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Cohort Study

# Effectiveness of propofol on incidence and severity of emergence agitation on pediatric patients undergo ENT and ophthalmic surgery: Prospective cohort study design

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ABSTRACT

*Introduction:* Emergence agitation is a common problem that can occur after administration of general anesthesia and during recovery time especially in pediatric patients, which can result in life-threatening events if not managed adequately and timely. Usage of modern inhalational anesthetic agents like sevoflurane, isoflurane, and also halothane is a common cause for emergence agitation. Currently, the use of propofol is gaining acceptance largely on decreasing emergence agitation in addition to prevention of postoperative nausea and vomiting. The objective of this study was to assess the effectiveness of prophylaxis administration of propofol on incidence & severity of emergence agitation on pediatric patients undergo ENT & ophthalmic surgery under general anesthesia.

*Methods and material:* An institutional-based prospective cohort study was conducted on 90 patients. Patients who take 1 mg/kg of propofol were grouped into exposed while if propofol were not given grouped to non-exposed. Data were collected through intraoperative observation & by using WATCH & PAED score the patients were observed at 5, 15 & 30 min in the recovery room. Incidence of emergence agitation was analyzed by chi-square test & Mann Whitney *U* test was applied for the severity of emergence agitation. A P-value less than 0.05 was declared as statistically significant.

*Result:* From a total of 90 study participants 64% of the non-exposed group & 31% of the exposed group were developed emergence agitation which was statistically significant with $p = 0.002$. The severity of agitation was also higher in the non-exposed group than the exposed group at 5, 15 & 30 min with $p = 0.009$, 0.013, and 0.011 respectively.

*Conclusion:* Administering 1 mg/kg propofol before the end of surgery in pediatrics ENT & ophthalmic procedure under general anesthesia is effective in reducing incidence & severity of emergence agitation. Based on our findings we recommend using 1 mg/kg propofol at the end of surgery to reduce the occurrence of emergency agitation.

## 1. Introduction

Emergence from general anesthesia is a transition from deep sleep to recovering consciousness and it should be a smooth recovery. During this time life-threatening event called agitation may arise. Emergence agitation is described first by Eckenoff, in 1961 and it is a common phenomenon that occurs after the administration of general anesthesia [1,2].

Emergence agitation can occur in all age groups but is more prevalent in pediatrics' with incidence ranges from 20 to 80%. It occurs mostly within 30 min after the end of surgery and administration of anesthesia during recovery time. The child becomes uncooperative, restless, irritable, inconsolable, typical thrashing, crying and moaning during recovery from anesthesia [2–5].

Different causes that contribute to the occurrence of emergence agitation are like a type of surgery that is Ear, nose, throat (ENT) and ophthalmic surgeries, type of anesthesia mainly inhalational agents, pain and pediatrics age group [4,6–10].

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As there are different methods to reduce emergence agitation in pediatric patients; one of the safe methods is a prophylactic use of sub hypnotic dose of propofol at the end of surgery to decrease emergence agitation and making recovery from general anesthesia smooth [5,11,12]. Propofol is short-acting intravenous anesthetics that has characteristics of rapid onset and recovery with amnestic effect and is not associated with nausea and vomiting [13].

Pediatric patient's post-operative emergence agitation needs special consideration because they can deteriorate easily and life-threatening events can happen so prevention is better than cure. The purpose of this study was to assess the effectiveness of prophylaxis propofol on incidence & severity of emergence agitation on pediatric patients undergoes ENT & ophthalmic procedures under general anesthesia.

## 2. Methods & materials

An institutional-based prospective cohort study was employed from November 2018 to May 2019 in Saint Paul Hospital Millennium Medical College. Ethical clearance was obtained from the institutional review board before the start of the study. An Official support letter was written to the Hospital and permission for data collection was sought from the responsible authorities. Written informed consent was obtained from each study participant partner. This study is reported in line with STROCSS criteria [14]. The study was also registered in the research registry with the unique identification number of researchregistry6548 www.researchregistry.com. All elective ASA I & II age of 2–12 years old pediatric patients undergoes ENT & ophthalmic surgery under general anesthesia were included. Patients with a known psychiatric disorder, the one induced with propofol & ketamine, Children who took fentanyl at the end of the procedure, or the one who is on propofol infusion was excluded.

Data were collected from selected study participants using a pretested questionnaire to maintain the quality and consistency of data. Since RCT is not allowed to do by our institution we did a cohort study based on patient exposure status where 1 mg/kg propofol was given at end of surgery or not.

