Oculocardiac reflex and oculorespiratory reflex during strabismus surgery under general anesthesia using the laryngeal mask airway with maintenance of spontaneous respiration: A retrospective study

Sun Young Shin¹, Min Ju Kim² and Jin Joo²

Abstract

Objective: To determine (1) how the specific muscle undergoing surgical treatment affects the occurrence of the oculocardiac reflex (OCR) and oculorespiratory reflex (ORR) and (2) whether the depth of anesthesia influences the occurrence of the OCR and ORR in patients undergoing strabismus surgery with a laryngeal mask airway with maintenance of spontaneous respiration.

Methods: The medical records of patients who underwent strabismus surgery on the lateral rectus (LR) and medial rectus (MR) muscles from January 2017 to December 2017 were retrospectively reviewed.

Results: The incidence of the OCR was not significantly different between LR and MR operations in either pediatric or adult patients. The incidence of the ORR as indexed by the tidal volume (TV) was significantly higher during MR than LR surgery in pediatric patients (29.3% vs. 10.1%, respectively). The change in TV during muscle traction and the bispectral index were significantly correlated in both pediatric and adult patients ($r^2 = 0.034$ and 0.058, respectively).

Conclusions: The OCR was not influenced by the specific muscle undergoing surgery or the depth of anesthesia. The incidence of the ORR as indexed by the TV was higher during MR surgery in pediatric patients and was positively correlated with the depth of anesthesia.

¹Department of Ophthalmology, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

²Department of Anesthesiology and Pain Medicine, Seoul St. Mary’s Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

Corresponding author:
Jin Joo, Department of Anesthesia and Pain Medicine, College of Medicine, Seoul St. Mary’s Hospital, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Korea.
Email: jiyo1004@catholic.ac.kr
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Introduction
The oculocardiac reflex (OCR) is evoked by parasympathetic stimulation induced by manipulation of the eye or extraocular muscles; thus, it typically occurs during strabismus surgery. The afferent pathway of the OCR runs from the ophthalmic branch of the trigeminal nerve to the vagus nuclei, while the efferent pathway runs from the vagus nerve to the heart. The OCR is defined as a 10% to 20% reduction in the heart rate (HR) from the baseline value or the development of dysrhythmia. The incidence of the OCR ranges from 14% to 90% in previously published studies depending on the definition used. In most cases, the OCR resolves without treatment, but some patients develop cardiac arrest and, in very rare cases, sudden death. The OCR occurs more often in pediatric patients and in those undergoing surgery on the medial rectus (MR) muscle; however, it is less prevalent in pediatric patients when deeper anesthesia is induced.

The oculorespiratory reflex (ORR) manifests as shallow respiratory movement, bradypnea, and respiratory arrest caused by pressure in or manipulation of the eye. The afferent pathway of the ORR is identical to that of the OCR, but the efferent pathway has not yet been fully elucidated. Additionally, the exact definition of, incidence of, and risk factors for the ORR have not yet been clearly described. Because most strabismus surgeries are performed under general anesthesia with mechanical ventilation that requires neuromuscular blocking agents (e.g., rocuronium), very little clinical research has focused on the ORR.

Most strabismus surgeries are performed on an outpatient basis. Therefore, anesthesia using a laryngeal mask airway (LMA) to maintain spontaneous respiration has been suggested in patients undergoing strabismus surgery. However, few studies have focused on the OCR and ORR during strabismus surgery in relation to the depth of anesthesia, especially in terms of the specific extraocular muscle undergoing surgery. Therefore, we designed this retrospective study primarily to elucidate the occurrence of the OCR and ORR according to the specific extraocular muscle being operated on in both pediatric and adult patients undergoing strabismus surgery with an LMA and maintenance of spontaneous respiration. The secondary aim was to determine whether the depth of anesthesia influences the occurrence of the OCR and ORR.

