

Ketamine or Atropine: Which One Better Prevents Oculocardiac Reflex during Eye Surgery? a Prospective Randomized Clinical Trial

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Abstract- Profound bradycardia during eye surgery is a potentially serious event. In clinical practice oculocardiac reflex (OCR) is most often encountered during squint surgery. The objective of this study was to assess the occurrence of OCR and prove the effect of ketamine as an induction drug and anticholinergic premedication (atropine) to prevent OCR. This study comprised 90 patients (aged 4-10 years) operated for squint surgery under general anesthesia. Patients were divided into three groups. Using block randomization, each patient enrolled in one of the three groups based on organized random table prepared by statistician. Group K received ketamine as an induction drug, Group A was premedicated with intravenous injection of atropine and Group C did not receive any premedication. Patients were monitored during operation for any bradycardia or dysrhythmias. The observed data showed occurrence of 63% OCR in Group C as compared to 43% in group A and only 20% in Group K. Current study showed that induction with ketamine in the patients of squint surgery under general anesthesia definitely obtunds OCR and prevents any untoward effects of dysrhythmias during eye surgery.

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Introduction

Oculocardiac reflex (OCR) because of its incidence (32-90%) and also serious possible outcomes is potentially one of the most significant and serious anesthesiologist concerns during pediatric eye surgical procedures especially during corrective strabismus surgery (1).

There is not a gold standard method for OCR prevention. It may show diverse clinical unwanted effects from bradycardia to complete heart block and arrest (2, 3). Traction on the extraocular muscles or pressure on the eyeball and stimulation of any of the orbital contents, including the periosteum causes bradycardia, atrioventricular block, ventricular ectopy, or asystole (4). Applying an appropriate preventive method to blunt OCR or reduce the incidence of this reflex is subject to many studies and

may play a significant concern in managing anesthesia for these patients. In this clinical trial study authors intended to compare the effects of atropine as a chronotropic anticholinergic drug with ketamine and a placebo to find which one could better prevent OCR.

Materials and Methods

The study protocol was accepted by review and ethical committee of our department. We obtained written informed parental consent to perform this study. We did a pilot study for sample size calculation and then during 30 months period 90 children aged between 4 -10 years and with ASA physical status I or II, were selected to undergo surgical correction of strabismus in Farabi Eye Hospital.

Patients with a history of heart conduction block,

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vasovagal responses, medication that cause heart conduction system disturbances, and patients who had a contraindication for using ketamine or propofol were excluded from the study. Children and their parents were visited before the scheduled procedure for preoperative examination and explanation of study plan, probable side effects and asked for permission for participation in the experiment.

On the day of surgery, the children were advised to drink sweet and clear drinks until four h before operating room scheduled time. Using block randomization, each patient enrolled in one of three groups based on organized random table prepared by statistician: atropine (Group A), ketamine (Group K) and placebo (Group C), correspondingly. Baseline vital signs were recorded, and a peripheral IV line was established after using Emla cream 30 min prior to catheterization. After infusion of 3-5 ml/kg ringer lactate solution, induction of anesthesia was performed based on different protocols. The syringes contained study drugs were prepared and infused by anesthesiologist who was not involved in data collection and patient management during operation.

Three-lead electrocardiogram and noninvasive blood pressure monitoring were applied, and baseline measurements were recorded. Induction of general anesthesia was done in our patients as follows: group C as control group (propofol, 2 mg/kg, fentanyl, 1 µg/kg, and atracurium, 0.5 mg/kg), group K (ketamine, 1.5mg/kg, fentanyl, 1 µg/kg, and atracurium, 0.5 mg/kg) and group A (atropine, 0.15 mg/kg, propofol, 2mg/kg, fentanyl, 1 µg/kg, and atracurium 0.5 mg/kg. A tracheal tube with suitable size was placed three minutes after atracurium administration, and anesthesia was maintained with 1.5MAC isoflurane and a mixture of 50% oxygen in 50% nitrous oxide.

Systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded immediately before and 1, 15, 30, 45, and 60 min after induction and heart rate (HR) were recorded continuously. We used mechanical ventilation IPPV with 10ml/kg tidal volume and respiratory rate of 14/min to preserving SPO₂ and ETco₂ in normal limits. We set alarm of monitoring devices for more range base on basal vital sign.

