns
Operative time (min)	Mean ± SD	35.6 ± 4.8	34.3 ± 6.4	0.253 ns
Wake up time (min)	Mean ± SD	7.2 ± 1.8	7.4 ± 2.3	0.629 ns
Time of stay in recovery room (min)	Mean ± SD	42.3 ± 5.4	41.8 ± 6.7	0.682 ns
Pain during stay in recovery room N (%)	None	31 (62%)	29 (58%)	0.838 ns
	Mild	11 (22%)	13 (26%)	0.814 ns
	Moderate	5 (10%)	7 (14%)	0.758 ns
	Intense	3 (6%)	1 (2 %)	0.609 ns
Use of analgesic medication in recovery room N (%)		19 (38%)	21 (42%)	0.659 ns

min :minutes, SD : standard deviation , ns: not significant

Table 4. Comparison of Pediatrics Anesthesia Emergence Delirium (PAED) scores of the studied groups at three assessment time-points

PAED score	Propofol group (n = 50)		Saline group (n = 50)		*P. value between groups*
	Mean	SD	Mean	SD	
at 5 min.	**8.3**	2.4	**12.8**	3.7	< **0.001 sig**
at 10 min.	**5.6**	1.9	**11.2**	3.2	< **0.001 *sig***
at 15 min.	**3.2**	1.1	**8.1**	2.9	< **0.001 *sig***
P. value within group	**<0.001 sig**		**<0.001 sig**		

min : minutes, sig: significant

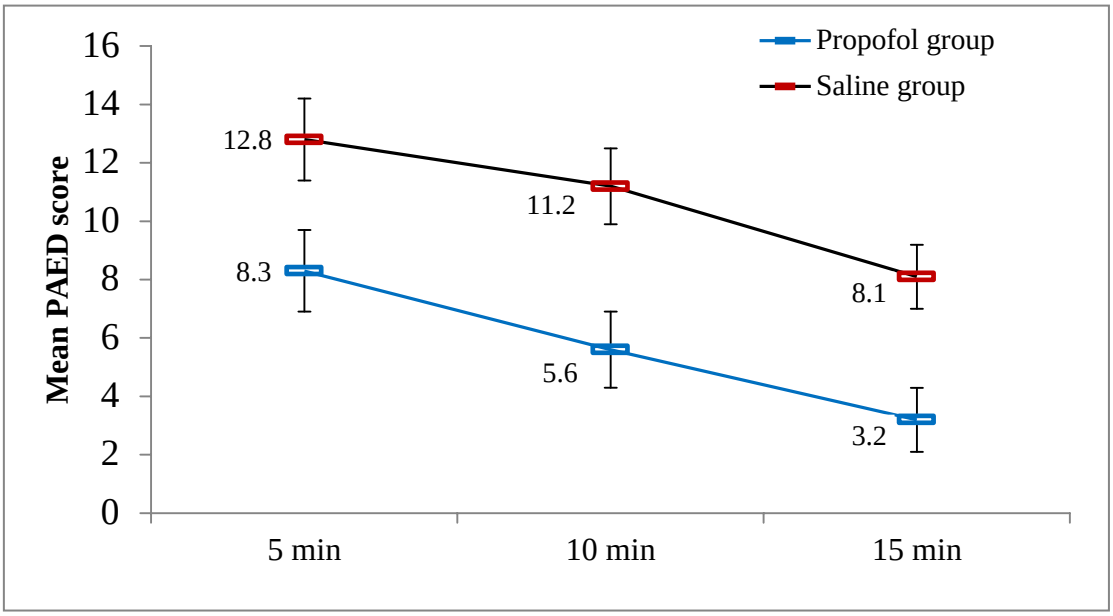

Figure 1. Changes in postoperative PAED scores of the studied group across the assessment time points