The protocol and routine procedures before, during, and after surgery at the study site were as follows:

On arrival of the patients to the operative theatre, and after application of the routine hospital monitoring protocol, HR, noninvasive blood pressure, and SPO2 have been recorded before induction of anesthesia. Anesthesia was induced by inhalational agent or thiopental 3–5 mg/kg, suxamethonium 1–2 mg/kg & fentanyl 1–2 μg/kg. These patients were maintained with halothane or isoflurane and vecuronium 0.08 mg/kg was used for muscle relaxation. Paracetamol 15 mg/kg and pethidine 1 mg/kg were given for analgesia for all patients. Before the end of surgery 1 mg/kg, propofol was given to the patient. During each procedure, the data collectors observed the intraoperative procedures and those patients who fulfill the inclusion criteria will be included in our study and then intraoperative data were recorded. So based on intraoperative observation, the one who took 1mg/kg of propofol is grouped into an exposed & if propofol is not administered they were called a non-exposed group. After transfer to PACU, data collectors were filled the data using WATCHA & PAED score, which determines the presence of emergence agitation and severity respectively at the time interval of 5, 15, and 30 min, and other parameters on the questionnaire were filled. A score of 3 or 4 on the WATCHA scale was considered as emergence agitation & a PAED score greater or equal to 12 was considered as severely agitated which was measured by observing the child's behavior.

Two BSc holder anesthetists were selected to collect data and one-day training was given on how to collect data One MSc holder anesthetist was assigned for assistance and supervision. We investigators did not participate in intraoperative as well as postoperative management of the patients.

For this study, the following definitions were used:

**Anxiety**: a feeling of worry, nervousness, or unease about something with an uncertain outcome.

**Calm**: patient not showing nervousness, anger, emotions, violence, or confrontation activity.

**Emergence agitation**: children scoring 3 or 4 after general anesthesia using the Watcha scale

**Maladaptive behavior**: is a type of behavior that inhibits a person's ability to adjust to certain situations.

**PAED SCALE**: is used to measure the severity of emergence agitation with a score of $\geq$12.

**Sleep**: altered state of consciousness easily aroused by external stimuli.

**Watcha scale**: this is a simple scale for determining the presence of ED in clinical practice; it has better specificity and sensitivity. It defines emergence delirium at a score of 3 and 4.

### 2.1. Sample size & sampling technique

The Sample size was determined by taking previous study result which was an incidence of agitation in unexposed was 47.2% and 19.5%, in exposed; by considering 80% power & 95% confidence interval 45 patients in each group was needed [11].

From situational analysis total of about 200 patients are estimated to undergo ENT & ophthalmic procedures under GA & who took prophylaxis propofol or not. Based on our sample size the sampling interval become 2, the first patient was selected by lottery method & the rest was selected by every 2nd interval based on their exposure status until the required sample size was reached.

### 2.2. Data processing and analysis

Data were entered in Epi-info 7 and exported SPSS Version 20 for analysis. The data were tested for normality using histogram and Shapiro–Wilk normality test and homogeneity of variance by Levene's test. Since the data was not normally distributed Comparison of numerical variables between study groups was done using the Manny Whitney *U* test & presented as median and IQR. Frequency and percentage were used to describe categorical variables and statistical differences between groups were tested using Chi-square. Statistical Significance was declared at p-value $<0.05$.

## 3. Results

### 3.1. Socio-demographic and perioperative characteristics

A total of 90 patients were included for this prospective cohort study based on their exposure status in which the one who took prophylaxis propofol was exposed & the one who not took as non-exposed and their data was analyzed. A result of the Mann-Whitney *U* test & chi-square revealed there was no statistically significant difference between the groups concerning age, ASA physical status, sex, duration and type of surgery, and type of maintenance of inhalational agents with p-value $>$ 0.05 (Table 1).

### 3.2. Incidence of emergence agitation between the groups

A Chi-square test was used to analyze the presence of emergence agitation between exposed & non-exposed groups (see Fig. 1). The incidence of emergence agitation was 31% in the propofol (exposed) group and 64% in the non-exposed group which was statistically significant with a p-value of 0.002 (Fig. 2).

