

PAEDIATRICS

Influence of the anaesthetic depth on the inhibition of the oculocardiac reflex during sevoflurane anaesthesia for paediatric strabismus surgery

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Background. It remains controversial whether the anaesthetic depth as assessed by bispectral index (BIS) influences the oculocardiac reflex (OCR) during strabismus surgery. We investigated whether BIS-guided sevoflurane titration may help to optimize the anaesthetic depth for inhibition of the OCR during paediatric strabismus surgery.

Methods. Eighty-four patients (aged 2–12 yr) undergoing strabismus surgery were randomly allocated to one of the three groups ($n=28$ for each) according to target BIS value of 40, 50, and 60. The end-tidal sevoflurane concentration with 50% N_2O/O_2 was adjusted towards target BIS. The incidence of OCR and the lowest heart rate (HR) were recorded in relation to the end-tidal sevoflurane concentration.

Results. The incidence of OCR was higher in Group BIS-60 (71.4%) than in Groups BIS-40 (10.7%) ($P<0.001$) or BIS-50 (32.1%) ($P=0.003$), with no difference between Group BIS-40 and Group BIS-50. The lowest HR [beats min^{-1} , mean (SD)] during traction on the extraocular muscle was lower in Group BIS-60 [112.3 (SD 17.8)] compared with Group BIS-40 [129.3 (11.2)] ($P<0.001$), with no difference between BIS-40 and BIS-50 [121.4 (16.3)], and between BIS-50 and BIS-60. The end-tidal sevoflurane concentration was different between the three groups ($P=0.001$).

Conclusions. We confirmed that OCR is relevant to the depth of anaesthesia. BIS values of 40–50 seem adequate for the inhibition of OCR. The results suggest that BIS may be a valuable tool during sevoflurane anaesthesia for strabismus surgery in children.

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It has been accepted that depth of anaesthesia influences the incidence of oculocardiac reflex (OCR).¹ However, controversy still exists on the role of the anaesthetic depth in causing OCR. Some textbooks emphasize that inappropriate anaesthetic depth increases the potential for arrhythmias with the OCR, recommending that the anaesthetist should ensure that the depth of anaesthesia is adequate if the patient seems sensitive to manipulation of the extraocular muscles (EOMs).^{1–2} However, others describe that it is unclear whether the anaesthetic depth could influence the incidence of OCR during general anaesthesia.^{3,4}

Assessing the depth of anaesthesia is difficult in children.⁵ The Bispectral Index (BIS[®], Aspect Medical Systems, Norwood, MA, USA) has been used to assess the depth of anaesthesia in several studies.^{6–8} Recently, reports also indicated that BIS facilitated the administration of volatile anaesthetics^{9–11} and showed that the end-tidal sevoflurane concentrations were closely correlated with the BIS values.^{10,12}

In this study, we aimed at investigating whether BIS-guided sevoflurane titration may help to optimize the anaesthetic depth in order to inhibit the OCR during strabismus surgery in children. To our knowledge, there has

been no study on the role of BIS decreasing the incidence of OCR.

Methods

After having obtained institutional review board approval and written informed consent from their parents, we studied 84 healthy children undergoing elective strabismus surgery performed by a single ophthalmologist. Children between the age of 2 and 12 yr, ASA physical status I, were eligible to enter the study. We excluded children with any neurological disease or taking chronic medications known to affect EEG or ECG recordings. The children were randomly divided into three groups ($n=28$ for each) according to the target BIS value (by picking one of the cards marked 40, 50, or 60 from a closed box by the parent or the child indicating the target BIS level, with predetermined range of ± 4). As such, the children were allocated to Group BIS-40, BIS-50, or BIS-60, respectively.

