Comparison of intravenous single dose Lidocaine and single dose Propofol in controlling emergence agitation in children for surgery under sevoflurane anesthesia: a randomized controlled trial

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OBJECTIVE: To determine the efficacy and safety of intravenous single dose lidocaine versus single dose propofol in controlling emergence agitation in children aged 2-6 years old for surgery under sevoflurane anesthesia in Philippine Children's Medical Center.

MATERIALS AND METHODS: This was a double-blind, randomized controlled trial of 64 children aged 2-6 years who had surgery under general anesthesia using sevoflurane. Patients were randomly assigned into 2 equal groups – the experimental (Lidocaine, L) group and the control (Propofol, P) group. Five (5) minutes prior to the discontinuation of sevoflurane, the patient assigned to the L group was given Lidocaine at 1.5 mg/kg IV while the patient assigned to the P group was given Propofol 1 mg/kg IV. Patients were monitored using Pediatric Anesthesia Emergence Delirium (PAED) and Face, Legs, Activity, Cry, and Consolability (FLACC) scales 5 minutes after giving the medication until discharge from the PACU. Data was collected using a data abstraction form.

RESULTS: There were no statistically significant differences between the 2 groups in terms of emergence agitation (RR= 0.5, 95% CI [0.098, 2.54], p-value= 0.672) and post- operative pain (RR:0.6, 95% CI [0.033, 1.91], p-value = 0.426). No adverse events were observed in both groups.

CONCLUSION: Both Lidocaine and Propofol are effective in preventing emergence agitation.

KEYWORDS: *emergence agitation, propofol, lidocaine, PAED scale, FLACC scale*

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INTRODUCTION

During post-anesthesia recovery, emergence agitation (EA), often referred to as emergence delirium, has become more common due to the use of sevoflurane for pediatric anesthesia. The peak incidence of EA in children is between 2 to 6 years old, with a prevalence of 20-80%, which lasts for 10-15 minutes. [1] Recurrent and persistent short-lived agitation, sobbing, confusion, disorientation, restlessness and alterations in cognition are some of the characteristics of EA. [2] This can interfere with surgical healing, be upsetting for caregivers and parents, and increase parental unhappiness with a child's care. [3] Several medications including Midazolam, Ketamine, Alpha 2 Agonists, and Propofol, have been investigated to reduce the likelihood of emergence agitation. [4] The most routinely utilized drug for prevention of EA is Propofol, since it spares the side effects of opioid, if pain is well controlled. [5] However, it may produce side effects such as delayed awakening, hypotension, bradycardia, and even asystole. [6] Lidocaine is a local anesthetic that is currently investigated for prevention of emergence agitation, but also with side effects such as nausea and vomiting, seizure, arrhythmia, and local anesthetic systemic toxicity. Several trials have shown that lidocaine has a potential to reduce the incidence of EA. [7] The use of Lidocaine as a treatment for EA has recently been investigated, but studies regarding this are lacking and have contradictory results, which is why this study was undertaken. Lidocaine is affordable and easily accessible so, if it proves to be helpful for EA, it may be cost-effective. This study aimed to examine the effect of intravenous (IV) single dose lidocaine versus IV single dose propofol in controlling EA in children aged 2-6 years old for surgery done under sevoflurane anesthesia at the Philippine Children's Medical Center.

Prevention is always preferred to cure since patients may quickly deteriorate and enter situations that are life-threatening. The dissociative state of consciousness known as EA occurs in pediatric patients and is characterized by incoherence, restlessness, uncontrollable pacing, and inconsolability. The fundamental cause of the illness is still unclear, despite their being observable connections with patient, surgical, and anesthetic variables. [8] EA can be upsetting for the patient as well as their parents and other caregivers. It increases the risk of falling and increases the chance that bandages, endotracheal tubes, drains, and IV catheters may be inadvertently removed. As a result, patients must be constantly monitored in the recovery area, and it may be necessary to physically restrain the patient.[9] Compared to other inhalation anesthetics, Sevoflurane has a pleasant smell, better cardiovascular stability and less tendency to irritate the airways, making it to be the drug of choice in maintaining anesthesia. Due to its property of

