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*Original Article*

# Comparison of effects of thiopental, propofol or ketamine on the cardiovascular responses of the oculocardiac reflex during strabismus surgery

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## Abstract

**BACKGROUND:** The oculocardiac reflex (OCR), which is most often encountered during strabismus surgery in children, may cause bradycardia, arrhythmias and cardiac arrest following a variety of stimuli arising in or near the eyeball. The main purpose of this study was to evaluate the effects of various anesthetic regimens on modulation of the cardiovascular effects of the OCR during strabismus surgery.

**METHODS:** Three hundred ASA physical status I-II patients, scheduled for elective strabismus surgery under general anesthesia, randomly allocated in a double blind fashion to one of the three anesthetic regimens: group P: propofol (2 mg/kg), alfentanil 0.02 mg/kg and atracurium 0.5 mg/kg at induction; group K: ketamine racemate (2 mg/kg), alfentanil 0.02 mg/kg and atracurium 0.5 mg/kg at induction; group T: thiopental (5 mg/kg), alfentanil 0.02 mg/kg, and atracurium 0.5 mg/kg at induction. Mean arterial pressure (MAP) and heart rate (HR) were recorded just before induction, at 1, 15, 30, 45 and 60 minutes after induction. OCR was defined as a 20 beats/minute change in HR induced by traction compared with basal value.

**RESULTS:** Mean HR (± SD) during total period of surgery in group P was significantly slower than that in group K (111.90 ± 1.10 vs. 116.7 ± 0.70, respectively; P<0.05). Mean HR changes (± SD) in group K was significantly higher than that in group P (11.2 ± 1.44 vs. 8.7 ± 1.50 respectively, P<0.05). MAP changes (± SD) was significantly lower in patients in group P compared with patients in group K or T (12.5 ± 1.13 vs. 19.3 ± 0.80 or 18.9 ± 0.91, respectively; P<0.05). Incidence of OCR was significantly lower in patients in group K compared with patients in group T or P (9% vs. 16% and 13%. Respectively; P<0.05).

**CONCLUSIONS:** Induction of anesthesia with ketamine is associated with the least cardiovascular changes induced by OCR during strabismus surgery.

**KEY WORDS:** Oculocardiac reflex, strabismus surgery, ketamine, propofol, thiopental.

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The oculocardiac reflex (OCR), which is most often encountered during strabismus surgery in children, may cause bradycardia, arrhythmias and cardiac arrest following a variety of stimuli arising in or near the eyeball [1-3]. The incidence of OCR has been estimated from 32% to 90% in earlier studies [4-7]. Prophylactic anti-cholinergic is recommended and adequate cardiac monitoring must accompany these interventions, as immediate action may be required. OCR may be manifested by bigeminey, ectopic beats, nodal rhythm and AV block due to traction on extraocular eye muscles (EOM) [8-10]. Various manoeuvres to prevent or minimize the OCR have been studied before. In contrast, the

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effects of anesthetic regimens on the reflex have received little attention. The hemodynamic response to the OCR was divided into two phases by Braun and colleagues [11]. The first phase, cholinergic, causes bradycardia and the second phase of the reflex, adrenergic, is described as counterregulation (CR). In addition, a hemodynamic release reaction (RR) is frequently observed during ocular traction release. Anesthetics may influence these various stages of the reflex in different ways. So, we designed this randomized double blind study to determine the effect of various anesthetic regimens (propofol/alfentanil/atracurium vs. ketamine/alfentanil/atracurium vs. thiopental/alfentanil/atracurium) on the cardiovascular responses of the OCR during strabismus surgery.

## Methods

After obtaining institutional approval and written informed consent, 300 patients (2-18 years, ASA physical status I or II) who were to undergo elective strabismus surgery were included in a prospective randomized controlled study. Patients with trauma to eye, ASA III or IV, who had contraindication for using thiopental, ketamine or propofol, had cardiovascular diseases or had taken cardiovascular drugs were excluded from the study. On the day of surgery, all patients arrived in the operating room without premedication. Standard monitoring was applied (the lead II electrocardiogram, pulse oximetry and noninvasive blood pressure monitor). The baseline blood pressure and heart rate (base) were recorded after a resting period of 5 minutes. In a double blind fashion and using random number lists, patients were randomly allocated to one of the three groups according to the agents to be used for the induction of anesthesia.