Anaesthesia

Food or milk products were allowed until 6 h before surgery and clear liquids until 2 h before surgery. Anaesthesia was standardized for all patients except for end-tidal sevoflurane concentrations according to target BIS values. Patients were premedicated with i.m. atropine 0.01 mg kg^{-1} . All patients were induced with thiopental 5 mg kg^{-1} and 4% sevoflurane in 50% N_2O in O_2 . The fresh gas flow was set at 5 litre min^{-1} . Rocuronium 0.8 mg kg^{-1} was used to facilitate tracheal intubation. Patients were then connected to an anaesthesia circuit. Then, the fresh gas flow decreased to 3 litre min^{-1} . No sedatives or opioids were used. After tracheal intubation, ventilation was controlled and an end-tidal CO_2 level was kept between 30 and 35 mm Hg. Peripheral oxygen saturation was maintained at $>97\%$. Body temperature was maintained in the range of $35.5\text{--}36.5^\circ\text{C}$. During anaesthesia, the inhaled concentration of sevoflurane was adjusted to achieve a stable target BIS value. The depth of anaesthesia was maintained by keeping the BIS value constant, using sevoflurane and N_2O . Heart rate (HR) and systolic and diastolic arterial pressure were recorded 30 s before EOM traction. The S/5™ Anaesthesia Monitor (Datex-Ohmeda, Madison, WI, USA) was used for end-tidal gas analysis. End-tidal CO_2 and sevoflurane concentration, pulse oximetry, non-invasive arterial pressure, HR and rhythm disturbances (lead II ECG), and type of the operated EOM were monitored.

Bispectral index

After induction, a disposable standard adult BisSensor® strip (Aspect Medical Systems) was attached to the forehead according to the manufacturer's instructions. Before

starting BIS recording, we verified that all electrode impedances were $<5 \text{ k}\Omega$. Suppression ratio number, electromyographic activity, and signal quality index were also recorded. The smoothing rate was set at 30 s. Once the BIS value was stable in the target value before the traction of EOM, the end-tidal concentration of sevoflurane was recorded.

Definition of OCR

We defined OCR as $>10\%$ decrease in HR or occurrence of any arrhythmia induced by traction during the single muscle surgery of recession–resection type which performed on one EOM, according to Hahnenkamp and colleagues.¹³ Preliminarily, we had observed the ophthalmologist's procedure on the strabismus surgery and found that the tractions on EOM were very gentle, reducing the incidence of OCR. This observation made us change the definition of OCR from $>20\%$ to 10% decrease in HR. Average HR obtained during 30 s before muscle stimulation served as a baseline value. The lowest HR, incidence of arrhythmia, and the number of OCR episodes during traction were recorded.

Statistical analysis was performed by using one-way ANOVA with *post hoc* Scheffe test for parametric data, and by using χ^2 test for non-parametric data. $P<0.05$ was considered significant.

Results

All enrolled patients completed the study. Patient characteristics are given in Table 1. No statistical differences were found among the three groups with respect to age, gender, weight, end-tidal CO_2 , type of EOM operated on, and baseline HR.

The incidence of OCR was different among the three groups: the incidence of OCR was higher in Group BIS-60 compared with that of Group BIS-40 ($P<0.001$) or BIS-50 ($P=0.003$); however, no significant difference in OCR was found between Group BIS-40 and Group BIS-50 ($P=0.051$). The lowest HR during traction of EOM was lower in Group BIS-60 compared with Group BIS-40 ($P<0.001$), with no significant difference between Group

Table 1 Patient characteristics. No significant differences among the three groups. Data were expressed as numbers, mean (range), or mean (sd). HR, heart rate; M/L, medial/lateral rectus

	Group		
	BIS-40 ($n=28$)	BIS-50 ($n=28$)	BIS-60 ($n=28$)
Age (yr)	6.7 (4–12)	6.3 (2–9)	6.2 (2–12)
Sex (M/F)	13/15	14/14	15/13
Weight (kg)	28.1 (10.9)	26.4 (6.8)	26.4 (10.6)
End-tidal CO_2 (mm Hg)	32.5 (1.9)	32.6 (1.9)	32.7 (2.0)
Baseline HR (beats min^{-1})	130.5 (10.5)	131.4 (7.9)	133.8 (11.7)
Muscle of traction (M/L)	8/20	6/22	8/20

Table 2 The incidence of OCR according to BIS values. Data were expressed as numbers or mean (sd). OCR, oculocardiac reflex; BIS, bispectral index; ET-sevo, end-tidal concentration of sevoflurane; HR, heart rate. * $P=0.001$ between groups; † $P<0.005$ vs Group BIS-40 or vs Group BIS-50; ‡ $P<0.001$ vs Group BIS-40