low blood-gas solubility, anesthesia can be quickly induced and have a fast recovery with this drug. However, in the study of Kim, et al., 2012, using sevoflurane causes a higher incidence of EA than using Propofol as maintenance for anesthesia. It has been suggested that the presence of clinically silent sevoflurane-induced epileptogenic activity causes EA. [10] According to Cohen et al., 2003, the difference in the rate of recovery of the nervous system from sevoflurane anesthesia increases sensitivity to stimulation from the environment, leading to a state of functional dissociation and the EA in patients. [11] In the model of Sachedev and Kruck, EA happens due to alterations and relationship of gamma-aminobutyric acid (GABA) A receptors in the central nervous system, wherein the mechanism of excitement is described to ensue from decreased inhibitory signals from the globus pallidus interna and substantia nigra, and the inability to suppress thalamocortical neurons and brain stem neurons due to nervous system disorder. [12] The length of the surgery affects how long the anesthetic lasts. According to Lepousé C., et al., 2006, EA will not likely happen in surgical procedures done in less than ten minutes. [13] The Ramroop, R. et al., 2019, study found that EA is unlikely to occur in surgical operations lasting more than four hours. [14] In the study of Voepel-Lewis, et al., 2003, it showed that otorhinolaryngological and ophthalmological procedures were associated with EA. [15] Among the one hundred thirty four pediatric patients who had EA, in the study of Mohkamkar, et al., 2014, the most frequent surgical procedures done were otorhinolaryngological surgery, abdominal surgery, orthopedic, urology and ophthalmic surgery.[16] Regional anesthesia, and combined general with regional anesthesia significantly decreased the incidence of EA and pain scores, in the study of Li, et al., 2022. [17] In contrast with the study of Zhu, et al., 2022, there was no significant difference in the incidence of EA whether patients were given regional or general anesthesia. [18] Propofol is a sedative-hypnotic anesthetic drug that works by positively modulating the inhibitory activity of the neurotransmitter GABA. According to Lee, CJ, et al., 2010, it was found that giving children a single dose of propofol at the conclusion of the operation had a significant impact on lowering the incidence of EA after sevoflurane anesthesia. [19] In agreement with this, Haile, et al., 2021, recommended that giving 1mg/kg of Propofol at the end of surgery reduces EA in pediatric patients. [20] Lidocaine is a local anesthetic, an amide type, that works on sodium ion channels found on the interior surface of nerve cell membranes. Neutral, uncharged lidocaine molecules pass through neural sheaths and into the axoplasm at these channels, where they combine hydrogen ions to become ionized. The sodium channels are thus capable of being reversibly bound by the resulting lidocaine cations from the inside, maintaining them in an open condition that precludes

neuronal depolarization. As a result, with enough obstruction, the postsynaptic neuron's membrane would not eventually depolarize and would not be able to send an action potential. By not just stopping pain signals from reaching the brain, but also by stopping their creation in the first place. [21] Lidocaine is generally safe when used sparingly and as prescribed. It is extremely rare to encounter unusual responses or hypersensitivity with this drug. In addition, compared to other local anesthetics, lidocaine is thought to have a better safety profile. [22] These verdicts are supported by the study of Both, C.P. et al., 2018, that there were no indications of circulatory disruption and neurological impairment in pediatric trials, twenty-four hours after Lidocaine has been administered. [23] In a different study by Nakajima et al., 2020, it was examined that pediatric patients receiving intravenous lidocaine for procedures done under general anesthesia did not experience any negative side effects, such as seizures, arrhythmias, or allergic reactions, when the dose was kept below the toxicity threshold of 5 mg/kg. [24] There are a few researches that investigate the impact of this medication in reducing emergence agitation, notably in pediatric patients. In the study of Hall, EA, et al., 2021, giving of lidocaine 1.5mg/kg, effectively reduces acute post operative pain in pediatric patients. [25] Benefits of lidocaine in pediatric patients include reduced postoperative opioid usage, better pain management, sparing of anesthetic medications, improved gastrointestinal function, and stress response reduction. [26] When pediatric patients received lidocaine before being extubated in the Lee, et al. study, the incidence of EA following surgery was significantly reduced. [27] Rahimzadeh et al., 2014, also looked at IV lidocaine's efficacy. They observed a large reduction in EA when lidocaine was given, and an even greater reduction when it was combined with propofol. These findings prompted researchers to hypothesize that lidocaine may be useful by reducing the sympathetic response to unpleasant stimuli, such as extubation and the surgical site pain after surgery.[28] There are no studies yet comparing propofol and lidocaine for preventing emerging agitation in pediatric patients having surgery under sevoflurane.

The general objective of this study is to determine the efficacy and safety of intravenous single dose lidocaine versus single dose propofol in controlling emergence agitation in children aged 2-6 years old for surgery under sevoflurane anesthesia at the Philippine Children's Medical Center. Specifically, to compare the incidence of emergence agitation among each group (lidocaine group and propofol group) using Pediatric Anesthesia Emergence Delirium (PAED) score, postoperative pain between the two groups and to describe the incidence of the following adverse events 24 hours post operatively among the two groups: hypotension, seizure, arrhythmia, post operative nausea and vomiting (PONV) and

and symptoms of overdose such as perioral numbness, metallic taste, tongue paresthesia, dizziness, tinnitus, and blurred vision.

Materials and Methods

This is a double-blind, randomized, controlled trial of 64 children aged 2-6 years, with surgery lasting 10 minutes up to 4 hours under sevoflurane anesthesia. Patients were randomly assigned to receive either propofol 1mg/kg (control group), or lidocaine 1.5mg/kg (experimental group), at the end of surgery. The drug was administered by the research investigator who was also blinded. To ensure that the research investigator was blinded, medication was prepared by the OR nurse who did not take part in the research group evaluation and placed the medication in covered syringes. EA was assessed by the blinded research investigator using the PAED score and the Face, Legs, Activity, Cry, Consolability (FLACC) Behavioral Pain Assessment Scale until 30 minutes after surgery. PACU discharge using the Modified Aldrete score was also recorded. (seen in Appendix 1)

The target population of the study was pediatric patients aged 2-6 years old, with American Society of Anesthesiologists (ASA) physical status classification I-II, who underwent any kind of surgery under general anesthesia using sevoflurane. This age group was chosen as this is considered to be the peak incidence of EA in children, as demonstrated in literature of Stoelting, RK, et al., 2005.[1]

