# Oculocardiac reflex as a predictive sign of postoperative nausea and vomiting following strabismus surgey in children

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## Key points

Postoperative nausea and vomiting (PONV) is a major concern following strabismus surgery in children. Different strategies been used for prediction as well as treatment. Contrary to previous studies we concluded that oculocardiac reflex (OCR) can not be used as a predictor of PONV as previously reported. Hence administration of more than one anti-emetic, including dexamethasone or anti-cholinergics is not justified. Atropine in a dose of 3 µgkg-1 rather than higher doses is effective in the treatment of OCR.

#### Abstract

## Background

In this prospective, non-randomized study, we tested the hypothesis if oculocardiac reflex (OCR) can be used as a predictor of postoperative nausea and vomiting following strabismus surgery in children.

## Methods

88 children aged between 2 and 16 years undergoing strabismus surgery were enrolled in the study between 2009 and 2011. All anaesthetic drugs were given in a specific sequence using propofol, ondansetron, and fentanyl. Sevofurane, N2O/O2 used to maintain anaesthesia. All children received intravenous fluid maintenance, intravenous diclofenac, as well as subtenon block. The incidence of oculocardiac reflex as well as postoperative nausea and vomiting were recorded.

#### Results

76 patients developed OCR during surgery (86.4 %). There was no evidence of an association between OCR and postoperative nausea/vomiting (PONV). There was no evidence between the number of muscles operated on and PONV. Furthermore, there was no evidence of association between children who received atropine to treat bradycardia and reduction in the incidence of PONV. None of our patients required overnight admission.

## Conclusions

PONV following strabismus surgery in children is low and cannot be predicted from OCR. It seems that boys are more likely to develop PONV compared to girls.

**Keywords:** Nausea; oculocardiac reflex; strabismus; vomiting; children.

#### Introduction

Postoperative nausea and vomiting is a major concern following day case surgery due to its varied psychological and financial implications<sup>1, 2</sup>. The quoted incidence of PONV following strabismus surgery in children can be as high as 88%<sup>3</sup>. The use of modern anaesthetic agents as well as avoiding strong opioids, like morphine, has significantly reduced the risk<sup>4</sup>. Muscarinic receptors agonist, like atropine and hyoscine, has an anti-emetic effect<sup>5</sup>. Atropine is the most commonly used muscarinic agonist to treat OCR in strabismus surgery. Theoretically, it should reduce the incidence of PONV if administered.

The aim of the present study is to answer the following questions:

- 1. Does OCR increase the risk of PONV hence can be used as a predictor (as our primary aim)?
- 2. Does treatment of OCR with atropine reduces the incidence of PONV?
- 3. Can the sequence of anaesthetic drug administration affect the overall incidence of PONV?

## Methods

After the approval of the regional research and ethics committee (Ref: 08/H1203/84) and parents/guardians informed written consent, we conducted this prospective non randomized study. Using data from a previous study by Allen el al<sup>6</sup> a 65% incidence OCR is assumed. With a power of 80% and a significance level alpha = 0.05, a total of 88 patients would be needed to detect a difference between 47.1% of OCR patients with POV and 17.9% of non-OCR patients with POV, using a chisquare. One hundred patients were recruited over 2 years period. Twelve children were excluded from the study due to incomplete data as well as lack of consent. Eighty eight children aged between 2 and 16 years undergoing strabismus surgery were enrolled in the study. All children were ASA 1 or 2. Patients known to be allergic to fentanyl, propofol, ondansetron, atropine, diclofenac as well as re-do strabismus surgery were excluded. We followed our local fasting guidelines (2

hours for clear fluids and 6 hours for milk and solids). No pre-medications were given except topical local anaesthetic cream for the purpose of intravenous (IV) cannulation. After IV cannulation, anaesthesia was induced using the following drug sequence: 1 ml of the induction dose of propofol 1%, ondansetron 100 µgkg-1, and fentanyl 1 µgkg-1, followed by the remaining sleeping dose of propofol. Laryngeal mask was inserted and patients were maintained on N2O/O2/Sevoflurane on spontaneous ventilation mode. Each patient received IV diclofenec 1mg/kg as well as IV saline as a maintenance fluid therapy according to their body weight. At the end of surgery, 1 ml of levobupivacaine 0.5% was given by the surgeon in the subtenon area. Oculocardiac reflex was defined as at least a 10% decrease in heart rate below relative baseline. Surgeons were asked to release the traction on extra-ocular muscles if bradycardia was profound. Atropine in a dose of 3µgkg-1 was given to treat OCR only if the heart rate drops below 60 beats minute-1, this was repeated if necessary. Perioperative monitoring included gases, MAC, ECG, NIBP, SPO2, spirometry and temperatures.