Group P: Propofol (2 mg/kg), alfentanil 0.02 mg/kg and atracurium 0.5 mg/kg.

Group K: Ketamine racemate (2 mg/kg), alfentanil 0.02 mg/kg and atracurium 0.5 mg/kg.

Group T: Thiopental (5 mg/kg), alfentanil 0.02 mg/kg and atracurium 0.5 mg/kg.

Syringes containing drugs for induction of anesthesia were prepared, in a double blind fashion, by a collaborator not involved in data recording. Another blind collaborator administered drugs while a blind observer collected data. Tracheal intubation was performed 3 minutes after atracurium administration. Anesthesia was maintained with continuous propofol infusion at 100μg/kg/min and 50% nitrous oxide in oxygen. Mean arterial pressure (MAP) and heart rate (HR) were recorded just before induction, at 1, 15, 30, 45 and 60 minutes after induction. Before the traction of extraocular muscle began, the anesthetist had atropine immediately available. During the traction, the minimal heart rate was recorded. If the heart rate decreased from the basal heart rate by >20 beats/min, the anesthetist asked the surgeon to release the extraocular muscle. If OCR was not disappeared within 20 seconds by releasing tension on the muscle, atropine 0.01 mg/kg was injected intravenously. Patients were classified as OCR positive if maximal heart rate decrement was >20 beats/minute, OCR negative if the decrement was ≤ 20 beats/minute and arrhythmia positive if any cardiac arrhythmia other than bradycardia developed; otherwise they were classified as arrhythmia negative. A lead II ECG (Datex, Corp Helsinki, Finland) was recorded during stimulation of the reflex for detection of dysrhythmias. A sample-size estimate indicated that 300 patients would give a power of 80% at a level of 0.05 for detecting a significant difference ($P<0.05$) among groups. Data were analyzed using the SPSS (version 11) system. Parametric data were analyzed by one-way analysis of variance. Two-way analysis (group vs. time) of variance was used to test for differences in hemodynamic data among groups. The differences in gender between the groups, total number of patients developed OCR, bradycardias or arrhythmias were tested using Pearson's chi-squared test and Fisher's exact test when the anticipated number was less than 5. Significance was defined as $P<0.05$.

## Results

No patient required intravenous atropine for profound bradycardia during operation and OCR disappeared within 20 seconds by releasing tension on the muscle. Incidence of OCR was 12.7% (38 cases) in 300 patients. There were slightly more females than males (51.7% vs. 48.3%). Mean (SE) age was 6 (± 0.05) years. There were more patients aged over 5 than below that age (67% vs. 33%). Mean body weight was 23.9 (± 0.11) kg. Mean duration of anesthesia was 64.6 (± 1.83) minutes. There were no statistical differences among the three groups in demographic data (table 1). There were no significant differences in basal mean heart rate (HR) or mean arterial pressure (MAP) among the three groups. Mean HR during total period of surgery in group P was significantly slower than that in group K. Mean HR changes in group K was significantly higher than that in group P (figure 1). MAP changes was significantly lower in patients in group P compared with patients in group K or T (figure 2). No patient had arrhythmia in any group. Incidence of OCR was significantly lower in patients in group K compared with patients in group T or P by Kendall's W test statistic (table 1).

**Table1.** Data of patients undergoing strabismus surgery and hemodynamic responses to OCR during anesthetic regimens.

| | Anesthetic regimens and OCR | | |
|---|---|---|---|
| Parameter | T | K | P |
| Number (n) | 100 | 100 | 100 |
| Age (years) | 6.6 ± 0.20 | 6.70 ± 0.20 | 6.6 ± 0.20 |
| Weight (Kg) | 23.8 ± 0.20 | 23.9 ± 0.20 | 23.9 ± 0.20 |
| Sex (M/F) | 60/40 | 58/42 | 57/43 |
| Total surgery time (minutes) | 62.8 ± 0.23 | 62.3 ± 0.20 | 62.8 ± 0.20 |
| Basal HR (bpm) | 104.7 ± 1.141 | 05.2 ± 1.10 | 104.4 ± 1.17 |
| HR (bpm) (total surgery time) | 114.2 ± 0.73 | 116.7 ±0.70 | 111.90 ± 1.10§ |
| HR change (bpm) | 11.2 ± 1.44 | 13.5 ± 0.90* | 8.7 ± 1.50 |
| Basal MAP (mmHg) | 71.0 ± 0.84 | 72.3 ± 0.90 | 71.6 ± 0.87 |
| MAP change (mmHg) | 18.9 ± 0.91 | 19.3 ± 0.80 | 12.5 ± 1.13† |
| OCR [n (%)] | 16 (16) | 9 (9)# | 13 (13) |

OCR: oculocardiac reflex, HR: heart rate, MAP: mean arterial pressure, T:; thiopental, P: propofol, K: ketamine.
Data are given as mean ± SE. § *P*<0.05 for P versus K; * *P*<0.05 for K versus P; † for *P*<0.05 P versus K and T; # *P*<0.05 for K versus P and T (by Kendall's W test statistic).