Inclusion Criteria:

1. ASA Physical Status 1-2
2. Elective case
3. 2-6 years old
4. Male and female
5. Scheduled for any surgical procedure (ex. ophthalmologic, urologic, otorhinolaryngologic, abdominal, dental, neurologic cases) under general anesthesia using sevoflurane

Exclusion Criteria:

1. History of hypersensitivity to any of the study drugs used
2. Patients with history of hepatic or renal dysfunction
3. Patients with CNS dysfunction and sleep apnea
4. Patients with developmental delay, psychological, or psychiatric disorders
5. Procedures lasting less than 10 mins or more than 4 hours
6. Emergency cases

To achieve sufficient allocation concealment, randomization was carried out utilizing a computerized randomization tool (RANDOM.ORG- List Randomizer) prior

to the start of surgery. Sixty four children were included using consecutive sampling method and randomized into 2 groups. Random numbers were used to assign patients to the propofol group (control group P), or the lidocaine group (experimental group L) by the supervising investigator. Outcomes were monitored by the research investigator, who was blinded to the group allocation. Confounders were controlled using randomization and restriction.

Sample size was computed using Epi Info. Sample size was computed based on the results of the study of Shi, et al.[29], wherein the mean and standard deviation of PAED score for group A is 6.2 and 2.5; and for group B is 8.1 and 2.9. With an alpha of 0.05 and power of 0.8, the computed sample size was 64 or 32 patients per group.

The study commenced upon approval of the Technical Review Board and the Institutional Review Board and Ethics Committee of the Philippine Children's Medical Center. The patient was included in the study once parental consent was obtained by the research investigator, during the pre-operative assessment. Patients were randomly assigned into either one of the 2 groups – the experimental (Lidocaine, L) group and the control (Propofol, P) group. Baseline characteristics such as the patient's age, gender, weight, ASA classification, OR procedure done and duration of surgery were recorded. Recommended preoperative fasting intervals of 8, 6 and 2 hours fasting for solids, milk, and clear fluids, respectively were instructed to the enrolled patients. No premedication was administered to them. When the patient arrived at the operating room on the day of operation, the subject was hooked to standard monitors such as electrocardiography (ECG), pulse oximetry (SpO2), noninvasive blood pressure (NIBP), and temperature probe. General anesthesia was induced using the following agents: Midazolam 0.05-0.10 mg/kg/IV, Atropine 20 mcg/kg/IV, Fentanyl 2mcg/kg/IV, Propofol 2 mg/kg/IV, and Rocuronium 1mg/kg/IV (if for intubation). Anesthesia was maintained and titrated using Sevoflurane. Intravenous Paracetamol at 15mg/kg was given after induction and intravenous Ketorolac at 0.5mg/kg was given 30 minutes prior the end of the surgery. The research investigator was blinded to the treatment assignment.

If the patient was assigned to the Experimental (L) group, Lidocaine at 1.5 mg/kg was given 5 minutes prior to discontinuation of Sevoflurane. The same timing for the Control (P) group, but Propofol 1 mg/kg instead was given. All study drugs in their respective syringes were prepared, covered with colored paper and labeled with only the patients' name and hospital number by an OR nurse who did not participate in the process of evaluation of study groups. In addition, the intravenous line near the patient, where the prepared drug was administered was also covered with colored

paper and labeled with only the patients' name and hospital number by an OR nurse who did not participate in the process of evaluation of study groups. In addition, the intravenous line near the patient, where the prepared drug was administered was also covered with colored paper.

Once the patient was extubated and transferred to the PACU, the research investigator assessed the patient. Standard monitors were again placed. The patient's guardian was allowed to stay beside the child in the duration of his PACU stay. Adverse events including hypotension, seizure, deep sedation, arrhythmia, and PONV, perioral numbness, metallic taste, tongue paresthesia, dizziness, tinnitus, and blurred vision were observed and recorded by the research investigator during the recovery period. To ascertain if the patients had any of these occurrences, all of these side effects were clinically observed and evaluated; no diagnostic test was required. Patients were monitored for efficacy and safety outcomes, using FLACC and PAED scoring sheets, until the patients were discharged from the PACU. Parents of the participants were given a contact number of the research investigator and were free to report any side effects that occurred even after PACU discharge within 24 - 48 hours post-operatively. A checklist of the possible signs and symptoms to watch out for and report was provided by the research investigator to the participants' parent and/ or caregiver. The research investigator monitored for adverse events until 24-48 hours post operatively and made a phone-call at least once to all the participants' parent and/ or caregiver. Participants' caregiver had the right to withdraw their consent at any time and for any reason. When study-related injuries ensue and subjects were managed accordingly without charging them extra cost.

