The effect of ketofol anesthesia on intraocular pressure in pediatric strabismus surgery

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Abstract

Background/Aim: Keeping intraocular pressure (IOP) within normal limits is an important goal in the anesthetic management of pediatric strabismus surgery. While propofol is commonly used as an induction agent since it provides smooth laryngeal mask insertion, it has the undesirable side effect of dose-dependent cardiorespiratory depression. On the other hand, ketamine acts as a sympathetic cardiorespiratory stimulant; however, its effect on IOP is controversial. The aim of this study was to determine the effect of the combination of ketamine and propofol (ketofol) on IOP in pediatric strabismus surgery compared to propofol alone.

Methods: Participants included patients aged between 2 and 18 years who underwent strabismus surgery. They were divided into two groups according to type of anesthesia induction: propofol and ketofol. Patient characteristics, surgical data, hemodynamic parameters, oculocardiac reflex (OCR), and IOP were compared between the two groups.

Results: Forty-five children with a mean age of 7.7 years were enrolled in the study. The patients were assigned into two groups: propofol alone (n=26) and ketofol (n=19). The groups were similar in patient characteristics, surgical data, and hemodynamic parameters (P>0.05 for each). IOP was measured at four points: before anesthesia, at 1 minute following induction, at 3 minutes following laryngeal mask airway (LMA) insertion, and at the end of surgery. All IOP values were within normal limits. No significant differences in mean IOP values were found between the groups (P=0.05 for each). There was also no significant difference in OCR between the groups (P=1.000).

Conclusions: Compared to propofol alone, ketofol had a similar effect on IOP, OCR, and hemodynamic parameters. These results suggest that ketofol can be safely used in the induction of anesthesia in pediatric patients undergoing strabismus surgery.

Keywords: induction of anesthesia, intraocular pressure, ketamine, ketofol, propofol
Introduction

Strabismus surgery, a common procedure in children, involves the surgical intervention for the extraocular muscles that provide movement of the eyeball. This surgery is always performed under general anesthesia, and, as in other ophthalmic procedures, keeping intraocular pressure (IOP) within normal limits is an important goal. An increase of more than 10 mmHg in IOP reduces choroidal blood flow and ocular fundus vibrations in healthy eyes, while an increase of more than 5 mmHg may lead to choroidal and optic nerve ischemia in injured eyes [1].

All anesthetic drugs affect IOP, with varying severity depending on the depth of anesthesia [2]. Propofol is a widely preferred induction agent in pediatric strabismus surgery as it ensures smooth laryngeal mask airway (LMA) insertion by depressing airway reflexes [3]. It also has rapid induction and recovery times, with strong antiemetic effects. On the other hand, dose-dependent cardiorespiratory depression is the leading undesirable adverse effect of propofol, particularly at higher doses [4]. To minimize this potential hemodynamic instability, several combinations of pharmacological drugs have been introduced to anesthesia protocols. Although some clinical studies on cataract surgery have demonstrated that anesthetic drugs such as propofol and fentanyl do not significantly change IOP, the effect of ketamine on IOP remains controversial [5]. It is widely known that ketamine is not used alone as an induction agent because it causes excessive secretions and does not adequately suppress airway reflexes. However, unlike propofol, it acts as a sympathetic cardiorespiratory stimulant and has pain-relieving properties [6]. In the literature, several studies have shown that hemodynamic stability can be achieved with the combined use of ketamine and propofol in pediatric cases under general anesthesia with LMA [7–10]. However, most of those studies involved sedation and general anesthesia for non-specific surgical indications and were conducted on different patient cohorts consisting of both pediatric and adult groups. Because changes in IOP are more important in pediatric patients undergoing ophthalmic surgery, it is crucial for anesthesiologists to understand the effects of preferred anesthesia drugs on IOP in pediatric patients.

Therefore, this study aimed to determine the effect of ketofol-based anesthesia protocol on IOP in pediatric patients who underwent strabismus surgery.

Materials and methods

Study design

The study, which was approved by the Local Ethics Committee of Eskişehir Osmangazi University Faculty of Medicine (protocol number: 25, date: 22 November 2022), was conducted on pediatric patients who underwent elective surgery for strabismus under general anesthesia with LMA at Osmangazi University Hospital between October 2020 and June 2021. Patient data including age, gender, American Society of Anesthesiologist (ASA) physical status, operative findings, anesthetic medications, and complications were recorded. Intraoperative hemodynamic parameters including heart rate (HR), mean arterial pressure (MAP), pulse oximetry (SpO2), end-tidal carbon dioxide concentration (etCO2), minimal alveolar concentration (MAC) of sevoflurane, tidal volume (TV), peak airway pressure (PAP), and IOP were also noted. The patients were randomly assigned into two anesthesia induction groups—propofol alone and ketofol—and compared in terms of patient characteristics, surgical data, hemodynamic parameters, occurrence of ocular cardiac reflex (OCR), and IOP values.