During the traction, the lowest heart rate (HR) was recorded and if it was below basal HR by > 10% beats/min, the anesthetist asked the surgeon to discontinue traction of extraocular muscle (EOM). If OCR was not recovered within 20 seconds by releasing tension on the muscle, atropine 0.02 mg/kg was injected intravenously. Patients were classified as OCR

positive if maximal HR drop off was >10% beats/min, or arrhythmia appeared on the electrocardiogram during the traction of EOM. The severity of OCR graded as mild if HR decreased by less than 20% of the baseline, and moderate if it decreased 20-30% of the baseline and severe if it decreased more than 30% of the baseline. A lead II ECG tracing was applied during the procedure for finding dysrhythmias.

Prior to the completion of surgery, ondansetron 0.1 mg/kg was given as an antiemetic, and after the surgery, neuromuscular blockade was antagonized with neostigmine 0.04 mg/kg and atropine 0.02 mg/kg. The tracheal tube was removed after development of sufficient spontaneous ventilation. Following extubation, the patient was transferred to the post-anesthesia care unit (PACU) and remained there until transferred to the surgery ward. The PACU stay time and post-operative analgesia was recorded by an anesthesiologist blinded to the patient's randomization group.

We used SPSS version 15 for statistical analysis. Numeric statistics were presented as frequencies, and continuous variables were presented as mean and standard deviations. To compare mean of HR, systolic, diastolic and mean blood pressure and other quantitative data we used ANOVA test and Tukey-B post Hoc test. For comparison of incidence of OCR in three groups, we used Mann-Whitney test. A *P*-value<0.05 was considered to be statistically significant.

Results

Incidence of OCR in the control group was 63%, whereas this was 43% in the atropine group and 20% in the ketamine group.

Demographic characteristics are shown in Table 1, and there were no statistically significant differences in baseline data amongst three groups. We have no missing cases, and all enrolled cases were analyzed. The three groups were not statistically different regarding age, weight, sex, number of muscles, time of surgery, anesthesia, and post anesthesia care unit stay time.

Baseline heart rates, diastolic and systolic blood pressures, and their changes at different time intervals were shown in Figures 1-3. The frequency of the OCR and HR reduction and arrhythmias following extraocular muscle traction in different study group were shown in table 2.

Table 1. Demographic characteristics of three groups

Variables	Atropine	Ketamine	Control	P-value
Sex (F/M)	14/16	13/17	11/19	NS*
Age (years)	5.7± 2.1	6.9± 1.4	6.1± 1.8	NS
Weight (Kg)	12.8 ± 2.9	14.2 ± 4.1	13.6 ± 3.9	NS
NO. of Muscles (range)	2(1-3)	2(1-3)	2(1-3)	NS
Operation time (min)	55± 21	61± 17	66± 13	NS
Anesthesia time (min)	75 ± 12	80± 23	70± 18	NS
PACU stay time (min)	15±3	14±4	16±2	NS
Basal HR (bpm)	103.4±0.53	102.2±0.83	104.7±0.5	NS
Basal MAP (mmHg)	7.2±0.93	71.6±0.90	70.3±0.93	NS

*NS: Non-Significant

Table 2. The comparison of OCR, HR reduction and arrhythmia in three groups

Variables	Atropine	Ketamine	Control	P-value
Δ HR< 20%	4	3	6	0.025
Δ HR20-30%	5	2	5	0.02
Δ HR>30%	1	0	2	NS*
OCR occurred	13	6	19	0.01
Sinus bradycardia	10	5	13	0.015
Junctional rhythm	2	1	4	NS
Bigemini	1	0	2	NS

*NS: Non-Significant

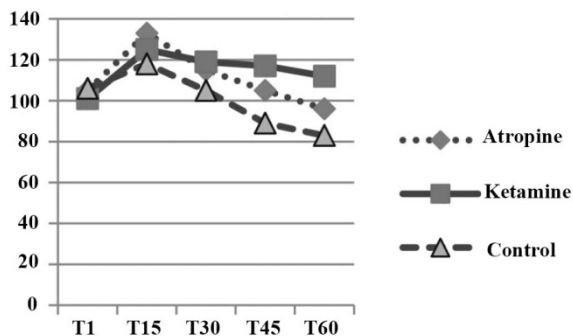


Figure 1. HR changes in three groups (P=0.02)

