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Comparison of Intravenous Infusion of Ketamine Versus Propofol for Post-Operative Complications in Children Undergoing Strabismus Surgery

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ABSTRACT

Background: To compare the post-operative complications like nausea, vomiting, pain, incidence of oculocardiac reflex, sedation, and agitation in the intravenous infusion of ketamine and propofol in children undergoing strabismus surgery. **Methods:** Sixty pediatric patients aged 5–15 years were enrolled for the study. Patients were assigned into 2 groups: Ketamine (K) (n=30) and Propofol (P) (n=30) using a computer-generated random number table. After pre-oxygenation with 6 L/min 100% O2, fentanyl 1 mcg/kg followed by ketamine 1 mg/kg or propofol 3 mg/kg was given. Further vecuronium 0.1mg/kg was given and after 3 minutes of IPPV patients were intubated. Anesthesia was maintained with intravenous infusion of ketamine 1–3 mg/kg/hr or propofol 6–9 mg/kg/hr with 50% oxygen and 50% air at 3L/min. **Results:** The consumption of antiemetics (P value<0.05) and analgesics (P value<0.05) in group K were significantly lower than in group P. Postoperative agitation score (P value<0.05), Face Pain Scale (P value<0.05) the incidence of oculocardiac reflex (P value<0.05), Ramsay Sedation Score (P value< 0.05) during awakening and at postoperative 30th min (P value< 0.05) in Group K were significantly lower than in Group P. **Conclusion:** Postoperative complications are less with the infusion of ketamine than propofol in children undergoing strabismus surgery.

Keywords: Ketamine, Pain, Pediatrics, Propofol, Strabismus.

INTRODUCTION

Strabismus, also known as crossed eyes or squint, is a visual condition where the gaze is misaligned. It is fairly common in children and affects roughly 2% - 5% of the population. Strabismus can affect either one or both eyes, with an eye turning in, out, up or down. Although it is never too late to try correction, the earlier this is done is better. The best results are usually obtained in children less than six years old. Strabismus surgery is extra-ocular surgery which involves repositioning of whichever ocular muscles are misaligned. The incidence of the oculocardiac reflex (OCR) during strabismus surgery has been variously reported as 14% to 90%, depending on the premedication, anesthetic agent, and the definition of OCR.[1] OCR occurs through the trigeminovagal reflex arc and can be triggered by mechanical stimulation such as pressure on the eye, intraorbital injections, or hematomas and especially by traction on extraocular muscles.[2] A variety of methods such as normoxia, normocapnia, premedication using atropine or glycopyrrolate, and adequate anesthetic depth have been used to prevent the OCR. However, none of them has been found to be satisfactory.[3]

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Strabismus surgery is normally carried out under general anesthesia (always so in children), although a local anesthetic technique may occasionally be used in adults. There are several ways of administering general anesthesia in strabismus surgery. Commonly a technique involving endotracheal intubation with the use of a neuromuscular blocking agent is used, although Laryngeal Mask Airways (LMA's) can also be used. During surgery, the eye must be immobile, as forced duction test (FDT) is required to be done. This is done to access the mechanical restriction to movement of the eye by moving it into each field of gaze, done by grasping the sclera near the corneal limbus with a pair of forceps. This test allows the surgeon to differentiate between a paretic muscle and a mechanical restriction limiting eye movement. As the muscle tone varies with the change in depths of anesthesia, some surgeons may prefer neuromuscular blockade.

Ketamine is in clinical use since 1970 as a unique intravenous (IV) anesthetic that produces a wide spectrum of pharmacological effects including sedation, catalepsy, somatic analgesia, bronchodilation, amnestic, dose-dependent anesthetic actions, it also activates sympathetic nervous system that increases the heart rate, blood pressure, and cardiac output.[4-7] The cataleptic state is an akinetic state with the loss of orthostatic reflexes without impairment of consciousness.[6,8] Ketamine is a water-soluble phencyclidine derivative. The ketamine molecule contains an asymmetric carbon atom with two enantiomers: The S (+) isomer and the R (−) isomer.[9] S-isomer of ketamine, reportedly enhances analgesia greater than the racemic mixture.[9]

Its mechanism of action is mainly by noncompetitive antagonism of the N-methyl D-aspartic acid (NMDA) receptor. It also interacts with opioid receptors, monoamine, cholinergic, purinergic, and adrenoreceptor systems as well as have local anesthetic effects.[10] It has got minimal effects on central respiratory drive and produces airway relaxation by acting on various receptors and inflammatory cascades and bronchial smooth muscles.[4,11] It increases salivation and muscle tone.[7] Ketamine can be used as premedication, induction, maintenance, and as postoperative analgesia alone or in combination with other drugs.