FLACC, PAED, and Aldrete scales were utilized to evaluate pain, the likelihood of emergence agitation, and the choice to discharge patient from the PACU, respectively. These tools have excellent validity and are widely accepted in the pediatric population, as these were evaluated in many nations, demonstrating their applicability in different ethnicities, cultures, and sociodemographic groups. Several studies have shown that among the 22 pain assessment tools, FLACC Scale was among the top 2 that scored high responsiveness, criteria validity, reliability, and internal consistency.[30] PAED scale is a reliable instrument to measure emergence delirium in pediatric population, as it shows a Cronbach's alpha value of 0.91, which indicates that the internal consistency of this tool falls within an acceptable level of reliability.[31] Over the past 40 years, Modified Aldrete Score is a well-known PACU discharge assessment tool that transformed the approach to assessing postoperative recovery in a straightforward, dependable, and repeatable manner based on common physiological parameters. As a result, it has greatly

improved postoperative patient safety and quality of care.[32]

FLACC Behavioral Pain Assessment Scale was used to evaluate the incidence and severity of pain for the participants. This scoring system is based on Face, Legs, Activity, Cry, Consolability scale. Each behavior was scored from 0-2, as described in table 4 (see in Appendix 4), and the total scores were tallied. The assessment was done once in a five minute interval from arrival to the PACU lasting to thirty minutes by the blinded anesthesiologist in charge of the case. A FLACC score of more than 4 for 5 minutes was considered as a patient in pain. Fentanyl (1mcg/kg) was administered for persistence of severe pain.

PAED score was used to evaluate EA occurrence of the participants. This tool consists of 5 criteria namely: 1. the child makes eye contact with the caregiver/ parent, 2. the child's action are purposeful, 3. the child is aware of his/her surrounding, 4. the child is restless, and, 5. the child is inconsolable. Each criterion was given a score between 0 and 4, as shown in table 5 (see in Appendix 4), and the total scores were tallied. A score of greater than or equal to 10, indicated that the child has EA and was given Midazolam (0.1mg/kg), as a rescue dose.

Another tool used in this study was the Modified Aldrete Score, which consists also of 5 criteria namely: 1. activity, 2. respiration, 3. circulation, 4. consciousness, and, 5. oxygen saturation. According to the characteristics listed in table 6 (see in Appendix 4), for each criterion, a score between 0 and 2 was assigned to it. The decision to transfer the patient from the PACU to the ward was made if the final score is greater than or equal to 9. Patients was assessed by the blinded anesthesiologist in charge of the case, and was assessed 1 hour post operatively, then hourly until the patient's score was 9 or above.

Demographic data, such as gender, age in years, duration of surgery in minutes, type of surgery and anesthesia technique, was presented as mean ± standard deviation and frequency (%). The assessed outcome was incidence of emergence agitation thru the use of PAED scores per group expressed as frequency and percentage.

The incidence of emergence delirium, postoperative pain, and adverse effects between lidocaine and propofol were compared using Chi-square test or Fisher exact test. Risk ratio was also computed for both EA and pain. Summary statistics for adverse effects, the incidence of hypotension, seizure, arrhythmia, PONV, perioral numbness, metallic taste, tongue paresthesia, dizziness, tinnitus, and blurred vision between the said comparators were included. P-values <0.05 was considered statistically significant.

Summary statistics were used to describe the clinicodemographic

characteristics of patients – frequency and percentage were used to summarize categorical variables, mean and standard deviation were used to summarize numeric variables. Chi-square or Fisher exact test was used to compare the incidence of EA and pain. Risk ratio was also computed using crude estimates data analysis technique. A p-value of < 0.05 is considered statistically significant.

The study was submitted to the Ethics Committee and Institutional Review Board of the Philippine Children's Medical Center and was then approved. Investigator adhered to the Good Clinical Practice and the study observed all Helsinki declaration rules. Ethical considerations during the study included voluntary participation and consent (parental permission), confidentiality (any identifying information was not available to, or accessed by anyone but the investigator, and there was also an insurance that such identifying information is excluded from any reports or published documents), anonymity (the identity of the participant remained unknown to the research team), and risk of harm (It is imperative that the evaluation process does not in any way harm (unintended or otherwise) participants, focusing on the risk to benefit ratio.

Possible risks included having adverse events such as hypotension, seizure, arrhythmia, PONV, perioral numbness, metallic taste, tongue paresthesia, dizziness, tinnitus, and blurred vision due to overdosage. In order to mitigate these risks, patients were weighed during preoperative assessment in order to determine the appropriate dosage of Propofol and Lidocaine. Additionally, emergency medications like phenylephrine and epinephrine for hypotension, midazolam for seizure, amiodarone for arrhythmia, and ondansetron for PONV, as well as reversal medication like intralipid for symptoms of overdosage such as perioral numbness, metallic taste, tongue paresthesia, dizziness, tinnitus, and blurred vision, were already on hand within the operating room. For study-related injuries, subjects were managed accordingly without charging them extra cost. Participants can withdraw from the study anytime without prejudice to their care. Participants' relative was instructed of their study-related responsibilities.

Risk of harm also required to measure the risk to benefit ratio as the study progressed. The study was beneficial to patients who have favorable outcomes, such as prevention of emergence agitation from developing, which did not interfere with surgical healing, did not cause distress for caregivers and parents, and lessened parental unhappiness with a child's care. The cost-effective prevention of emergence agitation following surgery for future pediatric patients became possible with the study's findings. There were no additional costs or financial benefit to the subjects of the study. Propofol and Lidocaine were free of charge to

to the patient, which was funded by the research investigator. In exchange for participating in the study, the patient was given 1 set of 8 crayons and a coloring book. Additionally, the relative's phone number was registered for a 2-day unlimited call and text promotion, which allowed the participant's relative to follow up with the research investigator. The research investigator covered the costs in the event of study-related damage, such as potential hospitalization, extra testing, or the need for emergency drugs.