Postoperative analgesics included oral ibuprofen 5-10 mg/kg TDS (if not contraindicated) and oral paracetamol 15 mg/kg QDS.

Patients were followed up in recovery area and visited in the ward prior discharge. To reduce the possibility of bias, data were retrieved from the nursing documentation. Any incidents of nausea / vomiting were recorded.

#### Results

Eighty eight patients aged between 2 and 16 years (median age of 6 years) were enrolled into our study. Female patients accounts for 56% of the total. The mean weight was 23.5 kg with a SD of 10.3. Table 1 shows patient's characteristics including the gender, age and weight. Of the 76 (86.4%) patients who developed intraoperative OCR, 6 (8%) had PONV, whilst of the 12 patients who did not develop OCR, 3 (25%) had PONV

Gender (N/%)	Male	39 (44%)	
	Female	46 (56%)	
Age (years)	Median	6	
	Range	2 - 16	
Weight (Kg)	Mean	23.5	
	SD	10.3	

**Table 1.** Patient's characteristics. Data are expressed asnumber (%), median (range) and mean (SD).

(Fischer exact test P=0.102). Children who did not develop intraoperative OCR were 3 times as likely to develop PONV as those who had OCR (Risk Ratio 3.2, 95% CI 0.8 to 12.7). Table 2 shows this relation between OCR and PONV in our group of patients. Twenty four patients required atropine treatment to reverse intraoperative bradycardia, of which 3 (12.5%) developed PONV. Fifty two patients did not need intraoperative atropine to treat OCR, of which 3 (5.8%) developed PONV (Fisher exact test P=0.37). Table 3 shows this relation between the incidence of PONV and atropine treatment for OCR. An interesting finding in our study was the difference in the incidence of PONV between male and female patients, 7 of the 32 male patients (22%) developed PONV compared to 2 of 47 (4.3%) female patients (Risk Ratio 5.1, 95% CI 1.1 to 24.7; Fisher exact P=0.027). There was not much difference between the number of muscle operated on and the overall incidence of PONV. Table 4 shows the relation between gender, number of muscles operated on

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and the incidence of PONV. Figure 1 shows oculocardiac reflex pathway (NYSORA permission).

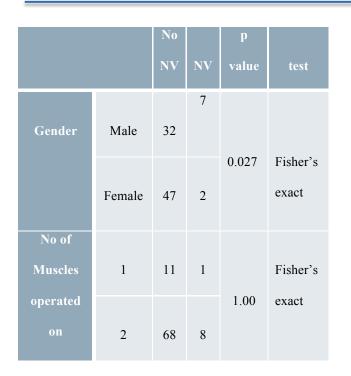
OCR	No PONV	PONV	Total
No	9	3	12
Yes	70	6	76
Total	79	9	88

**Table 2.** Relation between OCR and PONV(number of patients). P=0.102, Fischer exact test

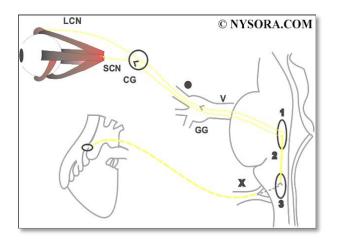
Treatment	No PONV	PONV	Total
No	49	3	52
Yes	21	3	24
Total	67	9	76

 Table 3. Relation between TTT received for OCR and PONV

 (number of patients), P==.37, Fischer exact te



**Table 4.** Relation between the gender and number of muscles operated on and PONV.



**Figure 1.** Oculocardiac reflex pathway. LCN = long ciliary nerve; SCN = short ciliary nerve; CG = ciliary ganglion; GG = geniculate ganglion; V = fifth cranial nerve; X = tenth cranial nerve; (1) main sensory nucleus of the trigeminal nerve; (2) short internuncial fibers in the reticular formation (3) motor nucleus of the vagus nerve.

