

# Incidence of the Oculocardiac Reflex using Isoflurane & Halothane during Enucleation Surgery under General Anaesthesia at NIO&H - A Comparative Study

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## Abstract

**Background:** The Oculocardiac reflex (OCR) is a well-known complication of ocular surgery involving direct or indirect manipulation of the eye or ocular adnexa. While most commonly associated with eye muscle surgery, with a reported incidence of 40-93%, it is prevalent during traction on the extraocular or eyelid muscles, compression of the globe, intraocular and retro bulbar injection, iris traction, retinal reattachment surgery and enucleation procedures and may manifest as a wide range of arrhythmias including ventricular bigeminy, bradycardia and asystole. Occurrence of the reflex in eye muscle surgery has been documented to increase with hypoxia and decrease with aging and premedication with anticholinergics, namely glycopyrrolate or atropine.

**Objective:** The purpose of our study was to determine the degree of change in heart rate (HR) and systolic blood pressure (SBP) during Enucleation surgery in patients anaesthetized with equipotent concentrations of Isoflurane or Halothane breathing via a laryngeal mask airway (LMA). **Methods:** The study was designed as a prospective randomized study. Fifty patients, having selected for Enucleation were randomized to Isoflurane (I) or halothane (H) in 66% nitrous oxide at 1.3 minimum alveolar concentration. Patients breathed through a laryngeal mask airway (LMA) and were not pretreated with anticholinergics. **Results:** The Oculocardiac reflex (OCR), defined as a 20% decrease in heart rate (HR) from baseline, dysrhythmias or sinoatrial arrest concomitant with ocular muscle traction occurred less frequently with Isoflurane than with halothane (I: 37%, H: 78%,  $P = 0.009$ ). The HR during induction was higher with Isoflurane (I:  $110 \pm 13$  bpm, H:  $100 \pm 15$  bpm,  $P = 0.002$ ). The lowest HR occurred with halothane (I:  $94 \pm 22$  bpm, H:  $72 \pm 19$  bpm,  $P = 0.001$ ). The incidence of dysrhythmias was higher in the halothane group (I 4%, H: 42%,  $P = 0.004$ ). Isoflurane may be a more suitable anaesthetic than halothane for operations involving traction on the ocular muscles with controlled respiration in patients because of reduced incidence of OCR with slightly higher airway irritability. **Conclusion:** Some patients experience a sudden slowing of the heart when the surgeon pulls on the eye muscles during Enucleation operations under anaesthesia. We found that Isoflurane was associated with a lower incidence of the OCR but relatively higher airway irritability compared with halothane. The oculocardiac reflex possesses the potential for significant morbidity and mortality. While some have documented factors affecting the OCR during eye muscle surgery, our data could not prove such a relationship during enucleation.

**Keywords:** Enucleation; Oculocardiac reflex (OCR); Isoflurane, Halothane, Inhaled anaesthesia

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## Introduction

The Oculocardiac reflex (OCR) is a well-known complication of ocular surgery involving direct or indirect manipulation of the eye or ocular adnexa<sup>1</sup>. While most commonly associated with eye muscle surgery, with a reported incidence of 40-93%<sup>2-5</sup>, it is prevalent during traction on the extraocular or eyelid muscles, compression of the globe, intraocular and retrobulbar injection, iris traction, retinal reattachment surgery and enucleation procedures<sup>6</sup> and may manifest as a wide range of arrhythmias including ventricular bigeminy, bradycardia and asystole. Cardiac disease, a light level of anaesthesia, myasthenia gravis, thyroid-associated ophthalmopathy, consumption of certain narcotics and most

importantly the age of the patient (young children with higher risk) have been suggested as predisposing risk factors for a potentially life threatening OCR<sup>7-9</sup>. Usually heart rate recovers after releasing the extra-ocular muscles (EOMs), if left untreated in rare cases results in intraoperative death<sup>10-12</sup>. Occurrence of the reflex in eye muscle surgery has been documented to increase with hypoxia and decrease with aging and premedication with anticholinergics, namely glycopyrrolate or atropine. There remains a paucity of literature on factors influencing the OCR during enucleation.