Patients and methods
Study population and ethical approval
The Institutional Review Board of Seoul St. Mary’s Hospital, The Catholic University of Korea approved this study (approval no. KC17RESI0365) and waived the requirement for obtaining informed consent because of the retrospective nature of the study. We reviewed the medical records of patients who underwent strabismus surgery at Seoul St. Mary’s Hospital from January to December 2017. Data abstraction was performed using the hospital’s electronic
charting system. Patients were excluded if they had an American Society of Anesthesiologists physical status of >III; underwent strabismus surgery on the superior/inferior rectus and oblique muscles; had bronchial asthma, chronic obstructive pulmonary disease, sleep apnea, or heart disease; or had no OCR and ORR data. Data on sex, age, body weight, the specific muscles operated on, HR, tidal volume (TV), respiratory rate (RR), minute ventilation (MV), and muscle traction time were collected. Patients aged <15 years were defined as children.

Anesthetic management

All patients scheduled to undergo strabismus surgery under general anesthesia at our hospital were routinely managed as follows. The patients were allowed to eat and drink until 8 hours before surgery. Intravenous access was established with a 20- to 24-gauge angiocatheter at the day surgery center (DSC). For pediatric patients who refused to enter the operating room alone, 0.05 to 0.10 mg of midazolam was intravenously administered at the DSC; otherwise, no premedication was administered. Basic monitoring, including electrocardiography, noninvasive sphygmomanometry, pulse oximetry, and measurement of the bispectral index (BIS), was performed in the operating room. For anesthetic induction, 1.5 to 2.0 mg/kg of propofol was administered, and an LMA (LMA® Flexible™ Airway; Teleflex, Westmeath, Ireland) fitted for age and weight was inserted when the patients were fully sedated. Anesthesia was maintained with sevoflurane at 2.0 to 2.5 vol%, 50% nitrous oxide, and 50% oxygen to maintain the BIS at 40 to 60. Spontaneous respiration was maintained with application of pressure support at 5 to 10 cmH₂O, preventing the peak pressure from exceeding 20 cmH₂O. At the end of surgery, the sevoflurane was discontinued and the LMA was removed. The patients were transferred to the post-anesthesia care unit and then to the DSC for discharge.

Data collection and statistical analyses

The ophthalmologist informed the anesthesiologist about the progress of the strabismus surgery, such as the extraocular muscle hooking and release, and the anesthesiologist recorded the cardiovascular and respiratory parameters at each point of the strabismus surgery. The lowest HR, TV, RR, and MV were recorded during hooking of the rectus muscle; all parameters were recorded at the moment of traction release. Changes in the HR, TV, RR, and MV were calculated as the lowest value during lateral rectus (LR) or MR muscle traction divided by the baseline value. The OCR was defined as a >20% reduction in the HR from the baseline value. The baseline HR was defined as the HR before surgical incision. The ORR was defined as a >20% reduction in the TV, RR, and MV from the baseline values. The baseline values of the respiratory parameters were defined as the values before surgical incision.

All data were analyzed using SPSS software ver. 20.0 (IBM Corp., Armonk, NY, USA). For demographic data, the χ² test or Fisher’s exact test and the t-test were used. The incidence rates of the OCR and ORR were compared between the LR and MR muscles using the χ² test. Linear logistic regression was performed to analyze changes in the HR, TV, RR, and BIS during muscle traction. Data are presented as mean ± standard deviation or number and percentage. A p-value of <0.05 was considered statistically significant.

Results

A total of 175 patients underwent strabismus surgery during the study period.
The data of 141 patients (89 children and 52 adults) who met the inclusion criteria were analyzed. The pediatric patients underwent 69 LR and 58 MR operations, while the adult patients underwent 44 LR and 42 MR operations (Figure 1). The mean muscle traction time was $161 \pm 50.0$ s in children and $156.1 \pm 42.5$ s in adults (Table 1).