## Discussion

Strabismus surgery is the most common ophthalmic paediatric surgery<sup>7</sup>. The incidence of PONV can be up to  $88\%^3$  without antiemetic prophylaxis with an admission rate up to 30% after the procedure<sup>8</sup>. Many

factors are to blame for such a high incidence including OCR and anaesthetic agents<sup>9</sup>. OCR is a trigemino-vagal reflex with its afferent pathway via the long and short ciliary nerves to the ciliary ganglion<sup>10</sup>. This send signals via the gasserian ganglion to the sensory nucleus of the trigeminal nerve, fibres in the reticular formation to connect with the motor nucleus of the vagus nerve. Efferent fibres then pass to the heart via the vagus nerve<sup>11</sup>(Fig. 1). Stimulation of the vagus nucleus leads to negative inotropic and chrontropic effect on the myocardium and consequently the clinical features seen with the OCR<sup>12</sup>. OCR is usually defined as a 10-20% drop in heart rate in response to a trigger<sup>13, 14</sup> which is normally traction on the ocular muscles but other triggers for the reflex include pressure on orbital structures, ocular trauma or a sudden increase in the intraocular pressure<sup>15</sup>.

Different studies reported an incidence of OCR up to 90% during strabismus surgery<sup>14, 16,17,18,19</sup>. In our study Seventy six (86.4%) of the 88 children studied developed OCR during their procedure. We looked for an association between this high incidence and the increased incidence of PONV following strabismus surgery.

There are very limited number of studies comparing the effect of OCR on PONV following strabismus surgery. Allen et al <sup>6</sup> concluded that children with a positive OCR were 2.6 times more likely to vomit than those without the reflex while Klockgether-Radke et al<sup>20</sup> found no statistical relationship. In our study, patients who developed OCR were 3 times less likely to develop PONV.

Based on our results, we could not find an association between the occurrence of OCR and PONV; hence it could not be used for possible preventive strategies. OCR was not a predictive sign for the development of PONV and hence administration of more than one antiemetic to this group cannot be justified. Most of the literature focused on the antiemetic prophylaxis for children undergoing strabismus surgery as this proved to shorten the time to discharge and improve the overall satisfaction at lower cost <sup>21</sup>. However, using more than one prophylactic antiemetic incurs not only an extracost but also more risk of side-effects<sup>21</sup>. We used ondansetron 100  $\mu$ gkg<sup>-1</sup> as a sole antiemetic agent and it was sufficient to reduce the incidence of PONV without an increased risk of side effects. Atropine is the main anticholinergic agent used to treat OCR. We administered atropine in a dose of 3  $\mu$ gkg<sup>-1</sup> to treat bradycardia below 60 beats minute<sup>-1</sup>; this was repeated if necessary. Small dose of atropine (2mcg/kg or less) would cause bradycardia. Hence a dose of 3mcg/kg was used with success to treat all cases of bradycardia following OCR. Of the 76 patients who developed OCR, 24 (31.5%) received one dose of atropine while the rest, 52 (68.5%), didn't need any pharmacological treatment. The incidence of PONV was not lower in those patients who received atropine. Chisakuta and Mirakhur found that anticholinergic prophylaxis does not prevent PONV following strabismus surgery in children and this is compatible with our findings<sup>22</sup>. From our results we feel it is not justifiable to administer atropine as a prophylaxis for strabismus surgery. We induced anaesthesia using the following drug sequence: 1 ml of the induction dose of propofol 1%, ondansetron 100  $\mu$ gkg<sup>-1</sup>, fentanyl 1  $\mu$ gkg<sup>-1</sup>, followed by the remaining sleeping dose of propofol. This sequence used for all patients. Propofol is known to decrease the incidence of PONV but increases the incidence of OCR<sup>18</sup>. Also, the use of opioids increases the incidence of both OCR and PONV<sup>7</sup>; however adequate hydration and good pain control reduce the incidence of PONV<sup>23</sup>. The overall incidence of PONV in our study was 10 % (9 patients) which is much lower than what is recorded in previous studies (27% to 88%) <sup>3</sup>. Although this is not evidence based but we believe that the sequence we used to administer the anaesthetic agents may have contributed to such a significant low incidence of PONV. Further studies are needed to establish our results.

Apparently there is no difference in the incidence of PONV between male and female paediatric populattion<sup>24</sup>. After puberty females are up to 3 times more likely to develop PONV. Interestingly, our study showed that female patients are less prone to PONV compared to male patients.

We may be criticized for bias as well as not having a control group. To reduce the possibility of bias, we increased the sample size and we used nursing documentation to retrieve data. As the incidence of PONV following strabismus surgery varied significantly, we could not conduct a double blind study as it was deemed unethical by the ethics committee not to administer anti-emetic therapy.

#### Conclusions

PONV is a small but major concern following strabismus surgery. OCR does not increase its incidence and cannot be used as a predictor or for preventative strategy.

Antiemetic prophylaxis, fluid administration, sub-tenon block and avoidance of potent opioids seem to be a reasonable strategy in avoiding overnight hospital stay.

