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ORIGINAL RESEARCH

The effect of anesthesia depth on the oculocardiac reflex in strabismus surgery

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Abstract The aim of this study was to investigate the effect of the bispectral index (BIS) guided depth of anesthesia to inhibition of the oculocardiac reflex (OCR) during pediatric strabismus surgery. Patients between the ages of 3 and 16 years who were scheduled for elective strabismus surgery were randomly assigned to two groups. In Group 1 (n: 32), the BIS values of the patients were maintained at <50; in Group 2 (n: 28), the BIS values of the patients were maintained at levels greater than or equal to 50 with 4–7 % desflurane in a 50 % O_2–air mixture by titrating the concentration during the surgery. The heart rates, presence of dysrhythmia, anticholinergic drug usage and the type of the operated extra ocular muscle were recorded. The incidence of OCR was 25 % in Groups 1 and 64.3 % in Group 2, ($p < 0.05$). Moreover, the incidence of OCR in group 2 was higher in medial rectus (MR) traction (78.9 %) than in lateral rectus (LR) traction (33.3 %) ($p = 0.035$), with no significant difference in Group 1 between MR (21.1 %) and LR (26.7 %) tractions ($p = 0.83$). We found that the lower BIS values are associated with the lower incidence of OCR in pediatric patients undergoing strabismus surgery. And our findings confirmed that the deeper anesthesia has a protective effect against the OCR.

Keywords Anesthesia · General · Strabismus · Consciousness monitors · Pediatrics

1 Introduction

The oculocardiac reflex (OCR) is one of the main challenges of pediatric anesthesiologists during strabismus surgery. The stimulus is triggered by pressure on the extraocular muscles (EOM) or eyeball, which transfers signals through the trigeminal nerve and ultimately results in a stimulation of the vagus nerve. The vagal stimulation leads to decreases in both heart rate and contractility of the heart. The incidence of the OCR decreases with age and tends to be more pronounced in young, healthy patients, which is clinically significant for pediatric anesthesiologists [1]. Sinus bradycardia is the most common

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manifestation of OCR, however, atrioventricular block, ventricular fibrillation, and even asystole may occur. It has also been reported that OCR may even be fatal in pediatric patients [2].

The incidence of OCR varies from 16 to 82 % depending on the anesthetic agent, premedication, and the definition of OCR being used. OCR is usually defined as a decrease in heart rate of more than 20 % from the baseline heart rate. It has been suggested that the anesthetic agents used during surgery influence the incidence of OCR. Recently, reports have proposed that sevoflurane or desflurane are associated with a lower incidence of OCR than propofol or remifentanil [3]. Sevoflurane and desflurane have similar effects on ORC incidence and can be used with a low OCR incidence rate during pediatric strabismus surgery [3, 4]. To date, the only successful way to interrupt an OCR is to stop the EOM traction, and then proceed with caution as the surgery is continued [1].

The depth of anesthesia is another presumed factor having an impact on OCR incidence [5, 6]. However, there are few studies that clearly show the effect of the anaesthesia depth on OCR. Recently, Yi and Jee [5] showed that bispectral index (BIS)—guided depth of anesthesia values of 40–50 allow for a lower incidence of OCR in strabismus surgery in children under sevoflurane anaesthesia. To the best of our knowledge, there are no studies comparing the BIS-guided anesthetic depth and surgically treated EOM on OCR incidence rates. In this study, we investigated the effect of the BIS-guided depth of anesthesia with desflurane on the inhibition of the OCR during pediatric strabismus surgery. We also evaluated the role of the anesthetic depth during medial or lateral rectus muscle traction on OCR incidence rates.

2 Methods

After approval of the Gaziosmanpasa University Clinical Research Ethics Committee (13-KAEK-138), this prospective study was conducted from August 2013 to May 2015. Prior to performing any procedures, we obtained the written informed consent from the patients' parents. A total of 64 children aged 3–16 years, with a physical status ASA I, who were scheduled for elective strabismus surgery under general anesthesia were enrolled into this prospective, randomized, single-blinded study. Patients who had neurological or cardiovascular disease, or were receiving antiepileptic or other medications known to affect EEG or ECG were excluded. The children were randomly divided into two groups according to the BIS value. In Group 1, the BIS values of the patients were maintained at levels 49–40; in Group 2, the BIS values of the patients were maintained at levels 50–59 by titrating desflurane concentration.

All surgical procedures were performed by the same ophthalmologist and the perioperative anesthetic management was standardized. Patients did not receive premedication before anesthesia induction and a peripheral venous cannula was inserted during the preoperative period. Patients who were given premedication or refused to obtain venous access during the preoperative term were also excluded.