The incidence of the OCR during LR versus MR operations was not significantly different in either pediatric or adult patients (42.0% vs. 46.6% and 34.1% vs. 38.1%, respectively). The overall incidence of the ORR in terms of the TV was 12.2%. The incidence of the ORR in terms of the TV was significantly higher during MR surgery (29.3%) than during LR surgery (10.1%) in children ($p < 0.05$); however, there was no significant difference in adult patients. The incidence of the ORR in terms of the RR

![Figure 1. Patient flow diagram.](image)

### Table 1. Patient characteristics.

|                          | Pediatric | Adult |
|--------------------------|-----------|-------|
| Total                    | 89        | 52    |
| Sex, male/female         | 41/48     | 26/26 |
| Age, years               | $6.6 \pm 2.8$ | $39.2 \pm 16.6$ |
| Body weight, kg          | $26.6 \pm 10.9$ | $63.7 \pm 7.7$ |
| Number of operated muscles, LR/MR | 69/58 | 44/42 |
| Baseline heart rate, beats/minute | $97.7 \pm 15.1$ | $72.6 \pm 11.6$ |
| Baseline tidal volume, mL/kg | $4.0 \pm 1.5$ | $4.4 \pm 1.2$ |
| Baseline respiratory rate, breaths/minute | $24.3 \pm 6.7$ | $17.7 \pm 7.1$ |
| Baseline minute ventilation, L/minute | $2.6 \pm 1.0$ | $4.0 \pm 1.5$ |
| Baseline BIS             | $82.3 \pm 17.5$ | $97.5 \pm 1.0$ |
| Muscle traction time, s  | $161.0 \pm 50.0$ | $156.1 \pm 42.5$ |

Categorical variables are shown as number, and other variables are shown as mean ± standard deviation. LR, lateral rectus; MR, medial rectus; BIS, bispectral index.
and MV was not significantly different between LR and MR surgeries in either pediatric or adult patients (Table 2). The overall incidence of the OCR was not significantly different between pediatric and adult patients. The incidence of the ORR in terms of the TV was significantly higher in pediatric patients than that in adult patients (18.9% vs. 2.3%, p < 0.001), while there was no significant difference in the incidence of the ORR in terms of the RR and MV between pediatric and adult patients (Table 3).

The change in the HR during muscle traction and the BIS showed a negative correlation in pediatric patients, but this was not statistically significant (Figure 2a). The change in the TV during muscle traction and the BIS were significantly correlated in both pediatric and adult patients ($r^2 = 0.034$ and 0.058, respectively; p < 0.05) (Figures 2b and 3b), while the change in the RR during muscle traction and the BIS showed no significant correlation in either group (Figures 2c and 3c). The change in the MV during muscle traction was correlated with the BIS in pediatric patients ($r^2 = 0.043$, p < 0.05), but not in adult patients (Figures 2d and 3d).

**Discussion**

Strabismus surgery is one of the most common ophthalmologic surgeries performed under general anesthesia, especially in pediatric patients. To the best of our knowledge, this is the first study to compare the incidence rates of the OCR and ORR during LR and MR strabismus surgeries in patients undergoing general anesthesia using an LMA with spontaneous respiration; moreover, it is the first study to investigate the incidence rates of the OCR and ORR in relation to the depth of anesthesia. This study showed that the incidence of the OCR was not significantly different between LR and MR surgeries in either pediatric or adult patients; in addition, it was not correlated with the depth of anesthesia. In pediatric patients, the incidence of the ORR in terms of the TV was higher during MR surgery than during LR surgery. Changes in the TV during rectus muscle traction were correlated with the depth of anesthesia, while changes in the RR during rectus muscle traction were not

**Table 2. Incidence of OCR and ORR.**

|       | LR muscle | MR muscle | p value |
|-------|-----------|-----------|---------|
| OCR   |           |           |         |
| Total | 44 (38.9) | 43 (43.0) | 0.737   |
| Pediatrics | 29 (42.0) | 27 (46.6) | 0.546   |
| Adults | 15 (34.1) | 16 (38.1) | 0.709   |
| ORR   |           |           |         |
| TV    |           |           |         |
| Total | 8 (7.1)   | 18 (18.0) | 0.312   |
| Pediatrics | 7 (10.1)  | 17 (29.3) | 0.008*  |
| Adults | 1 (2.3)   | 1 (2.4)   | 0.722   |
| RR    |           |           |         |
| Total | 1 (0.9)   | 2 (2.0)   | 0.192   |
| Pediatrics | 1 (1.4)   | 1 (1.7)   | 0.532   |
| Adults | 0 (0.0)   | 1 (2.4)   | 0.307   |
| MV    |           |           |         |
| Total | 3 (2.7)   | 7 (7.0)   | 0.217   |
| Pediatrics | 2 (2.9)   | 6 (10.3)  | 0.106   |
| Adults | 1 (2.3)   | 1 (2.4)   | 0.722   |

Variables are shown as number (percentage). LR, lateral rectus; MR, medial rectus; OCR, oculocardiac reflex; ORR, oculorespiratory reflex; TV, tidal volume; RR, respiratory rate; MV, minute ventilation. *p < 0.05.