Anaesthesia using the laryngeal mask airway (LMA) with controlled ventilation is a suitable anaesthetic technique for patients undergoing Enucleation surgery in inpatient settings. Most of the anaesthesiologists prefer to secure the airway of patients 4 years and older undergoing enucleation or any eye muscle surgery with an LMA<sup>13</sup>.

During Enucleation surgery, traction on the ocular muscles causes abrupt changes in the cardiovascular and respiratory systems. The medial rectus muscle (MR) is more reflexogenic than the other EOMs, and the OCR occurs most frequently during resection of the MR<sup>3,14</sup>. The oculocardiac response (OCR) is defined as a decrease in heart rate (HR) of more than 20% of the baseline value, dysrhythmias, or sinoatrial arrest<sup>15,16</sup>. Because Halothane is associated with a lower HR<sup>17</sup> and a higher incidence of dysrhythmia<sup>18</sup>, we hypothesized that Isoflurane might cause less severe OCR than halothane during enucleation surgery with controlled respiration.

The purpose of our study was to determine the degree of change in HR, SBP, MAP and SpO<sub>2</sub> during Enucleation surgery in patients anaesthetized with equipotent concentrations of Isoflurane or Halothane breathing via a LMA.

## Methods

The study protocol was approved by NIO&H Ethical Review Committee. The study was designed as a prospective randomized study. Patients of ASA physical status I or II, scheduled to undergo Enucleation surgery were eligible to enter the study. Patients and their parents were

seen 1 week before the planned operation in the anaesthesia pre assessment clinic. All the patients (IV or inhalational induction) were asked for consent for participation in the trial.

Patients were allowed food and milk products on the evening before surgery until midnight. On the day of surgery, the patients were advised to drink sweet drinks if operation delayed. Patients were not pre medicated. Parents accompanied their patients into the operating room and were present during the induction of anaesthesia. Before the induction a Clip- Tip Spo<sub>2</sub> probe was attached to a finger or toe. Anaesthesia was induced through a face mask with oxygen in 66% nitrous oxide (N<sub>2</sub>O) via the Modified Jackson Rees system or Bain system with fresh gas flows sufficient to eliminate rebreathing.

Patients were randomly allocated to the study groups at the time of the induction of anaesthesia by having a nurse pick a colored card out of an opaque box with equal numbers of purple and red cards signifying Isoflurane (Group I) and halothane (Group H), respectively. The overpressure technique was used for induction. After four breaths of oxygen and N<sub>2</sub>O, the vaporizers were set at the maximal concentration deliverable, 5% for Isoflurane or 5% for halothane.

After loss of consciousness, a three-lead electrocardiogram and noninvasive blood pressure monitoring were applied. Clinical readiness for LMA insertion was jaw relaxation. The presence of an IV line was not a prerequisite for this procedure. An appropriately sized LMA was placed and checked for absence of obstruction. If hypoventilation was present at this time, ventilation was briefly assisted manually. Vaporizers were then adjusted to an approximate MAC multiple of 1.3 for either anaesthetic, 1.2% in the Isoflurane group and 0.5% in the halothane group. In calculating equipotent concentrations the following data were used. The MAC reducing effect of 60% N<sub>2</sub>O on Isoflurane 1.2% is 1 MAC [MAC is 1.2% in this age group]; 66% N<sub>2</sub>O adds approximately 0.24 MAC when combined with Isoflurane; Isoflurane contributes 1 MAC and N<sub>2</sub>O 0.24 MAC=1.24 total MAC. 0.5% halothane is 0.55 MAC, [1 MAC is 0.91% in this age group<sup>(19)</sup>]; 66%N<sub>2</sub>O adds 0.66 MAC; halothane

contributes 0.55 MAC and N<sub>2</sub>O contributes 0.66 = 1.21 total MAC.

Ringer's lactate was administered via an IV cannula. Paracetamol in adequate dose but no opiates or prophylactic anticholinergics was given.