Following data analysis, the paper-based data collection forms were stored in locked cabinets for five years in a designated place before being shredded. Encoded data was password protected and was kept on a different USB drive, which was only accessible by the researcher and will be removed and disposed of after five years.

RESULTS

This study included 64 pediatric patients aged 2-6 years with an ASA classification of I-II, who underwent various surgeries under general anesthesia using sevoflurane. Participants were evenly divided between the two exposure groups, with 32 children receiving a single dose of intravenous lidocaine and 32 receiving a single dose of propofol.

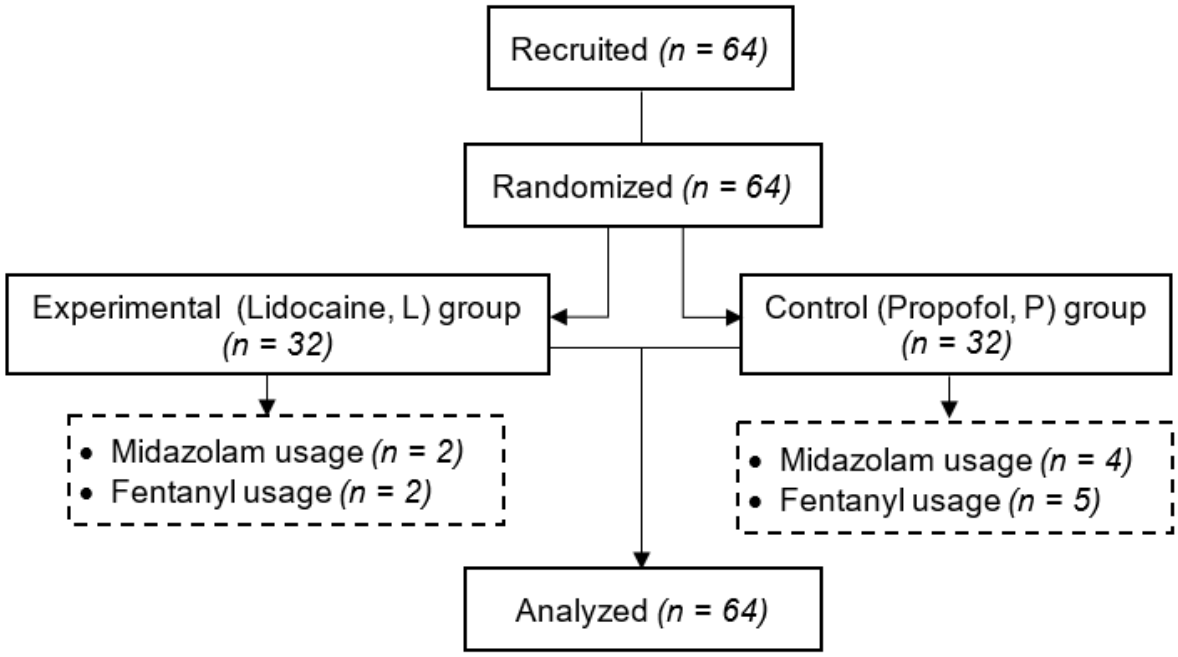

Table 1 shows the clinicodemographic characteristics of the patients in both groups. Group P and L participants are comparable in terms of gender, age, weight, duration of surgery and type of surgery.

Table 1. Clinicodemographic Distribution of Patients

	Propofol group (n= 32)	**Lidocaine group (n=32)**	**p-value**
Gender *			
Male	25 (78)j	25 (78)j	1.000
Female	7 (22)j	7 (22)j	
Age (years) +	3.41 ± 1.41	3.5 ± 1.22	0.777
Weight (kg) +	15.46 ± 5.08	16.48 ± 4.23	0.425
Duration of Surgery (minutes) ±	113.78 ± 76.07	111.81 ± 73.38	0.995
Type of Surgery d			
Head and Neck	9 (28)j	6 (19)j	0.774
Lower Abdomen	22 (69)j	25 (78)j	
Orthopedic	1 (3)j	1 (3)j	
Anesthesia Technique d			
General Anesthesia	10 (31)j	7 (22)j	0.572
Combined General and Regional Anesthesia	22 (69)j	25 (78)j	

* Chi-square
+ t-test
± Mann Whitney
d Fisher Exact
j (%)

Table 2 shows the incidence of EA among the 2 groups. Risk ratio was computed to be 0.5 [95% CI 0.098, 2.54] - i.e., the risk of having EA in patients given Lidocaine prior to end of anesthesia is 50% less as compared to those given Propofol. The results, though, were not statistically significant.