### 3.3. Postoperative emergence agitation severity using PAED scale

A Mann-Whitney *U* test discovered a statistically significant difference in the severity of emergence agitation in PACU between propofol &

**Table 1**
Socio-demographic and perioperative data of pediatric patients who underwent general anesthesia for ENT and ophthalmic surgeries at saint Paulo's hospital millennium medical college 2018/2019.

| Variables | | Exposed group (n = 45) | Non-exposed group(n = 45) | p-value |
|---|---|---|---|---|
| Age in year | | 4(2–12)* | 5(2–12)* | 0.11 |
| Sex | | | | |
| Female | | 23(51.1%) | 21(46.7%) | 0.67 |
| Male | | 22(48.9%) | 24(53.3%) | |
| Duration of surgery | | 1(1–3)* | 1(1–3)* | 0.5 |
| ASA I | | 44(97.8%) | 45(100%) | 0.31 |
| ASA II | | 1(2.2%) | 0(0%) | |
| Type of surgery | ENT | 27(60%) | 22(48.9%) | 0.29 |
| | Ophthalmic | 18(40%) | 23(51.1%) | |
| Types of inhalational agent | Halothane | 13(28.9) | 11(24.4) | 0.63 |
| | Isoflurane | 32(71.1) | 34(75.6) | |

Values are presented as* = median (IQR), and number (%) and p-value <0.05 is statistically significant. Mann Whitney *U* test and chi-square test were applied.

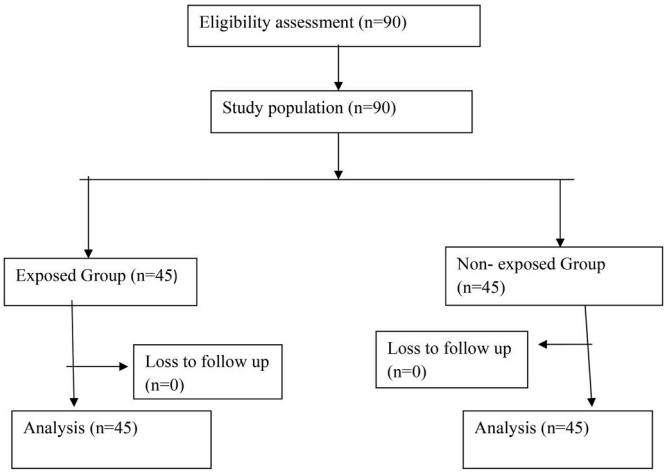


**Fig. 1.** a study flowchart for patient's enrolment.

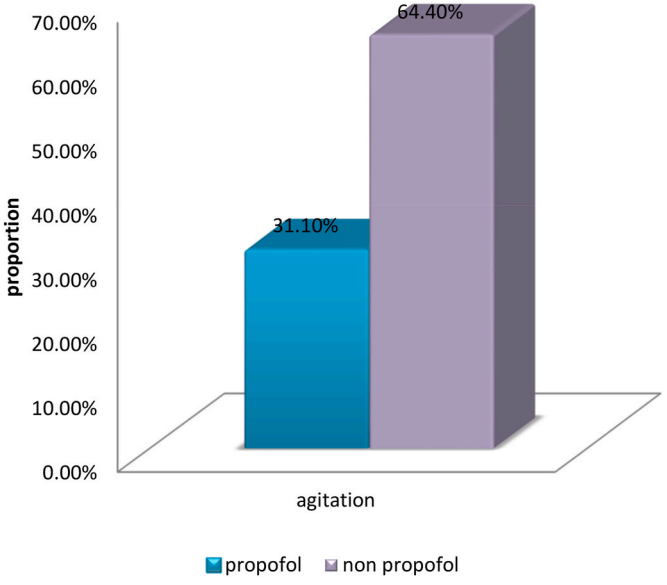


**Fig. 2.** Incidence of emergence agitation between propofol and non-propofol group. Postoperative emergence agitation severity using PAED scale.

non-propofol groups at 5, 15 & 30 min with a p-value of 0.009, 0.013 & 0.011 respectively (Fig. 3).

## 4. Discussion

Post-operative emergence agitation is the most commonly encountered problem in the post-anesthesia care unit especially in pediatric patients who are recovering from general anesthesia [15]. An agitated child in the recovery room is distressing for the caregiver to manage and also can result in life-threatening events like self-harm, disrupting intravenous lines, surgical dressings which result in bleeding, falling accidents, and may even result in death [4,15].

In our study, there was a significant reduction of incidence of emergence agitation (31%) in patients who took propofol at the end of surgery than those who not took propofol group (64%) with p = 0.002.

In agreement with our finding study conducted by Aoud et al. showed that there was a high incidence of agitation (47.2%) in a non-propofol group versus (19.5%) of a propofol group with a p-value of 0.01 [11]. The incidence is a little bit higher in our study than in Aoud el. Al due to we included different types of surgery instead of a specific procedure and volatile agent used for maintenance was halothane and isoflurane so maybe those differences cause a difference in incidence. Similarly study done by I Abu-Shawan et al. which evaluates the effectiveness of 1 mg/kg of propofol given at the end of surgery showed that there was a significant difference in the incidence of emergence agitation on a patient who took propofol (4.8%) & the one who not took propofol (26.8%) with p < 0.05 [16,16] which was comparable to our result. A study was done by costi. et al., Zahi Almajali, and bong et al. also agree with our result & conclude that administration of propofol would reduce the occurrence of emergence agitation [5,17,18].