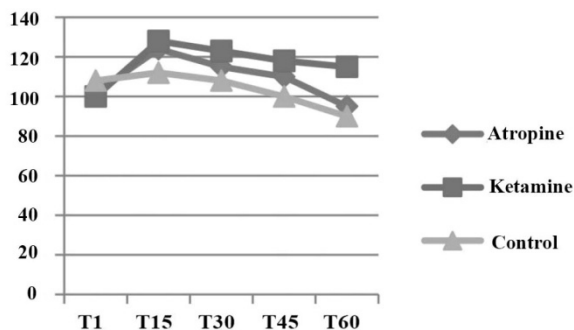


Figure 2. Systolic blood pressure changes in three groups (P>0.05)

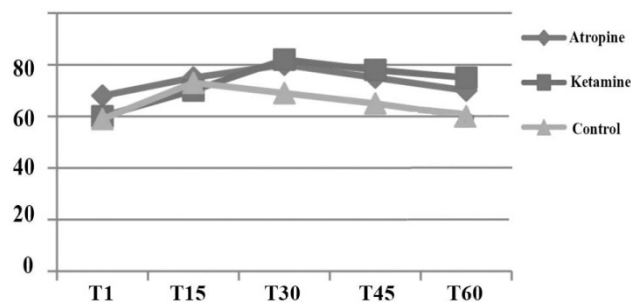


Figure 3. Diastolic blood pressure changes in three groups (P>0.05)

Discussion

Current findings show the OCR incidence was 63% in the control group, whereas this was 43% in the atropine group and 20% in the ketamine group. According to Choi study, the incidence of OCR in patients who propofol, ketamine, halothane or sevoflurane were used as a main anesthetic, the incidence of OCR was lowest in the continuous ketamine infusion, followed by sevoflurane, halothane and propofol (5).

Pretreatment with intravenous anticholinergics such as atropine or glycopyrrolate decreases the incidence of OCR and is indicated in patients with a history of conduction disturbances, vasovagal responses, or β-blocker therapy (6). Atropine increases firing of the sinoatrial node (SA) and

conduction through the atrioventricular node (AV) of the heart, opposes the actions of the vagus nerve, blocks acetylcholine receptor sites (7). Both IV and IM form of atropine is effective in the reduction in the rate of the OCR in children undergone strabismus corrective surgery. However, even higher doses cannot completely protect against OCR in children (8).

Moreover, atropine cannot totally prevent either bradycardia or hypotension but also may cause bigeminy and increase ectopic beats, and these arrhythmias are more persistent than the OCR. In addition, atropine is ineffective to abolish inhibition of adrenergic vasoconstriction as demonstrated after electrical stimulation of spinal trigeminal tract and trigeminal nuclear complex (9-10). The mechanism by which ketamine stimulates the circulatory system remains mysterious (5). Although ketamine's primary site of action appears to be the phencyclidine receptor on the N-methyl-D-aspartate (NMDA) receptor complex, additional activity on opiate and quisqualate receptors is suggested. Ketamine profoundly inhibits muscarinic signaling (11). Ketamine also causes the sympathoneuronal release of norepinephrine, which can be detected in venous blood (12). Ketamine inhibits the efferent cardiac vagal drive by its central action, not baroreflex function. This central vagolysis is probably the cause of its positive chronotropic effects. It is believed that ketamine may induce an increase in HR by bearing an inhibitory effect on parasympathetic receptors, where the agent has a greater affinity for nicotinic-AChRs over muscarinic-AChRs. Ketamine inhibits nicotinic cholinergic excitation in cardiac preganglionic parasympathetic neurons of the nucleus ambiguus of the brainstem (13). The hypothesis is that the ketamine will inhibit the chemical release produced by vagal stimulation throughout the parasympathetic system by blocking the nAChRs within the cardiac ganglion and mAChRs at the target tissue.

However, by testing the effects of ketamine on each of these receptors, it is predicted that there will be evidence to suggest that ketamine has a greater effect on the nAChRs at the ganglia (14). In conclusion, we found that ketamine was associated with a lower incidence of the OCR and may be the better choice as an induction drug for eye surgery.

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