Propofol is an intravenous agent used commonly for the induction and maintenance of anesthesia procedural, and critical care sedation in children. Propofol is chemically described as 2, 6-diisopropylphenol and it is formulated in a white, oil-in-water emulsion with a pka of 11. The emulsion form makes it very useful for the intravenous delivery of fat-soluble agents but also inheritably unstable vehicles that provide fertile media for bacterial proliferation and carry the potential risk of iatrogenic sepsis after contamination. Propofol is readily oxidized to quinine which turns the suspension yellow in colour after approximately 6 hours of exposure to air. Propofol inhibits N-methyl-d-aspartate (NMDA)-receptors in hippocampal neurons and this may have contributed to the positive effects on the mood state after operation.[12] As the clearances of propofol depends on postnatal age, there is a risk for its accumulation in preterm, and in the first two weeks of postnatal life.[13] Propofol infusion syndrome has to be kept in mind if propofol is usedat doses greater than 4 mg/kg/h of longer than 48 hours especially in pediatric patients.[14]

While propofol has advantages over inhalational anesthesia, like less postoperative nausea and emergence delirium in children, pain on injection remains a problem even with the newer formulations. As there are currently less published data comparing intravenous infusion of propofol and ketamine without using volatile agents, we aimed to compare propofol and ketamine with a special emphasis on the incidence of pain, agitation, sedation, OCR, PONV, and consumption of analgesics during strabismus surgery in children.

MATERIALS AND METHODS

This randomized prospective double blind control study was conducted in Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University. The study was conducted in 60 pediatric patients aged 5 to 15 years scheduled for strabismus correction surgery under general anesthesia. Written informed consent was obtained from all the parents of patients before being included in the study.

Patients excluded include those with ASA physical status greater than I; those who were younger than 5 years or older than 15 years; those who had hypertension, psychiatric disorders, drug allergy, cardiovascular and clotting disorders, and those whose families did not approve inclusion.

After checking the anesthesia machine and preparing emergency and anesthetic drug, patients were taken inside the surgery room, a 22-gauge cannula was inserted into a vein in the dorsum of the hand and saline was infused at a rate of 3 ml/kg/h. Standard ASA monitors including electrocardiography, arterial blood pressure, end-tidal CO_2, temperature probe, and pulse oximetry were attached. Ketamine and Propofol 1% were prepared in an unlabeled, impermeable, red 50 ml syringe by an assistant for intravenous infusion. All patients were randomly allocated through computer-generated random table number to the following two groups of 30 patients each:

Group K- ketamine (n =30) and Group P- propofol (n =30).

None of the patients were pre-medicated. After pre-oxygenation with 6 L/min of 100% O2, fentanyl 1 mcg/kg was given, ketamine 0.1 mg/kg or propofol (1%) 3mg /kg was slowly given as inducing agent, followed by vecuronium 0.1 mg/kg as a muscle relaxant. After 3 min of IPPV airway was secured with supraglottic devices or ETT and was confirmed by capnography. The patient was shifted to controlled positive pressure ventilation and then was handed over to the surgeon. Anesthesia was maintained by intravenous infusion of ketamine1–3 mg/kg/hr or propofol (1%) 6–9 mg/kg/hr with 50% oxygen and 50% air at 3L/min.

During the traction, the minimal heart rate was recorded. If the heart rate decreased by 20% beats/min from the basal line,[15] the surgeon was asked to release the extraocular muscle and 0.01 mg/kg of atropine intravenously was given if bradycardia did not improve. Intravenous anesthetics were stopped 5 minutes before ending the operation and extubation was performed after the complete reversal of neuromuscular blockade. Postoperatively consumption of antiemetic, analgesics, incidence of oculocardiac reflex, and following scores were noted.

The numeric rank score for Postoperative nausea and vomiting

0 = no nausea

1 = vomiting once

2 = vomiting twice or more times [16]

Faces Pain Scale (FPS) Score for postoperative pain by choosing face 0, 2, 4, 6, 8, or 10, counting left to right, so 0 = no pain and 10 = very much pain.

Ramsay Sedation Score (RSS) during awakening and after 30 min recorded on a numerical scale.
1 = anxiety and completely awake
2 = completely awake
3 = awake but drowsy
4 = asleep but responsive to verbal commands
5 = asleep but responsive to tactile Stimulus
6 = asleep and not responsive to any stimulus

Emergence agitation (behavior score) for post-operative agitation
1 = sleeping
2 = awake and calm
3 = irritable and crying
4 = inconsolable crying
5 = severe restlessness and disorientation purposelessly wanting to get out of the bed.

Nausea and vomiting were treated with Ondensatron 0.15mg/kg and Nonopioid analgesic like paracetamol 15mg/kg was given to the patients who had FPS >=3 after the surgery.

RESULTS

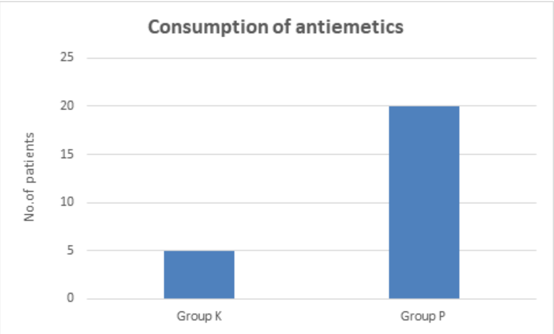

Figure 1: Consumption of antiemetics in study groups.