Standard monitoring included electrocardiography, pulse oximetry, capnography, body temperature and non-invasive blood pressure monitoring that were all applied before anesthetic induction. Heating pads were used during anesthesia to avoid hypothermia. Anesthesia was induced using intravenous thiopental (5 mg/kg) and fentanyl (1 mcg/kg). Tracheal intubation was performed in all patients after providing muscle relaxation by rocuronium (0.6 mg/kg). Controlled mechanical ventilation was adjusted to sustain end-tidal CO_2 levels between 30 and 35 mmHg. Anesthesia was maintained with 4–7 % desflurane in a 50 % O_2–air mixture by titrating the concentration according to the BIS monitoring to maintain the target BIS values. After anesthesia induction, the BIS values of all patients were monitored by applying sensors to the patients' foreheads according to the manufacturer's recommendations (BIS XP, A 2000, version 3.31, Aspect Medical Systems, Newton, Mass, USA). Additionally, the BIS monitor was concealed from the ophthalmologist during the surgery.

After the ophthalmologist's notification about EOM traction, the BIS value, heart rate (HR), systolic and diastolic arterial pressures, and muscle type were recorded by the anesthesiologist 30 s before and after the EOM traction. The HR before the traction was accepted as the basal HR. The BIS value was accepted as debatable if the BIS value changed more than 10 units during a 30 s interval; in patients where this occurred, the patient was excluded from the study.

OCR was defined as a sudden reduction in HR of more than 20 % from the baseline HR, a HR below 60 beats/min, or dysrhythmia during EOM traction during the surgery on one EOM; during these instances, the lowest HR and the presence of a dysrhythmia were recorded. Treatment of OCR consisted of stopping the traction on the EOM. If the HR still did not return to baseline values or if severe bradycardia developed (HR $<$ 60 beats/min), intravenous atropine (0.01 mg/kg) was administered.

The primary outcome of our study is the incidence of the oculocardiac reflex. Sample size was determined using a power analysis. We aimed a power of 80 % (beta = 0.2) with a 5 % significance level (alpha = 0,05) for a study to detect a 50 % reduction in oculocardiac reflex from a basal incidence of 77 % which was reported by Hahnenkamp et al. [7]. The minimum sample size was calculated as 26

patients in each group. We recruited 64 patient into the study to allow for dropouts.

Categorical variables were compared using the Chi square (χ^2) test. Normality was tested using a one sample Kolmogorov–Smirnov test. Normally distributed variables were presented as the mean ± SD and compared using the Student's t test. All statistical analyses were performed using SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). A p value of <0.05 was considered to be statistically significant.

3 Results

Sixty-four patients were enrolled into the study. Four patients were excluded from the study for failing to keep the target BIS values. There were a total of 32 patients in Group 1 and 28 patients in Group 2. The mean age of each group was 9.96 (range 3–16) years for Group 1 and 8.85 (range 3–16) years for Group 2. The patient characteristics are shown in Table 1. There were no differences among the two groups with respect to age, gender, type of EOM operated on, or eye laterality.

The OCR incidence was significantly different between groups. OCR occurred more in Group 2 (n = 18, 64.3 %) compared to Group 1 (n = 8, 25 %) ($p = 0.02$).

In general, the surgical stimulus stopped immediately when OCR was observed and most patient's HR returned to baseline values. However, it was necessary to use intravenous atropine in five patients: one patient (3.1 %) in Group 1 (during traction on the lateral rectus muscle), and four patients (14.3 %) in Group 2 (one of them during traction on the lateral rectus muscle and the others during traction on medial rectus muscles) ($p = 0.175$).

In Group 2, the EOM type had an effect on the incidence rate of OCR; these OCR incidents occurred during traction on the medial rectus muscle of 15 patients (78.9 %) compared with only three patients (33.3 %) following traction on lateral rectus muscle ($p = 0.035$). However, in Group 1, OCR occurred in four patients (21.1 %) with medial rectus muscle traction, which was similar to the four patients (26.7 %) experiencing OCR following lateral rectus muscle traction ($p = 0.83$) (Table 2).

Table 2 Incidence of OCR according to type of manipulated EOM

Type of manipulated EOM	Incidence of OCR		p value
	Group 1	Group 2	
Lateral rectus [n, (%)]	4 (26.7)	3 (33.3)	0.48
Medial rectus [n, (%)]	4 (21.1)	15 (78.9)	0.01*
Total [n, (%)]	8 (25)	18 (64.3)	0.02*

OCR oculo cardiac reflex, *EOM* extra ocular muscles. Chi square test
* $p < 0.05$

4 Discussion

One of our main findings was that the depth of the anesthesia was one of the related factors in the occurrence of OCR in patients undergoing strabismus surgery. BIS values under 50 were associated with a lower incidence of OCR. Moreover, the OCR incidence was higher with traction on the medial rectus muscle compared with the lateral rectus muscle.