**Table 3. Comparison between pediatric and adult patients.**

|       | Pediatric | Adult | p value |
|-------|-----------|-------|---------|
| OCR   | 56 (44.1) | 31 (36.0) | 0.259   |
| ORR   |           |       |         |
| TV    | 24 (18.9) | 2 (2.3) | 0.000*  |
| RR    | 2 (1.6)   | 1 (1.2) | 1.000   |
| MV    | 8 (6.3)   | 2 (2.3) | 0.322   |

Variables are shown as number (percentage). OCR, oculocardiac reflex; ORR, oculorespiratory reflex; TV, tidal volume; RR, respiratory rate; MV, minute ventilation. *p < 0.05.
correlated with the depth of anesthesia in either pediatric or adult patients.

The OCR is an important phenomenon during strabismus surgery; thus, both anesthesiologists and ophthalmic surgeons closely monitor potential signs of the OCR to prevent its occurrence. Retrobulbar block, premedication with anticholinergics, and gentle tension during muscle traction have been suggested to reduce the incidence of the OCR.\textsuperscript{12,16,17} Previous studies of the association between the OCR and operations on specific extraocular muscles have produced conflicting results. In some studies, the OCR occurred more frequently during MR surgery than during LR surgery because of the differences in the afferent pathways involved.\textsuperscript{3,4,7,18} Other studies showed no relationship between the OCR and the specific extraocular muscle on which the operation was performed.\textsuperscript{1,6,19,20} In our study, LR and MR surgeries showed no differences in the incidence of the OCR in either pediatric or adult patients; moreover, changes in the HR during muscle traction were not associated with the depth of anesthesia. Changes in the HR during muscle traction were negatively correlated with the depth of anesthesia in pediatric patients, as in previous studies; however, this correlation was not statistically significant. We presume that this discrepancy with previous results was due to the maintenance of spontaneous respiration during surgery in our study population. Notably, respiration modulates sympathetic nerve activity, and a more rapid RR is associated with a higher level of sympathetic activity.\textsuperscript{21} Additionally, negative intrathoracic pressure during spontaneous inspiration causes a slight increase in the HR because of vagal withdrawal and

\textbf{Figure 2.} Relationship between BIS and changes in (a) HR, (b) TV, (c) RR, and (d) MV during muscle traction in pediatric patients. BIS, bispectral index; HR, heart rate; TV, tidal volume; RR, respiratory rate; MV, minute volume.
lung hyperinflation, which may occur during mechanical ventilation and leads to bradycardia due to vagal overstimulation.\textsuperscript{22} In contrast to the findings of previous studies involving general anesthesia with mechanical ventilation, the patients in our study maintained their spontaneous respiration; the resulting sympathetic stimulation offset the parasympathetic reflex that occurred during extraocular muscle manipulation.

The ORR has not been well characterized for anesthesiologists or ophthalmologic surgeons because most studies to date have been experimental in nature. Although the efferent pathway of the ORR has not been clearly elucidated, it appears to be independent of the vagus nerve because intravenous atropine enhances the ORR; moreover, as in the OCR, the afferent pathway stimulates the pneumotaxic respiratory center to send a signal to the medullary respiratory area through the phrenic nerve and other respiratory nerves.\textsuperscript{13} The ORR is prevented by retrobulbar block.\textsuperscript{15}

Allison et al.\textsuperscript{11} reported that the ORR occurred in a manner that led to a reduced TV without significant declines in the RR in pediatric patients who underwent strabismus surgery with the use of an LMA to maintain spontaneous respiration; this result is identical to the result of our study. We used sevoflurane, the respiratory effect of which has not yet been fully elucidated,\textsuperscript{11,23–26} and we found that the overall incidence of the ORR in terms of the TV was 12.2\% in pediatric patients. The incidence rate was higher during MR surgery than during LR surgery, which might have been a result of the different afferent pathways involved.\textsuperscript{19} However, the overall incidence rate of the ORR in terms of the RR and MV was <5\% and did not differ