	Group		
	BIS-40 (n=28)	BIS-50 (n=28)	BIS-60 (n=28)
BIS (range)	38–43	47–53	58–63
ET-sevo (%)*	2.1 (0.2)	1.7 (0.3)	1.3 (0.2)
Incidence of OCR (%)	3 (10.7)	9 (32.1)	20 (71.4)†
Lowest HR (beats min ⁻¹)	129.3 (11.2)	121.4 (16.3)	112.3 (17.8)‡

BIS-40 and Group BIS-50 or between Group BIS-50 and Group BIS-60. The number of OCR episodes was not different in patients with OCR among the three groups during the traction (one for each group). End-tidal sevoflurane concentration was different among the three groups with significant difference between Group BIS-40 and Group BIS-50, between Group 50 and Group 60, and between Group 40 and Group 60 ($P=0.001$). Arrhythmia (premature ventricular contraction) occurred in one patient of Group BIS-60 (Table 2).

In all patients demonstrating OCR, HR, arrhythmia, or both returned to baseline value after release of the muscle and required no other treatment. With arterial pressure being within 20% of preinduction value, no patient required treatment.

Discussion

Strabismus surgery involves traction on EOMs, inducing OCR. Although not consistently reliable, various prophylactic measures have been used for the reduction of OCR.^{13–15} The aim of this study was to investigate whether the depth of anaesthesia may influence the occurrence of OCR and whether BIS-guided sevoflurane titration may help to optimize the anaesthetic depth in order to inhibit OCR during paediatric strabismus surgery. In this study, we confirmed that depth of anaesthesia influences OCR. We found that BIS target values of 40–50 seem adequate to inhibit OCR. The results suggest that BIS may be a valuable tool for monitoring the depth of sevoflurane anaesthesia during strabismus surgery in children.

Children are most predisposed to the OCR during strabismus surgery, because of a relative increase in vagal tone.¹⁶ Several investigators have suggested that the vagolytic effect induced by anaesthetics may decrease the incidence of OCR.^{14 15 17 18} Sevoflurane depresses the parasympathetic tone in children,¹⁹ hereby demonstrating that sevoflurane inhibits the vagal activity more than other anaesthetics and as such, a comparatively greater depression of the vagal activity by sevoflurane could lead to a less pronounced bradycardia and decreased incidence on stimulation of the OCR.^{17 18} Accordingly, depressing

the vagal activity may be of great importance in reducing the incidence of OCR. We hypothesize that the deeper plane of anaesthesia with higher concentrations of sevoflurane, as evidenced by lower BIS value in our study, would result in a more pronounced vagolytic effect, thereby decreasing the incidence of OCR. However, this could be in contrast with the reports showing that sevoflurane has little or no effect on cardiac parasympathetic tone.²⁰

It has been confirmed that BIS was inversely proportional to the end-tidal concentration of sevoflurane, providing accurate clinical information in children.¹² Furthermore, BIS correlates with the clinically assessed hypnotic component of anaesthesia induced by sevoflurane in children²¹ and end-tidal sevoflurane concentrations are more closely correlated with BIS than with mean arterial pressure or HR in children undergoing sevoflurane anaesthesia for tonsillectomy and adenoidectomy.¹⁰ Our results, in which end-tidal sevoflurane concentrations were significantly different between the groups depending on the BIS values, accord with these previous observations, indicates that the BIS index is a useful monitor for ‘depth of anaesthesia.’ However, as anaesthesia can be defined by its hypnotic and analgesic components and the BIS index primarily measures the effects of hypnotics,²² the depth of anaesthesia as assessed by BIS indicates the level of hypnosis rather than overall depth of anaesthesia. As a result, it is reasonable to state that the component of anaesthesia that is relevant to OCR is its hypnotic component.