OCR is a parasympathetic response following EOM traction or ocular compression. The afferent loop of the OCR pathway involves the ophthalmic division of the trigeminal nerve with the efferent loop being the vagus nerve. The only objective feature of the OCR while the patient is anaesthetized is an abnormal electrocardiogram. Although there are different definitions given among various studies, it has usually been accepted that a drop in heart rate of 20 % or more after an ocular stimuli is defined as a positive OCR. However, many factors affect the incidence of OCR. The OCR is much more likely to occur in children than in adults during strabismus surgery [1]. Hypercarbia and hypoxemia are important adjuvant factors of the OCR [8]. Factors closely associated with the risk of

Table 1 Patients' characteristics

	Group 1 (n = 32)	Group 2 (n = 28)	p
BIS value	43.0 ± 2.9	56.5 ± 3.8	<0.001$^{\alpha,*}$
Age (year)	9.96 (3–16)	8.85 (3–16)	0.219$^{\alpha}$
Sex (M/F)	20/12	14/14	0.33$^{\beta}$
Right eye [n, (%)]	12 (37.5)	11 (39)	0.88$^{\beta}$
Muscle of traction (M/L)	17/15	19/9	0.37$^{\beta}$

BIS bispectral index, *M* male *F* female, *M/L* medial/lateral rectus
* $p < 0.05$
$^{\alpha}$ Student test
$^{\beta}$ Chi square test

OCR include the general anesthesia agents used, the surgical interventions including tension applied by the surgeon on EOMs, and the EOM that is being surgically treated [9–11].

Several studies have examined the anesthesia management of patients undergoing strabismus surgery [3, 4]. The anesthetic drugs are one of the main topics in attempts to prevent OCRs from occurring [3, 4, 9]. It is speculated that ketamine may reduce OCRs due to its cardiostimulatory effect, but some studies have reported contradictory results [7, 12]. However, Choi et al. [3] recently showed there was very little effect of ketamine on OCR, but propofol and remifentanil were more relevant to OCR than sevoflurane or desflurane. Inhalational anesthetic agents mostly increase HR due to their vagolytic activity, especially with desflurane. Thus, Oh AY et al. [4] hypothesized that desflurane would be associated with a lower incidence of OCR than sevoflurane; however, their results suggested that desflurane and sevoflurane had similar effects on OCR with an OCR incidence of 26.0 % in the sevoflurane group and 28.0 % in the desflurane group. They further proposed that both agents could be safely used during strabismus surgery in pediatric patients. In the current study, we used desflurane as an inhalation anesthetic for general anesthesia and found that the OCR was 43.3 % in all patients. Our total OCR incidence was higher than the results reported in the Oh AY et al. [4] study. We believe this difference may have been due to the depth of the anesthesia. Moreover, a recent study has shown that the OCR incidence decreases with an increased depth of anesthesia [5]. Oh AY et al. [4] did not use any neuromonitoring to assess the depth of anesthesia. Additionally, it has been shown that the equivalent concentrations of the different volatile anesthetics do not results in similar BIS values [13]. However, we realized that the OCR incidence is closely associated with the depth of general anesthesia and the incidence of OCR was 25 % in Group 1 and 64.3 % in Group 2. Thus, our findings confirm that the deeper anesthesia produces a protective effect from the OCR. This protective effect may be based on the effects of the anaesthetic drugs on the cortical and subcortical areas in the brain. The small dose of the anaesthetics lead to suppressed thinking, focused attention and working memory. The increased anaestetic dose can act subcortical areas and suppress the nociceptive and autonomic reflexes [14, 15].

Anticholinergic prophylaxis decreases the incidence of OCR [16]. However, systemic prophylactic anticholinergic administration is associated with ventricular arrhythmias [17]. Therefore, the routine use of prophylactic atropine in any pediatric ophthalmic surgery is not recommended by many pediatric anesthetists. We did not routinely use systemic anticholinergic prophylaxis in our pediatric strabismus surgeries. Intravenous atropine was administered only if the HR did not increase after the release of muscle tension. According to our results, it can be said that the depth of anesthesia reduces the usage of systemic anticholinergic agents that are associated with cardiac arrhythmias.

Surgery-related factors including the type of manipulated EOM and the quantitative traction force are closely related to OCR [10, 11]. As tension was increased, bradycardia occurred rapidly and became deep. Also, the OCR incidence rates vary according to the type of manipulated EOM. Of the rectus muscles, the inferior rectus caused the greatest bradycardia while the lateral rectus caused the least [18]. However, there are few comprehensive studies that have evaluated this association that included all of the EOMs. Therefore, there is no consensus on the association between OCR and surgical treatment of specific EOMs in the literature [19]. Some studies concluded that medial rectus surgery is most strongly associated with OCR [9, 12]; however, others have reported no association between the treatment of specific muscles and OCR [19]. We found that the incidence of OCR was significantly higher in the medial rectus compared to the lateral rectus in Group 2 but not in Group 1. These results suggest that traction on the medial or lateral rectus muscle may not associated with the OCR incidence rates in patients with deep anesthesia (BIS value <50).

There are some limitations in this study. First, the BIS monitoring was our only data source for determining the depth of anesthesia. Unfortunately, the performance of the monitors predicting the level of consciousness may be affected by certain drugs like neuromuscular blockers or environmental and patient conditions. Second, the sample size of our study was relatively small. Third, the duration and the force of the tension applied to the EOM were not measured.

In conclusion, we found that the lower BIS values are associated with a lower OCR incidence in pediatric patients undergoing strabismus surgery. The type of stretched EOM traction appears to be not important in patients with BIS values <50. However, further studies with larger sample sizes are needed. These results support the notion that the usage of intraoperative neuromonitoring, such as BIS, for the adjustment of anesthesia depth may increase safety by preventing OCRs during desflurane anesthesia for strabismus surgery in children.

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Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest to declare.

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