Table 2. Incidence of Emergence Agitation using PAED scoring

	Propofol group (n= 32)	**Lidocaine group (n=32)**	**RR [95% CI]**	**p-value**
(+) EA	4	2	0.5 [0.098, 2.54]	0.672
(-) EA	28	30		

Table 3 shows the incidence of pain among the 2 groups. Two out of thirty two patients in Lidocaine group, while 5/32 patients in the Propofol group had moderate to severe pain post operatively necessitating rescue medications. These results however, were not statistically significant. Risk ratio for the incidence of pain is computed to be 0.6 which means that the risk of having breakthrough pain in patients given Lidocaine prior to the end of the surgery is 40% less as compared to those given Propofol (RR:0.6, 95% CI [0.033, 1.91], p-value = 0.426)

Table 3. Incidence of Moderate to Severe Pain using FLACC Scoring

	Propofol group (n= 32)	**Lidocaine group (n=32)**	**RR [95% CI]**	**p-value**
(+) pain	5	2	0.6 [0.033, 1.91]	0.426
(-) pain	27	30		

There were no adverse events reported among the participants, indicating that all children tolerated the interventions without complications during the study period. All participants were assessed as transferable to the ward based on the MAS (Modified Aldrete Score), indicating that all children met the criteria for safe postoperative recovery and transfer. Three to five minutes were spent on the phone with the patients' relatives to inquire about their status after discharge.

Discussion

Majority of the participants in the Propofol and Lidocaine groups did not experience EA, demonstrating the effectiveness of both interventions in preventing EA. The results of the study may be applicable to other ASA 1-2 patients who were scheduled for any surgical procedure, but must be used with caution in patients who have a history of hypersensitivity to propofol or lidocaine, as well as those who have developmental delays, hepatic, renal, or CNS dysfunction, psychological disorders, or psychiatric disorders. Emergence agitation is a condition that is mostly associated to pediatric patients. When a patient who is awake and sedated exhibits violent behavior, an observer watches for signs and symptoms, including confusion, pain, and a slow pace transition. The patient may need pharmaceutical treatment in some situations. This research looked at the intra-operative administration of lidocaine or propofol concurrent with the intra -operative use of Sevoflurane anesthesia. The improvement provided by these drugs will optimize the quality of recovery of the patient.

Propofol inhibits GABA A receptors, which are responsible for central nervous system excitement. Propofol markedly reduced the incidence of EA in patients who had sevoflurane anesthesia, as demonstrated by Lee, CJ, et al., 2010. [19] The results of this research are consistent with the findings of Eshetie, et al.'s, 2020, study, which suggests that propofol be administered before the conclusion of surgery in order to prevent emergence agitation.[2] Lidocaine also lowers the incidence of EA due to its inhibition to sodium ions from depolarizing neurons, which results in no action potential.[19] According to Hall, EA, et al., 2021, there is also a disruption of pain signals, which explains why giving Lidocaine to pediatric patients effectively reduces their acute postoperative pain.[25] Incidence of EA was lower when lidocaine was compared to a placebo, but was higher when compared to propofol, esmolol and magnesium sulfate.[7] In this study, compared to Propofol, Lidocaine causes 50% less emerging agitation and post-operative pain to pediatric patients aged 2-6 years old. Lidocaine works by a multimodal manner, inhibiting several pain receptors such as muscarinic (M1, M3) and N-methyl-D-aspartate (NMDA) [25], which explains the lower incidence of post-operative pain in this study. On the other hand, only a few patients had post-operative pain with propofol, which was not statistically significant in this trial, since it inhibits proinflammatory cytokines and reduces lipopolysaccharide-induced reactive oxygen species formation.[29]

Contrary to the findings of Cohen et al.'s, 2003, study, which showed that pain and inconsolability persisted for hours after discharge from the recovery room, no untoward events were observed following discharge from the PACU to home, which is similar to that of Rahimzadeh et al., 2014. [11, 28] Adverse effects can be avoided by using the right dosages of propofol and lidocaine [28], which were utilized in this study at 1mg/kg and 1.5mg/kg, respectively. Since no adverse side effects were observed, both Lidocaine and Propofol are safe to use in pediatric patients. The strength of this research is that it includes a variety of surgeries, as opposed to previous studies that only focus on a particular kind of surgery. However, there is a limitation in the variability of cases, since there is only 1 case for each group who had orthopedic surgery. Lidocaine is less expensive than Propofol, which proves that it can be a cost effective alternative to prevent emergence agitation and acute post operative pain. Reduced emergence agitation would lead to higher parental satisfaction, lower hospital expenses, and better overall patient outcomes. Although the relative risks suggested a potential benefit, a wide range of confidence intervals of possible outcomes could mean that we cannot ascertain at this stage that the observed reactions are attributed to a true treatment effect. It is recommended that the results be interpreted with caution.

Conclusion

Both lidocaine or propofol significantly prevented the occurrence of emergence agitation in post-anesthesia care unit and decreased the risk of postoperative pain. Emergence agitation to pediatric patients occurred less when given Lidocaine, than Propofol. Both Propofol and Lidocaine can safely be used to prevent EA in children. Comparisons between other medications, such as midazolam and lidocaine or propofol are suggested. It is recommended to do research on combined medications which prevents children between the ages of 2 to 6 years old on having emergence agitation.

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References

1. Stoelting RK, Barash PG, Cullen BF. Clinical Anesthesia (Clinical Anesthesia (Barash)). 5th ed. [place unknown]: Lippincott Williams & Wilkins; 2005. 1584 p.