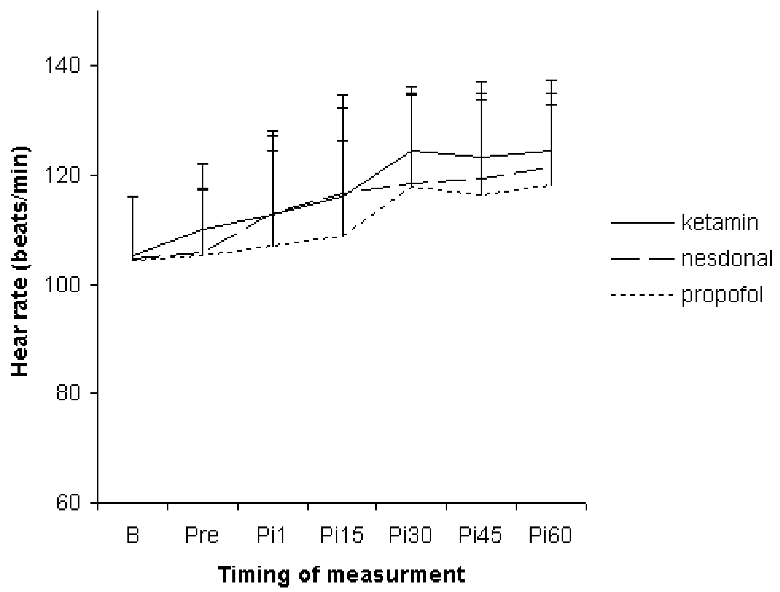


**Figure 1.** Heart rate changes during surgery based on anesthetic regimes used for induction of anesthesia. Mean heart rate changes in group ketamine was significantly higher than that in propofol group. HR: heart rate, PreI: Pre Induction, PI: Post Induction.

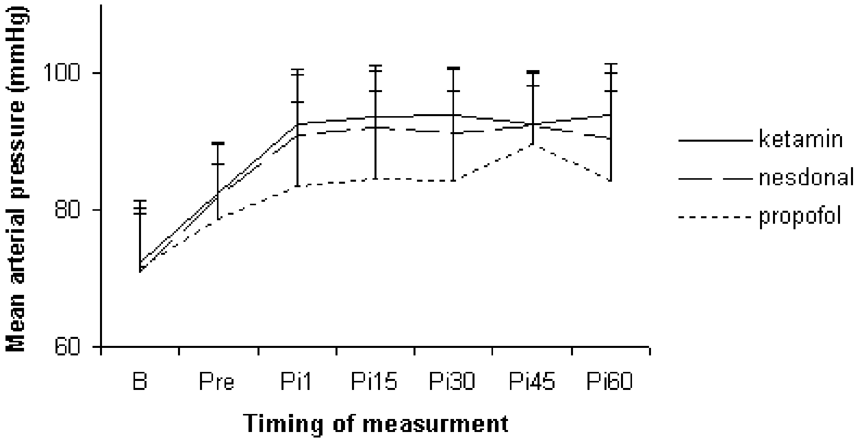


**Figure 2.** Mean arterial pressure changes during surgery based on anesthetic regimens used for induction of anesthesia. Mean arterial pressure changes was significantly lower in patients in group propofol compared with patients in group ketamine or thiopental. MAP: mean arterial pressure, PreI: Pre Induction, PI: Post Induction.