Figure 3. Relationship between BIS and changes in (a) HR, (b) TV, (c) RR, and (d) MV during muscle traction in adult patients. BIS, bispectral index; HR, heart rate; TV, tidal volume; RR, respiratory rate; MV, minute volume.
between the LR and MR surgeries. Based on these findings, the ORR may be defined as a change of in the TV during muscle traction. Meanwhile, maintenance of the MV during traction of the MR and LR muscles indicates that muscle traction does not interfere with spontaneous respiration in a comprehensive sense.

Among the respiratory parameters, only the TV decreased with a greater depth of anesthesia in both pediatric and adult patients, although the correlations were marginal. In other words, the TV increased as the depth of anesthesia decreased (i.e., became lighter), which might be considered a result of stimulation of muscle hooking, such as pain. However, all patients were anesthetized deep enough to maintain a BIS of <60 even without using rocuronium, which may lower the BIS regardless of the actual depth of anesthesia. We consider that the higher incidence of the ORR in terms of the TV in pediatric than adult patients is the reason that the BIS and MV showed a significant correlation only in pediatric patients.

One limitation of this study is that the OCR and ORR occurring during superior rectus, inferior rectus, and oblique muscle surgery were not analyzed because of the lower number of procedures performed on these muscles. Most strabismus surgeries are performed on the horizontal rectus extraocular muscles, such as the LR and MR muscles. Therefore, we only included patients who had undergone surgeries on two horizontal rectus muscles. Ha et al. reported that the incidence of the OCR was significantly higher in the first operated muscle than in the second operated muscle in patients who underwent two muscle surgeries because of the adaptation to the subsequent stimulation. In the present study, we focused only on the effect of the MR and LR muscles on the OCR and ORR, including patients undergoing surgery on one or two muscles. We did not analyze whether the OCR or ORR differed according to the order of the operated muscles in our study. This might have influenced the results of this study by introducing bias. Nevertheless, this study is considered sufficiently meaningful as the first study to analyze the OCR and ORR depending on the specific muscle being operated on and the depth of anesthesia in patients undergoing strabismus surgery with an LMA to maintain spontaneous respiration.

In summary, the OCR was not influenced by either the specific muscle being operated on or the depth of anesthesia. The ORR in terms of the TV occurred more frequently during MR surgery in pediatric patients and was positively correlated with the depth of anesthesia in both pediatric and adult patients. Thus, we propose that young age and MR surgery are risk factors for the ORR during strabismus surgery under general anesthesia with spontaneous respiration. Additionally, we do not advise deepening anesthesia to prevent the ORR when using an LMA with spontaneous respiration because the OCR is not correlated with the depth of anesthesia. However, further prospective observational studies should be performed to clarify the relationship between the ORR and the depth of anesthesia as well as to validate the risk factors for the ORR during strabismus surgery with the use of an LMA to maintain spontaneous respiration.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