2. Eshetie D, Getinet H, Abdissa Z, Mollalign M. Incidence and associated factors of emergence agitation after general anesthesia and surgery among pediatric patients: A prospective follow-up study. Int J Surg Open [Internet]. 2020 [cited 2024 Jan 18];27:25-31. Available from: https://doi.org/10.1016/j.ijso.2020.10.005

3. Reduque LL, Verghese ST. Paediatric emergence delirium. Contin Educ Anaesth Crit Care Amp Pain [Internet]. 2013 Apr [cited 2023 May 18];13(2):39-41. Available from: https://doi.org/10.1093/bjaceaccp/mks051

4. Xiao Y, Jin X, Zhang Y, Huang T, Zhou L, Gao J. Efficacy of propofol for the prevention of emergence agitation after sevoflurane anaesthesia in children: A meta-analysis. Front Surg [Internet]. 2022 Oct 3 [cited 2023 May 18];9. Available from: https://doi.org/10.3389/fsurg.2022.1031010

5. Rosen HD, Mervitz D, Cravero JP. Pediatric emergence delirium: Canadian Pediatric Anesthesiologists' experience.

Pediatr Anesthesia [Internet]. 2015 Nov 12 [cited 2023 June 10];26(2):207-12. Available from: https://doi.org/10.1111/pan.12812

6. Kim S, Hahn S, Jang MJ, Choi Y, Hong H, Lee JH, Kim HS. Evaluation of the safety of using propofol for paediatric procedural sedation: A systematic review and meta-analysis. Sci Rep [Internet]. 2019 Aug 22 [cited 2023 June 10];9(1). Available from: https://doi.org/10.1038/s41598-019-48724-x

7. Pamintuan, N. E., & De la Cerna, A. (2023).Efficacy of intravenous lidocaine in controlling emergence agitation in children for surgery under Sevoflurane anesthesia: a meta-analysis. Philippine Children's Medical Center Journal, 19(1), 50-64

8. Nair S, Wolf A. Emergence delirium after paediatric anaesthesia: new strategies in avoidance and treatment. BJA Educ [Internet]. 2018 Jan [cited 2023 June 10];18(1):30-3. Available from: https://doi.org/10.1016/j.bjae.2017.07.001

9. Evidence-Based Clinical Decision Support System| UpToDate | Wolters Kluwer [Internet]. UpToDate; [cited 2023 July 18]. Available from: https://www.uptodate.com/contents/emergence-delirium-and-agitation-in-children

10. Kim YS, Chae YK, Choi YS, Min JH, Ahn SW, Yoon JW, Lee SE, Lee YK. A comparative study of emergence agitation between sevoflurane and propofol anesthesia in adults after closed reduction of nasal bone fracture. Korean J Anesthesiol [Internet]. 2012 [cited 2023 July 18];63(1):48. Available from: https://doi.org/10.4097/kjae.2012.63.1.48

11. Cohen IT, Finkel JC, Hannallah RS, Hummer KA, Patel KM. Rapid emergence does not explain agitation following sevoflurane anaesthesia in infants and children: a comparison with propofol. Pediatr Anesthesia [Internet]. 2003 Jan [cited 2023 July 18];13(1):63-7. Available from: https://doi.org/10.1046/j.1460-9592.2003.00948.x

12. Psychiatrist.com: JCP, PCC, and The CME Institute [Internet]. [cited 2023 July 18]. Available from: https://www.psychiatrist.com/wp-content/uploads/2021/02/15830_pathophysiology-agitation.pdf

13. Lepousé C, Lautner CA, Liu L, Gomis P, Leon A. Emergence delirium in adults in the post-anaesthesia care unit. Br J Anaesth [Internet]. 2006 Jun [cited 2023 July 18];96(6):747-53. Available from: https://doi.org/10.1093/bja/

14. Ramroop R, Hariharan S, Chen D. Emergence delirium following sevoflurane anesthesia in adults: prospective observational study. Braz J Anesthesiol (Engl Ed) [Internet]. 2019 May [cited 2023 July 18];69(3):233-41. Available from: https://doi.org/10.1016/j.bjane.2018.12.012

15. Voepel-Lewis T, Malviya S, Tait AR. A Prospective Cohort Study of Emergence Agitation in the Pediatric Postanesthesia Care Unit. Anesthesia Amp Analg [Internet]. 2003 Jun [cited 2023 July 19]:1625-30. Available from: https://doi.org/10.1213/01.ane.0000062522.21048.61

16. Mohkamkar, M., Farhoudi, F., Alam-Sahebpour, A., Mousavi, S.-A., Khani, S., & Shahmohammadi, S. Postanesthetic emergence agitation in pediatric patients under general anesthesia. Iranian journal of pediatrics. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4268839/

17. Li T, Dong T, Cui Y, Meng X, Dai Z. Effect of regional anesthesia on the postoperative delirium: A systematic review and meta-analysis of randomized controlled trials. Front Surg [Internet]. 2022 Jul 26 [cited 2023 July 19];9. Available from: https://doi.org/10.3389/fsurg.2022.937293