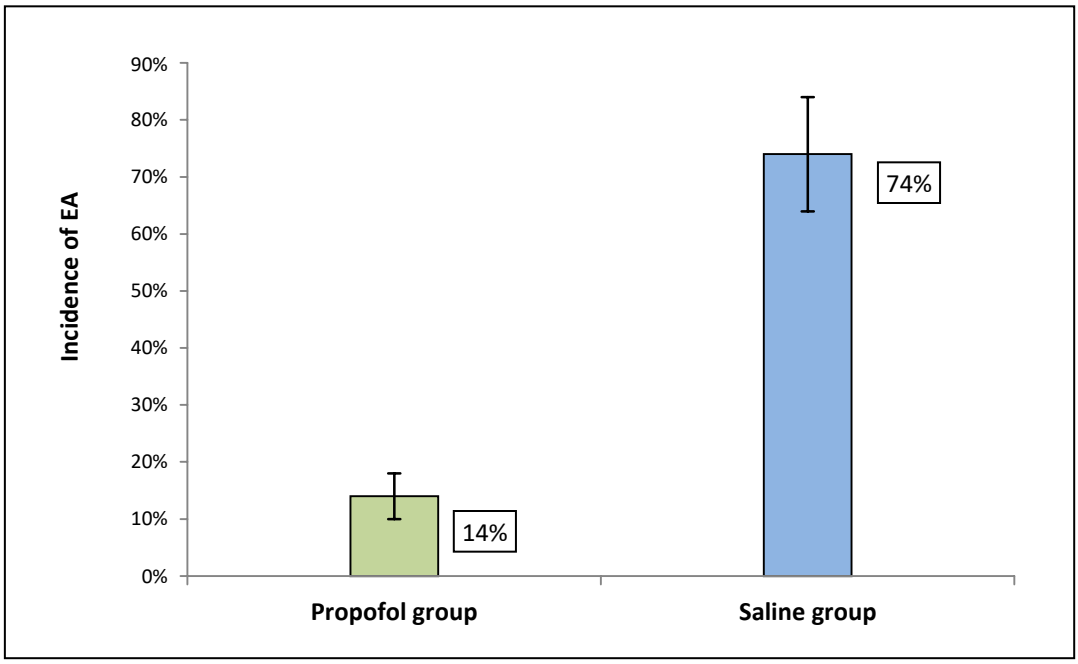

Figure 2. Overall incidence of postoperative emergence agitation in both studied group

Table 5. Incidence of postoperative emergence agitation in both studied group at different assessment time

Time of assessment	**Incident EA**	Propofol group (n = 50)		Saline group (n = 50)		Relative risk (95%CI RR)	P. value
		No.	%	No.	%		
at 5 min	**Yes**	6	12.0	30	60.0	0.26 (0.14 - 0.47)	**<0.001 sig**
	No	44	88.0	20	40.0		
at 10 min	**Yes**	1	2.0	6	12.0	0.48 (0.616 – 1.14)	0.214 ns
	No	49	98.0	44	88.0		
at 15 min	**Yes**	0	0.0	1	2.0	0.00	1.00 ns
	No	50	100.0	49	98.0		
Overall incident EA		7	14.0	37	74.0	0.21 (0.10 – 0.41)	**<0.001 sig**

RR: relative risk, CI: confidence interval of the RR, ns: not significant, sig: significant

Table 6. Correlation of PAED score with patients characteristics

Parameter	Correlation Coefficient (R)	P. value
Age	-0.511	**0.007 sig**
Gender	0.010	0.832 ns
Weight (kg)	0.111	0.528 ns
BMI (kg / m²)	0.032	0.722 ns
Duration of anesthesia	-0.249	0.132 ns
Physical status (ASA class)	-0.224	0.139 ns