After the operative field was prepared, HR (average of 3 s) was noted, and this was taken as baseline. The OCR was considered present if the HR decreased by 20% from this value or if dysrhythmias or sinoatrial arrest occurred during traction of the ocular muscles. If the HR did not increase after release of muscle tension, atropine 0.02 mg/kg was administered.

After surgery was completed, the child was given 100% oxygen, and the LMA was removed under deep anaesthesia with the vaporizer on maintenance concentrations. The child was then turned on his or her side and transported to the recovery room.

## Results

Demographic data are given in Table 1. Fifty patients were studied, and there were no statistically

significant differences. The number of muscles operated on was similar, and the average duration of surgery was 45 min.

The incidence of the OCR is presented in Table 2. Baseline HR was higher in the Isoflurane group ( $P = 0.002$ ). The OCR occurred less often in the Isoflurane group (I: 38%, H: 79%;  $P = 0.009$ ). Halothane was found to have the lower mean lowest HR during OCR. There was no difference in the baseline systolic blood pressure (I:  $102 \pm 12$  mm Hg, H:  $98 \pm 12$  mm Hg). Dysrhythmias were seen after traction on the ocular muscles and were more common in the halothane group (I 4%, H: 42%;  $P = 0.004$ ). One child in the Isoflurane group experienced nodal rhythm. In the halothane group, five patients had nodal rhythm, one had irregular sinus rhythm, one had a transient sinus arrest, that is, a missing P wave with a delayed QRS by 0.4 s, and three had ventricular extra systoles. One of the patients in the halothane group had severe ventricular extra systoles on traction of the ocular muscles and was switched to isoflurane for the maintenance anaesthetic.

**Table 1:** Demographic Data

Characteristics	Isoflurane (n=25)	Halothane (n=25)	P value
Sex (% female)	35.0	59.0	0.161
Age (year)	6.0±1.5	8.0±1.7	0.075
Weight (kg)	17.8±4.0	22.0±4.5	0.059
Muscles operated (number)	2.8±1.2	2.8±1.0	0.872
Duration of surgery (min)	43±10	45±17	0.711

Values are mean ± sd

These patients included three, all receiving halothane, who had irritable airways with laryngospasm and coughing, four patients who had Spo<sub>2</sub> values < 95% (I: 2, H: 2), and four who had PETCo<sub>2</sub> > 60 mm Hg (I: 1, H: 3). One patient receiving halothane had a persistent irritable airway and could not be settled, even after deepening the level of anaesthesia, and was switched to IV propofol for maintenance. This patient was excluded from the analysis of the OCR but included in the results on complications.

**Table 2:** Cardiovascular data during surgery

Characteristics	Isoflurane (n=25)	Halothane (n=25)	P value
Systolic blood pressure (mm Hg)	101±12	97±12	0.24
HR(bpm)	110±13	100±15	0.002
<b>OCR</b>			
Patient with OCR (%)	37.0	78.0	0.009
Median number of episodes	0(0–1)	1.5 (1–2)	0.001
HR after OCR (bpm)	94±22	72±19	0.0005
Patient with dysrhythmias (%)	4.0	42.0	0.004

Values are mean ± sd, HR =Heart Rate, OCR=Oculocardiac Reflex

## Discussion

OCR is a Trigemino-vagal reflex characterized by clinical occurrence of bradycardia and other cardiac rhythm disturbances following manipulation on eye, especially after traction of external eye muscles. The afferent pathway is via ciliary ganglion to ophthalmic division of Trigeminal nerve and through Gasserian ganglion to main sensory nucleus in the fourth ventricle. The efferent pathway is via the Vagus Nerve<sup>20</sup>. Profound bradycardia during ophthalmic surgery is not rare and is potentially serious event. Little is known about predictability of OCR. The patients undergoing Enucleation surgery, the OCR occurred significantly less often with 1.3 MAC Isoflurane in N<sub>2</sub>O than with halothane. Baseline HR was higher in patients receiving Isoflurane. These findings have also been observed in similarly aged patients during controlled ventilation with 1 and 2 MAC, Isoflurane and halothane in 100% oxygen<sup>21,22</sup>. In that study, the authors postulated that the higher HR with Isoflurane was possibly caused by the differing effects of Isoflurane and halothane on the baroreflex<sup>22</sup>. The vagal nerve is involved not only in the baroreflex but also in the OCR. Because we found that the OCR occurred less often in the Isoflurane group, a comparatively greater depression of the vagal activity by Isoflurane could theoretically lead to a less pronounced bradycardia on stimulation of the OCR. We also observed considerably fewer dysrhythmias in patients receiving Isoflurane than in those receiving halothane. This has also been observed in other studies in patients<sup>22</sup>