In contrast to our finding RCT done by Jin Lee et al. in Korea on the effectiveness of 1 mg/kg propofol at the end of surgery showed that there was no significant difference in the incidence of emergence agitation between the groups [19].

The severity of emergence agitation was assessed using the PAED scale and we found that there was a statistically significant reduction in the severity of emergence agitation by administering propofol at the end of surgery. In our study, the PAED score was low in the propofol group compared to the non-propofol group at 5, 15, and 30 min with a p-value of 0.009, 0.013, and 0.011 respectively.

Our finding is in agreement with a study done in Egypt by Ali Abdullatif et al. which assesses that PAED score at arrival, 5, 15, and 30

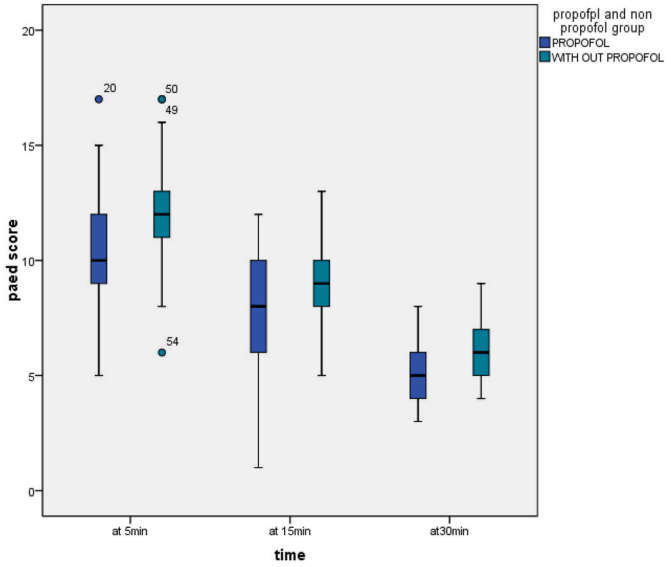


**Fig. 3.** Comparison of severity of emergence agitation between the groups.

min. Results revealed that severity of emergence agitation was lower in the propofol group at arrival, 5 and 15 but not at 30 min. The possible explanation for the difference in this time will be they include specific surgery (adenotonsillectomy) instead of all ENT procedures [20]. A study was done by Aoud. et al. which assesses the overall PAED score of a patient who took propofol & the one who did not take propofol showed that the mean PAED score was 8.6 ± 3.9 in the propofol group & 11.5 ± 4.5 in saline with a p-value of 0.004 [11].

In contrast to our finding lee et al. found that there was no significant difference in the severity of emergence agitation at 5, 15 & 30 min between the propofol & control groups. The possible explanation for this difference is the inhalational agent used in their study was sevoflurane while we used halothane & isoflurane [19].

Zahi Almajali also showed that there was a significant reduction in the severity of agitation in the propofol group [18].

In **Conclusion** administration of 1 mg/kg, propofol at the end of surgery for pediatric patients who undergo ENT and ophthalmic surgery under general anesthesia reduces incidence and severity of emergence agitation.

**Strength** Since most of the study conducted previously was done in a patient exposed to sevoflurane anesthesia or a specific type of surgery it was difficult to conclude about emergence agitation in pediatric patients induced by other induction agents or all ophthalmic and ENT surgery's, so our study is the first which incorporate a different type of surgeries and induction agent.

The main **limitation** of this study was since it was a cohort study it was difficult to make a controlled environment for patients.

More studies should be conducted with the randomized controlled trial and meta-analysis is needed to have great evidence.

**List of abbreviations** ASA-American society of anesthesiologist, EA-emergence agitation, ENT-ear nose, and throat, GA-general anesthesia

## Ethical approval

Ethical approval was secured from Addis Ababa University institutional review board.

## Sources of funding

Addis Ababa University funded the study but the university have no role in collection, analysis and interpretationof data.

## Author contribution

**Samrawit Haile** and **Leulayehu Akalu** have made substantial contributions to conception, design, analysis, and interpretation of data, participated in the critical review, and editing of the manuscript drafts for scientific merit and depth. **Timsel Girma** contributed to conception, design, and acquisition of data, analysis, and interpretation of data as well as on preparing the manuscript to this study.

## Registration of research studies

1. Name of the registry: research registry
2. Unique Identifying number or registration ID: 6548
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

## Guarantor

Timsel Girma

## Consent

All participants partners were asked to sign the informed consent form before their child data were collected. Participants patient privacy was kept confidential

## Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Declaration of competing interest

None

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102765.

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