ns: not significant, sig: significant

4. DISCUSSION

Postoperative behavioral changes, mainly EA, are a serious problem in the postoperative period of pediatric anesthesia that can have potential risks on patient safety (1–4). In our study, the overall incidence of EA was 14% in Propofol group and 74% in saline group. In the studies carried out on the subject, there is a great variability in the results due to various causes: lack of homogenization of the diagnostic method, pathophysiological triggering mechanisms that are not clear, the influence of the anesthetic agent is unknown and all the risk factors are not fully identified (1,3,47). In our study we have detected an incidence of EA is much lower in Propofol group, which is similar to that described in other studies, however there is a great variability of incidence in the literatures. In most of the articles reviewed that use the PAED scale to define EA (3,36,46,48,49), the incidence of EA in patients undergoing anesthesia with sevoflurane or desflurane ranges up to 80% (6,49–51). We included pediatric age group because postoperative EA have much concern in pediatric patients on daily practice for anesthesiologists and the parents, and large efforts tried to eliminate , prevent or reduce its incidence(5,52). Using PAED scale in our study to assess incidence of EA because this scale is more frequently used as it is proved to be more sensitive, valid with high accuracy (46,53,54). The present study revealed that PAED score significantly reduced with the time in both groups, but significantly larger reduction was reported in Propofol than saline group, from other point of view, patients in Propofol group had significantly lower PAED score across all measurement points of time. The reduction in PAED score of patients in saline group was expected, due to the fact that EA in children lasting for less than 15 minutes and resolved without intervention (54), the larger reduction in PAED scores in Propofol group could be attributed to the prophylactic dose of Propofol ; similar findings reported in previous studies conducted by Kim et al. (49), and Aouad et al. (40). The main moment of appearance of EA is in the first minutes after surgery, where EA is more frequent and more intense; We found that incidence of EA at 5 minutes was much lower in Propofol group than saline group, 12% vs. 60%, respectively, and the overall incidence of EA after 15 minutes, was much lower in Propofol group than controls, a RR below one indicates a protective (prophylactic) effect of Propofol, however, with progressing time of stay in recovery room incidence of EA reduced in both groups, this was expected as our study hypothesis based on the prophylactic effect of Propofol to prevent EA and the fact that EA is almost self-limited and not last for longer than 15 minutes. Our findings agreed that reported by Jiang et al. from China (2015) (7) and

another study from USA conducted by van Hoff et al. (36) which revealed that Propofol reduce the incidence and intensity of EA. Furthermore, Aouad et al. (40) in their study documented that administration of 1 mg/kg Propofol after the cessation of Sevoflurane at the end of surgery had good ameliorating effect to reduce the incidence and intensity of EA. Uezono et al.(35) observed much reduction in the incidence of EA and the risk of EA could be eliminated when Propofol infusion administered following Sevoflurane induction (21). Conversely, the present study disagreed that reported in some other previous studies that found no significant reduction in the incidence of EA in Propofol group; Bong et al. in 2015 from Singapore (48) did not reported a beneficial effect for a single dose of Propofol in child patients undergoing MRI under general anesthesia using Sevoflurane. Also, an earlier study in 2002 conducted by Cohen et al. (39) found that Propofol had no effect to reduce the incidence of EA in children undergoing adenotonsilectomies, this insignificant findings by Bong et al. and Cohen et al. (39,48) could be attributed to the nature of their studies, time of administration of Propofol, surgical procedures, awakening time, patients characteristics and other factors, (38,48). The present study proved that administration of Propofol reduced significantly the incidence and intensity of EA reflected by lower PAED score. This prophylactic effect of Propofol could be attributed to smooth recovery, remaining sedation at early stages of emergence as well as its effect to cause euphoria (40,48,51). Fortunately, none of our patients developed any type of adverse effects indicated the safe use of Propofol (36,48,49).

In our study, the main risk factor related to EA was age; younger children had significantly higher PAED score, these results are consistent with other previous studies on this topic who found a significant difference in the incidence of EA between preschool-age children and school-age children (35,47). Several subsequent studies have confirmed these results, and speak of an increase in the incidence of EA in children under 5 years of age (1,3,47,55) . The increase in the incidence of EA in preschool-age children may be due to the fact that their emotional liability is exacerbated when they are subjected to stressful situations in an unfamiliar environment, in addition to the immaturity that parts of the central nervous system still possess (56).

5. CONCLUSIONS

1. The overall incidence of postoperative emergence agitation was lower in pediatric patients receiving Propofol at a dose of 1 mg/kg before end of surgery compared to control group.
2. Propofol 1 mg/kg was safe and effective agent with significant ameliorating effect in prophylaxis and prevention against postoperative emergence agitation in pediatric patients undergoing surgeries under general anesthesia.
3. Incidence of postoperative emergence agitation was inversely associated with the patient's age, younger children had higher PAED score than older ones. Hence, age is the main risk factor for postoperative agitation, being more frequent and more intense in younger children.
4. Sex, weight, BMI, residence, Physical state, total anesthesia time and duration of surgery, do not influence the incidence or intensity of postoperative agitation .

Ethical Clearance

Ethical clearance and approval of the study are ascertained by the authors. All ethical issues and data collection were in accordance with the World Medical Association Declaration of Helsinki 2013 for ethical issues of researches involving humans, verbal and signed informed consent obtained from all parents or care guards of the patients. Data and privacy of patients were kept confidentially. The criteria for withdrawal or abandonment of the study were: refusal by the parents to sign the consent and participate in the study. The patient could withdraw from the study at any time he wanted.

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