Opioids can be used for strabismus surgery. One might argue that the addition of opioids can affect the incidence of OCR by improving analgesia. The BIS index is most accurate when used with anaesthetics consisting of a low or moderate dose of opioid analgesic and a volatile anaesthetic, and the addition of adequate opioid analgesia results in less or no change in the BIS value as long as a high-dose opioid technique is avoided.²² Thus, the usual doses of opioids, if used for strabismus surgery, are not likely to affect BIS value, and thereby may not change OCR response: rather, opioid analgesia using rapidly acting opioids (fentanyl, sufentanil, and remifentanyl) may intensify the OCR response in the absence of anticholinergic block during strabismus surgery.²³ We hypothesize that the hypnotic, rather than the (opioid) analgesic, component is more relevant to OCR. In contrast to opioid analgesia, regional analgesia can reduce the OCR alone²⁴ or in combination with general anaesthesia^{25 26} during which deafferentation produced by regional block changes hypnotic anaesthetic requirements and BIS response.²²

Both anaesthetic over- and underdosing can endanger children. BIS monitoring, by measuring continuous, real-time measurement of hypnosis, can give us information on the state of anaesthesia with optimal titration of anaesthetics based on individual requirements, with a reduction in the incidence of relative over- and underdosing.²⁷ BIS values between 40 and 60 have been recommended for

general anaesthesia. In our study, BIS values between 40 and 50 seem adequate for the inhibition of OCR during strabismus surgery. We believe that children and infants may additionally benefit from the use of BIS monitoring in order to avoid anaesthetic over- or underdosing during strabismus surgery. However, the indiscriminate use should be avoided because OCR is generally well controlled and rarely life threatening in most patients when ophthalmic surgeons are careful during the procedure. We suggest that the use of BIS monitoring should be limited to patients with conditions such as myocarditis,²⁸ breath-holding spells,²⁹ or Marcus-Gunn syndrome³⁰ in which OCR may be exaggerated.

In our study, only one patient presented arrhythmia which meets the definition of OCR, whereas many investigators reported a relatively high incidence of arrhythmias.¹⁷ Rocuronium was used in our study. Rocuronium, 0.4 mg kg⁻¹ given i.v. 2 min before tracheal intubation, is reported to reduce the incidence of arrhythmia but not of bradycardia probably as a result of vagolytic effect.¹⁵ We used 0.8 mg kg⁻¹ of rocuronium, and this might have contributed to the inhibition of arrhythmia in combination with sevoflurane. In addition, the ophthalmologist was always very careful for traction of EOMs, which might also avoid arrhythmia.

Paediatric strabismus surgery increases both OCR and postoperative nausea and vomiting (PONV), with a significant association between them.¹⁶ It is reported that the patients receiving large concentrations of sevoflurane resulting in BIS lower than 40 had an increased risk of PONV.³¹ On the basis of this observation and our present study in which BIS values of 40–50 seem adequate for inhibition of OCR, we speculate that BIS monitoring with the values above 40 may also help to decrease PONV in children after strabismus surgery, although we did not study PONV.

One limitation is that atropine and rocuronium were used in our study. We speculate that these drugs attenuated the OCR response. I.M. atropine might play a role in changing the definition of OCR from >20% to 10% decrease in HR. In addition, the attenuation of OCR response by the drugs might complicate the effect of anaesthetic depth assessed by BIS value on OCR, incurring a potential impact on the results of our study. It has been reported that i.m. prophylactic atropine decreases the incidence of OCR.² However, recent publications also describe that atropine for OCR prophylaxis is not universally effective,¹⁶ or even ineffective in the usual i.m. premedication regimen.¹ Considering these two contradictory views on the use of atropine and rocuronium, it is difficult to estimate how seriously the i.m. premedication of atropine influenced the results in our study.

The force of traction on EOM is an important determinant of OCR.³² In this regard, the type of surgery (resection vs recession) may influence the occurrence of OCR

because the force of traction may be stronger in resection than in recession. However, we could not find any study on the effect of the type of strabismus surgery on occurrence of OCR. As such, we did not differentiate between the resection and the recession in our study. Further study is needed.

In summary, we confirmed that differences in the hypnotic component of anaesthetic depth might influence OCR. BIS values between 40 and 50 seem adequate to inhibit vagal activity, hereby decreasing OCR. The results suggest that BIS may be a valuable tool helping to optimize anaesthetic depth for inhibition of OCR during sevoflurane anaesthesia for strabismus surgery in children.

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