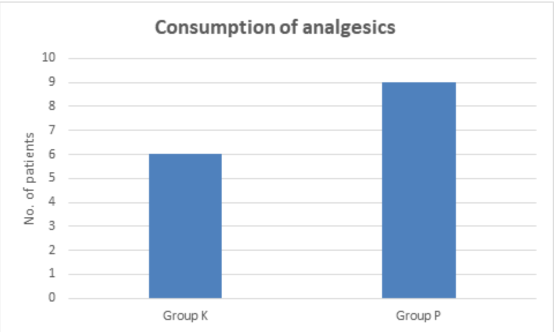

Figure 2: Consumption of analgesics in study groups.

At the end of the study, the data were analyzed on SPSS 20.0 software version. Mean +standard deviation (SD) or median (interquartile ranges) values or n (%) were calculated for different parameters recorded in the study. Consumption of antiemetics was compared using an independent sample t-test. Postoperative agitation score, FPS, were compared using the Kruskal–Wallis test.
The consumption of antiemetic (P=value<0.05) in Group K were significantly lower than in Group P [Figure 1]
Consumption of analgesics in group K were significantly lower than in group P (P value<0.05) [Figure 2]. Postoperative agitation score (P value<0.05), Face Pain Scale (P value<0.05), the incidence of oculocardiac reflex (p value<0.05) (Fig. 3), Ramsay Sedation Score (P value<0.05) during awakening and at postoperative 30th min (P value<0.05) in Group K were significantly lower than in Group P.

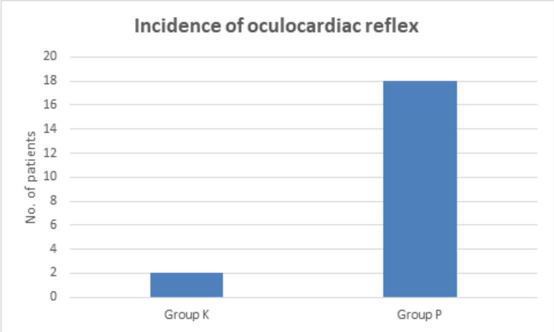

Figure 3: Incidence of oculocardiac reflex in study groups.

DISCUSSION

The main findings of the present study indicates that the infusion of ketamine is more effective than the intravenous infusion of propofol, in decreasing, the consumption of antiemetics and analgesics, incidence of oculocardiac reflex and the grades of Face pain Scale, agitation score and sedation score.
Pain stimulus to the patients was the same as all the procedures were done by the same surgeon with the same technique. There are some undesired effects of the surgery such as postoperative pain, anxiety, agitation, PONV, and OCR.[15,17-19] These effects are the most frequent complications secondary to anesthesia, and leading causes for distress in patients recovering from general anesthesia.[20,21]
Both propofol and ketamine are found to be safe and effective sedation for the short, painful procedures performed.[22] Pain itself can induce PONV.[23] The pain level during awakening affects the patient's agitation score. Although propofol produces dose-related sedation, amnesia, and anxiolysis, it is a poor analgesic and usually requires an adjunctive analgesic agent.[24] Moreover, it was reported that propofol has a pharmacokinetic profile leading to rapid induction and recovery times with minimal postoperative confusion.[24]
In the present study, it was found that the heart rate and mean arterial blood pressure was higher in group k than group P during intubation, incision, and extubation, but both were near the baseline in

between these events and during the postoperative period. Similar to Badrinath et al,[25] heart rate and mean arterial blood pressure were within an acceptable range consequently no patient needed treatment.[25]

In our study, the incidence of PONV and the consumption of antiemetics in Group P are significantly higher than in Group K. Although propofol, which provides hypnosis and amnesia, is antiemetic,[26] when used solely as an induction agent, propofol is not beneficial in reducing the incidence of nausea or vomiting. The low consumption of ketamine may be the reason for low incidence of PONV as larger dosages of ketamine were associated with a clinically significant increase in PONV.[23] Thorp et al,[27] reported that intravenous doses of ketamine-associated vomiting are neither related to the initial loading dose nor to the total dose but, the modest increase in receiving high cumulative doses (>7 mg/kg). Postoperative pain and the use of opioids analgesia in the perioperative period may have contributed to this.[28,29]

In the current study, the patients administered with propofol seem to be more prone to develop pronounced OCR. Tramer et al,[19] revealed that propofol, despite the use of anticholinergics, substantially increases the incidence of OCR. Propofol has the potency to increase the incidence of bradycardia by a central sympatholytic effect. Whereas ketamine seems to protect against the parasympathetic activation induced by OCR.[2] Choi et al,[30] reported that 1–2 mg/kg of ketamine for anesthetic induction results in a lower incidence of OCR than propofol in children undergoing strabismus surgery.

These above observations were on small study subjects which can be further confirmed on a larger sample size of the population.

CONCLUSION

Thus, it appears infusion of ketamine is more advantageous than the infusion of propofol for postoperative complications (nausea, vomiting, pain, incidence of oculocardiac reflex, sedation, and agitation) in children when used in strabismus surgery.

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