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References

1. Lai YH, Hsu HT, Wang HZ, et al. The oculocardiac reflex during strabismus surgery: its relationship to preoperative clinical eye findings and subsequent postoperative emesis. J AAPOS 2014; 18: 151–155.
2. Dewar KM. The oculocardiac reflex. Proc R Soc Med 1976; 69: 373–374.
3. Apt L, Isenberg S and Gaffney WL. The oculocardiac reflex in strabismus surgery. Am J Ophthalmol 1973; 76: 533–536.
4. Welhaf WR and Johnson DC. The oculocardiac reflex during extraocular muscle surgery. Arch Ophthalmol 1965; 73: 43–45.
5. Aletaha M, Bagheri A, Roodneshin F, et al. Oculocardiac reflex during strabismus surgery: experience from a tertiary hospital. Strabismus 2016; 24: 74–78.
6. Ha SG, Huh J, Lee BR, et al. Surgical factors affecting oculocardiac reflex during strabismus surgery. BMC Ophthalmol 2018; 18: 103.
7. Karaman T, Demir S, Dogru S et al. The effect of anesthesia depth on the oculocardiac reflex during strabismus surgery. J Clin Monit Comput 2016; 30: 889–893.
8. Fayon M, Gauthier M, Blanc VF, et al. Intraoperative cardiac arrest due to the oculocardiac reflex and subsequent death in a child with occult Epstein-Barr virus myocarditis. Anesthesiology 1995; 83: 622–624.
9. Ghai B, Makkar JK and Arora S. Intraoperative cardiac arrest because of oculocardiac reflex and subsequent pulmonary edema in a patient with extracocular cysticercosis. Paediatr Anaesth 2006; 16: 1194–1195.
10. Barry Smith G, Hamilton RC and Carr CA. Ophthalmic anaesthesia. 2nd ed. London: Arnold, 1996. p. 216–219.
11. Allison CE, De Lange JJ, Koole FD, et al. A comparison of the incidence of the oculocardiac and oculorespiratory reflexes during sevoflurane or halothane anesthesia for strabismus surgery in children. Anesth Analg 2000; 90: 306–310.
12. Arnold RW, Bond AN, McCall M, et al. The oculocardiac reflex and depth of anesthesia measured by brain wave. BMC Anesthesiol 2019; 19: 36.
13. Yi C and Jee D. Influence of the anaesthetic depth on the inhibition of the oculocardiac reflex during sevoflurane anaesthesia for paediatric strabismus surgery. Br J Anaesth 2008; 101: 234–238.
14. Blanc VF, Jacob JL, Milot J, et al. The oculorespiratory reflex revisited. Can J Anaesth 1988; 35: 468–472.
15. Khurana AK, Khurana I, Yadav RN, et al. An experimental model of oculorespiratory reflex. Br J Anaesth 1992; 76: 76–78.
16. Braun U, Feise J and Muhlendyck H. Is there a cholinergic and an adrenergic phase of the oculocardiac reflex during strabismus surgery? Acta Anaesthesiol Scand 1993; 37: 390–395.
17. Gupta N, Kumar R, Kumar S, et al. A prospective randomised double blind study to evaluate the effect of peribulbar block or topical application of local anaesthesia combined with general anaesthesia on intraoperative and postoperative complications during paediatric strabismus surgery. Anaesthesia 2007; 62: 1110–1113.
18. Ohashi T, Kase M and Yokoi M. Quantitative analysis of the oculocardiac reflex by traction on human extraocular muscle. Invest Ophthalmol Vis Sci 1986; 27: 1160–1164.
19. Blanc VF, Hardy JF, Milot J, et al. The oculocardiac reflex: a graphic and statistical analysis in infants and children. Can Anaesth Soc J 1983; 30: 360–369.
20. Stump M and Arnold RW. Iris color alone does not predict susceptibility to the oculocardiac reflex in strabismus surgery. Binocul Vis Strabismus Q 1999; 14: 111–116.
21. Narkiewicz K, Van De Borne P, Montano N, et al. Sympathetic neural outflow and chemoreflex sensitivity are related to spontaneous breathing rate in normal men. Hypertension 2006; 47: 51–55.
22. Shekerdemian L and Bohn D. Cardiovascular effects of mechanical ventilation. Arch Dis Child 1999; 80: 475–480.
23. Doi M and Ikeda K. Respiratory effects of sevoflurane. Anesth Analg 1987; 66: 241–244.
24. Doi M, Takahashi T and Ikeda K. Respiratory effects of sevoflurane used in combination with nitrous oxide and surgical stimulation. *J Clin Anesth* 1994; 6: 1–4.

25. Komatsu H, Chujo K, Morita J, et al. Spontaneous breathing with the use of a laryngeal mask airway in children: comparison of sevoflurane and isoflurane. *Paediatr Anaesth* 1997; 7: 111–115.

26. Yamakage M, Tamiya K, Horikawa D, et al. Effects of halothane and sevoflurane on the paediatric respiratory pattern. *Paediatr Anaesth* 1994; 4: 53–56.

27. Schuller PJ, Newell S, Strickland PA, et al. Response of bispectral index to neuromuscular block in awake volunteers. *Br J Anaesth* 2015; 115: i95–i103.