18. Zhu X, Yang M, Mu J, Wang Z, Zhang L, Wang H, Yan F. The Effect of General Anesthesia vs. Regional Anesthesia on Postoperative Delirium—A Systematic Review and Meta-Analysis. Front Med [Internet]. 2022 Mar 28 [cited 2023 July 19];9. Available from: https://doi.org/10.3389/fmed.2022.844371

19. Lee CJ, Lee SE, Oh MK, Shin CM, Kim YJ, Choe YK, Cheong SH, Lee KM, Lee JH, Lim SH, Kim YH, Cho KR. The effect of propofol on emergence agitation in children receiving sevoflurane for adenotonsillectomy. Korean J Anesthesiol [Internet]. 2010 [cited 2023 July 19];59(2):75. Available from: https://doi.org/10.4097/kjae.2010.59.2.75

20. Haile S, Girma T, Akalu L. Effectiveness of propofol on incidence and severity of emergence agitation on pediatric patients undergo ENT and ophthalmic surgery: Prospective cohort study design. Ann Med Surg [Internet]. 2021 Sep [cited 2023 July 19];69:102765. Available from: https://doi.org/10.1016/j.amsu.2021.102765

21. Beecham, G. B., Nessel, T. A., & Goyal, A. Lidocaine - StatPearls - NCBI Bookshelf. Lidocaine. https://www.ncbi.nlm.nih.gov/books/NBK539881/

22. Heath C, Hii J, Thalayasingam P, von Ungern-Sternberg BS, Sommerfield D. Perioperative Intravenous Lidocaine Use in Children. Pediatr Anesthesia [Internet]. 2022 Nov 24 [cited 2023 July 28]. Available from: https://doi.org/10.1111/pan.14608

23. Both CP, Thomas J, Bühler PK, Schmitz A, Weiss M, Piegeler T. Factors associated with intravenous lidocaine in pediatric patients undergoing laparoscopic appendectomy – a retrospective, single-centre experience. BMC Anesthesiol [Internet]. 2018 Jul 18 [cited 2023 July 28];18(1). Available from: https://doi.org/10.1186/s12871-018-0545-1

24. Nakajima D, Kawakami H, Mihara T, Sato H, Goto T. Effectiveness of intravenous lidocaine in preventing postoperative nausea and vomiting in pediatric patients: A systematic review and meta-analysis. PLOS ONE [Internet]. 2020 Jan 28 [cited 2023 July 28];15(1):e0227904. Available from: https://doi.org/10.1371/journal.pone.0227904

25. Hall EA, Sauer HE, Davis MS, Anghelescu DL. Lidocaine Infusions for Pain Management in Pediatrics. Pediatr Drugs [Internet]. 2021 May 26 [cited 2023 July 28];23(4):349-59. Available from: https://doi.org/10.1007/s40272-021-00454-2

26. Heath C, Hii J, Thalayasingam P, von Ungern-Sternberg BS, Sommerfield D. Perioperative Intravenous Lidocaine Use in Children. Pediatr Anesthesia [Internet]. 2022 Nov 24 [cited 2023 July 28]. Available from: https://doi.org/10.1111/pan.14608

27. Lee JY, Kim CH, Kim SH, Kim JS, Lee KY. Intravenous Lidocaine Prior to Extubation Reduces Emergence Agitation and Cough in Pediatric Adenotonsillectomy under Sevoflurane Anesthesia. Korean J Anesthesiol [Internet]. 2007 [cited 2023 July 28];53(4):458. Available from: https://doi.org/10.4097/kjae.2007.53.4.458

28. Rahimzadeh P, Faiz SH, Alebouyeh MR, Dasian A, Sayarifard A. Appropriate Anesthesia Regimen to Control Sevoflurane-Induced Emergence Agitation in Children: Propofol–Lidocaine and Thiopental Sodium–Lidocaine: A Randomized Controlled Trial. Iran Red Crescent Med J [Internet]. 2014 Jul 5 [cited 2023 July 28];16(7). Available from: https://doi.org/10.5812/ircmj.16388

29. Shi S, Gan L, Jin CN, Liu RF. Effects of propofol combined with lidocaine on hemodynamics, serum adrenocortico-tropic hormone, interleukin-6, and cortisol in children. World J Clin Cases [Internet]. 2022 Aug 26 [cited 2023 July 28];10(24):8506-13.

Available from: https://doi.org/10.12998/wjcc.v10.i24.8506

30. Chan AY, Ge M, Harrop E, Johnson M, Oulton K, Skene SS, Wong IC, Jamieson L, Howard RF, Liossi C. Pain assessment tools in paediatric palliative care: A systematic review of psychometric properties and recommendations for clinical practice. Palliat Med [Internet]. 2021 Dec 29 [cited 2023 July 28];36(1):30-43. Available from: https://doi.org/10.1177/02692163211049309

31. Epulef V, Muñoz S, Alarcón AM, Vial M. Spanish version of the Pediatric Anesthesia Emergence Delirium scale: translation and cross-cultural adaptation. BMC Anesthesiol [Internet]. 2022 Nov 14 [cited 2023 July 28];22(1). Available from: https://doi.org/10.1186/s12871-022-01893-1

32. National Center for Biotechnology Information [Internet]. Aldrete Scoring System - StatPearls - NCBI Bookshelf; [cited 2023 July 28]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK594237/.