and may be attributed to the lack of effect of Isoflurane on myocardial conduction as compared with halothane<sup>22</sup>. During OCR, one possible explanation for this apparent discrepancy is a lower cardiac output with halothane when compared with an equivalent MAC of Isoflurane<sup>23</sup>.

The crucial issue in this study is whether the compared alveolar vapor concentrations were equipotent. The principle of overpressure induction consists of the creation of the steepest possible gradient between inspired and alveolar vapor concentrations to hasten the achievement of a specified endpoint. The endpoint chosen determines the MAC reached and will be similar to the accepted MAC for that endpoint. The inspired vapor must then be immediately reduced to prevent overdosing. If this is not done, this technique may create potentially dangerous large tissue vapor concentrations, similar to the circumstances seen with intubation under deep volatile anaesthesia.

The endpoint in this study was readiness for LMA insertion which was between two and three minutes after beginning the induction for both anaesthetics. Therefore, both were equipotent at the time that the vaporizer was switched off and the mask removed for LMA insertion.

We chose to use the overpressure technique with Isoflurane and halothane as it had been shown to be associated with minor complications<sup>24</sup>. We found that there were more respiratory complications with



Isoflurane than with Halothane. Also it is worth to be noted that controlled ventilation has no significance in lowering the risk of OCR<sup>25</sup>.

As halothane has a slower uptake and washout than Isoflurane, the time to the achievement of maintenance alveolar concentrations may have differed and have led to discrepancies. An average of 10 minutes passed from the time that the vaporizer concentration was reduced to the time surgery began. During this time, the remaining monitors were applied and the operative field was prepared. End tidal and inspired vapor concentrations had then reached equilibrium. The OCR were determined only after surgery started.

In determining equipotent maintenance concentrations, the term "MAC multiple" has been used, although it is not known what distortions arise from this concept. Moreover, the use of N<sub>2</sub>O creates further difficulties in calculating equipotency. When N<sub>2</sub>O and halothane are used together in patients, it has been stated that MAC multiples of halothane and N<sub>2</sub>O can be simply added when the total MAC is 1. The evidence suggests that MAC multiples of Isoflurane and N<sub>2</sub>O are less than purely additive, and the hypothesis is that they act at a common site of action or mechanism. Furthermore, the amount of the MAC-reducing effect of N<sub>2</sub>O on Isoflurane is different for MAC skin incision, as it is for MAC tracheal intubation. The MAC multiples we used were 1.21 for the Isoflurane group and 1.24 for the halothane group. Considering the many points where inaccuracies can enter in the concept of MAC multiples, we feel that the comparison of the two anaesthetics in our study was acceptable.

## Conclusion

In conclusion, patients undergoing inpatient Enucleation surgery must be intensively monitored for bradycardia or other arrhythmias. We found that Isoflurane was associated with a lower incidence of the OCR but relatively higher airway irritability compared with halothane. If skillfully used Isoflurane may be the better choice of inhaled anaesthetic for this procedure. The oculocardiac reflex possesses the potential

for significant morbidity and mortality. While some have documented factors affecting the OCR during eye muscle surgery, our data could not prove such a relationship during enucleation. Also it is worth to be noted that controlled ventilation had no significance in lowering the risk of OCR. The lack of statistical significance in our study was likely the result of a small sample size. Further research will prove beneficial in this area.

**Conflict of Interest:** Nothing to declare.

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