## Discussion

Although OCR is a frequent and frightening challenge to anesthetists during strabismus surgery, there have been very few studies investigating the influence of anesthetic regimens on the incidence of the OCR. The incidence of OCR determined in earlier studies ranged from 32% to 90%, depending upon methods of stimulation and evaluation criteria [12,13]. We demonstrated that clinically used anesthetics have divergent effects on this response. Of particular interest was ketamine as the only anesthetic with sympathetic action. Our study showed that patients receiving propofol or thiopental were more prone to develop pronounced OCR compared with patients in ketamine group. The enhanced vagal tone associated with OCR may act in synergy with the cardiovascular depressant and vagotonic properties of the propofol/alfentanil or thiopental/alfentanil combination [14]. This corresponds to the analysis of randomized controlled trials by Tramer et al., which revealed that propofol, despite the use of prophylactic anticholinergics, substantially increases the incidence of OCR [15]. Despite the fact that group P had the lowest HR at baseline, HR decrease during traction on an extraocular eye muscle was still the greatest in this group. In contrast, ketamine seems to be protective against the parasympathetic activation induced by the OCR. Only in nine out of one hundred patients significant OCR were elicited. In view of the hypothesis that the OCR consists of an initial parasympathetic phase, followed by a sympathetic phase [11], ketamine anesthesia may, by increasing sympathetic tone, counteract vagal stimulation during the first phase of the OCR.

## Conclusion

Our data suggest that induction of anesthesia with ketamine is associated with the least cardiovascular changes induced by OCR during strabismus surgery.

## References

1. ASCHNER B: **[Successful therapy of non-infectious rheumatoid arthritis; constitutional therapy, plus the use of cantharides and vesicants.].** *Hippokrates* 1950, 21**:** 452-458.
2. Dagnini G: **Intorno ad un riflesso provocato in alcuni emiplegici collo stimolo della cornea e colla pressione sulbulbo oculare.** *Bull Sci Med* 1908, 8**:** 380-381.
3. Ghai B, Makkar JK, Arora S: **Intraoperative cardiac arrest because of oculocardiac reflex and subsequent pulmonary edema in a patient with extraocular cysticercosis.** *Paediatr Anaesth* 2006, 16**:** 1194-1195.

4. Blanc VF, Hardy JF, Milot J, Jacob JL: **The oculocardiac reflex: a graphic and statistical analysis in infants and children.** *Can Anaesth Soc J* 1983, 30**:** 360-369.
5. Goerlich TM, Foja C, Olthoff D: **[Effects of sevoflurane versus propofol on oculocardiac reflex--a comparative study in 180 children].** *Anaesthesiol Reanim* 2000, 25**:** 17-21.
6. KIRSCH RE, SAMET P, KUGEL V, AXELROD S: **Electrocardiographic changes during ocular surgery and their prevention by retrobulbar injection.** *AMA Arch Ophthalmol* 1957, 58**:** 348-356.
7. Gilani SM, Jamil M, Akbar F, Jehangir R: **Anticholinergic premedication for prevention of oculocardiac reflex during squint surgery.** *J Ayub Med Coll Abbottabad* 2005, 17**:** 57-59.
8. Pontinen PJ: **The importance of the oculocardiac reflex during ocular surgery.** *Acta Ophthalmol (Copenh)* 1966, Suppl-66.
9. Alexander JP: **Reflex disturbances of cardiac rhythm during ophthalmic surgery.** *Br J Ophthalmol* 1975, 59**:** 518-524.
10. Apt L, Isenberg S, Gaffney WL: **The oculocardiac reflex in strabismus surgery.** *Am J Ophthalmol* 1973, 76**:** 533-536.
11. Braun U, Feise J, Muhlendyck H: **Is there a cholinergic and an adrenergic phase of the oculocardiac reflex during strabismus surgery?** *Acta Anaesthesiol Scand* 1993, 37**:** 390-395.
12. Dewar KM: **The oculocardiac reflex.** *Proc R Soc Med* 1976, 69**:** 373-374.
13. RHODE J, GROM E, BAJARES AC, ANSELMI A, CAPRILES MA, RIVAS C: **A study of the electrocardiographic alterations occurring during operations on the extraocular muscles.** *Am J Ophthalmol* 1958, 46**:** 367-382.
14. Karanovic N, Jukic M, Carev M, Kardum G, Dogas Z: **Rocuronium attenuates oculocardiac reflex during squint surgery in children anesthetized with halothane and nitrous oxide.** *Acta Anaesthesiol Scand* 2004, 48**:** 1301-1305.
15. Tramer MR, Moore RA, McQuay HJ: **Propofol and bradycardia: causation, frequency and severity.** *Br J Anaesth* 1997, 78**:** 642-651.