## References

- D'Errico C, Voepel-Lewis TD, Siewert M, Malviya S. Prolonged recovery stay and unplanned admission of the paediatric surgical outpatient: an observational study. J Clin Anesth 1998; 10: 482-487.
- Patel RI, Hannallah RS. Anesthetic Complications following Pediatric Ambulatory Surgery. Anesthesiology 1988; 69: 1009-1012.
- Ingeborg D, Thilo M, Michael G, Christina B, Axel M, Gunter H. Reduction of Postoperative Nausea and Vomiting by dimenhydrinate suppositories after Strabismus Surgery in Children. Anaesthesia Analgesia 2000; 90:311-4.
- Wennstrom B, Reinsfelt B. Rectally administered diclofenac (voltaren) reduces vomiting compared with opioid (morphine) after strabismus surgery in

children. Acta Anaesthesiol Scand 2002; 46(4):430-434.

- Kovac AL. Prevention and treatment of postoperative nausea and vomiting. Drugs 2000; 59(2):213-43.
- Allen LE, Sudesh S, Sandramouli S, Cooper G, McFarlane D, Willshaw HE. The association between the oculocardiac reflex and post-operative vomiting in children undergoing strabismus surgery. Eye 1998; 12:193-196.
- Dell R, Williams B. Anaesthesia for strabismus surgery: a regional review. Br J Anaesth 1999; 82(5): 761-3.
- Isenberg SJ, Apt L, Yamada S. Overnight admission of outpatient strabismus patients. Ophthalmic surgery 1990; 21(8):540-543.
- Karanovic N, Carev M, Ujevic A, Kardum G, Dogas Z. Association of oculocardiac reflex and postoperative nausea and vomiting in strabismus surgery in children anaesthetized with halothane and nitrous oxide. Paediatric anaesthesia 2006; 16(9); 948-54.
- 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; 30:360-9.
- Jacques R, Kenneth M, Robert DR. Local & Regional Anesthesia for Eye Surgery. NYSORA.com 2009.
- Welters ID, Menges T, Gräf M, Beikirch C, Menzebach A, Hempelmann G. Reduction of postoperative nausea and vomiting by dimenhydrinate suppositories after strabismus surgery in children. Anesth Analg 2000; 90(2):311-4.
- Choi SR, Park SW, Lee JH, Lee SC, Chung CJ. Effect of different anesthetic agents on oculocardiac reflex in pediatric strabismus surgery. J Anesth 2009; 23(4): 489-93.

- 14. Yi C, 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(2): 234-8.
- Gayer S, Tutiven J. Anesthesia for pediatric ocular surgery. Ophthalmol Clin North Am 2006; 19(2): 269-78.
- Hahnenkamp K, Honemann CW, Fischer LG, Durieux ME, Muehlendyck H, Braun U. Effect of different anaesthetic regimes on the oculocardiac reflex during paediatric strabismus surgery. Paediatr Anaesth 2000; 10(6): 601-8.
- Karanovic N, Carev M, Ujevic A, Kardum G, Dogas Z. Association of oculocardiac reflex and postoperative nausea and vomiting in strabismus surgery in children anesthetized with halothane and nitrous oxide. Paediatr Anaesth 2006; 16(9): 948-54.
- Goerlich TM, Foja C, Olthoff D. Effects of sevoflurane versus propofol on oculocardiac reflex– a comparative study in 180 children. Anaesthesiol Reanim 2000; 25(1): 17-21.
- Tramer MR, Sansonetti A, Fuchs-Buder T, Rifat K. Oculocardiac reflex and postoperative vomiting in paediatric strabismus surgery. A randomised controlled trial comparing four anaesthetic techniques. Acta Anaesthiol Scand 1998; 42(1): 117-23.
- Klockgether-Radke A, Demmel C, Braun U, Mühlendyck H. Emesis and the oculocardiac reflex. Drug prophylaxis with droperidol and atropine in children undergoing strabismus surgery. Anesthesist 1993; 42(6): 356-60.
- 21. Kovac AL. Management of postoperative nausea and vomiting in children. Paediatr Drugs 2007(1); 9: 47-69.
- Chisakuta AM, Mirakhur RK. Anticholinergic prophylaxis does not prevent emesis following strabismus surgery in children. Paediatr Anaesth 1995; 5(2): 97-100.

- Williams AR, Conroy JM. The anesthetic management of the pediatric strabismus patient. J AAPOS 1998; 2: 113-5.
- Rowley MP, Brown TCK. Postoperative vomiting in children. Anaesth Intensive Care 1982; 10:309-13