Inclusion and exclusion criteria

Inclusion criteria were that the patients were between 2 and 18 years old, had an ASA physical status of 1 or 2, and were undergoing an elective surgery. Children with an ASA physical status ≥3, high IOP, previous ocular surgery, allergy to the study medications, irregular medical records, or any ophthalmic, cardiac, or central nervous system disease were excluded from the study.

Anesthesia management

The fasting time was at least 8 hours before the operation. No premedication was given to the children. After standard monitoring, anesthesia was administered via a face mask with inhalation of sevoflurane in 4 L/min oxygen (50%) and air (50%). Venous access was opened following sufficient loss of consciousness. The patients were randomly assigned to one of the two induction groups: remifentanil (1 μg/kg), lidocaine (0.5 mg/kg), and propofol (3–5 mg/kg) (propofol alone group) or propofol (2.5–3 mg/kg) plus ketamine (1.5 mg/kg) (ketofol group). LMA was used for airway control. Anesthesia was maintained with sevoflurane (with age-corrected 1–1.3 MAC) in 4 L/min oxygen (50%) and nitrous oxide (50%). Weight-appropriate continuous IV fluids (mixture of 0.45% NaCl and 5% dextrose) were given to the patients throughout the surgery. Standard monitoring was conducted for HR, MAP, SpO2, and etCO2.

OCR was defined as a 20% decrease in HR or the presence of dysrhythmia following the traction of extraocular muscle. In the case of OCR lasting for more than 5 seconds, the surgeon was warned to stop the traction of muscle and to wait until the HR returned to normal rhythm. IV atropine (0.01 mg/kg) was given to patients when a persistent OCR or rapid drop in HR <60/min was observed. The surgeon continued the surgery after the values returned to normal limits. All surgical interventions were performed by the same surgeon using standard techniques.

Measurement of IOP

IOP was measured four times during the procedure. The first measurement (baseline) was performed when spontaneous breathing was lost and the patient was fully immobilized. The other measurements were performed at 1 minute following induction of anesthesia, at 3 minutes following insertion of LMA, and at the end of the surgery. All measurements of IOP were performed using the same tonometry device (Tonopen XL, Reichert Technologies, Depew, NY) by the same ophthalmologist, who was blinded to the type of anesthesia protocol being used.

Statistical analysis

A power analysis based on the study by Aydoğan et al. [11] showed that a sample size of 37 patients was required to achieve 95% power with a 5% significance level to assess the differences between the two anesthesia groups. Statistical
analyses were performed using the Statistical Package for the Social Sciences (SPSS 23.0 software). Descriptive data were presented as numbers (%) for the categorical variables and as mean (standard deviation) for the continuous variables. Chi-square test, Mann-Whitney U test, and Fisher’s exact test were used to assess the differences between the groups. A P-value < 0.05 was accepted as the level of significance.

Results

Forty-five patients with a mean age of 7.7 years were included in the study. There were 23 (51.1%) boys and 22 (48.9%) girls. All patients had a preoperative ASA physical status of 1 or 2. All patients underwent strabismus surgery, including 19 (42.2%) single-eye and 26 (57.8%) double-eye procedures. The patients were classified into two anesthesia induction groups: propofol alone (n=26) and ketofol (n=19). The two groups were similar in basic characteristics and surgical data (Table 1).

Table 1: Comparison of two groups in terms of basic patient characteristics and surgical data

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Propofol alone (n=26)</th>
<th>Ketofol (n=19)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>8.5 (3.9) (1-17)</td>
<td>6.5 (3.4) (2-14)</td>
<td>0.108</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>31.8 (14.8) (14-65)</td>
<td>23.7 (11.4) (11-60)</td>
<td>0.053</td>
</tr>
<tr>
<td>Gender (F/M)</td>
<td>15 (57.7%)/11 (42.3%)</td>
<td>7 (36.8%)/12 (63.2%)</td>
<td>0.231</td>
</tr>
<tr>
<td>ASA status (ASA I/ASA 2)</td>
<td>20 (76.9%)/6 (23.1%)</td>
<td>17 (89.5%)/2 (10.5%)</td>
<td>0.211</td>
</tr>
<tr>
<td>Laterality</td>
<td>Unilateral 13 (50%)</td>
<td>6 (31.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bilateral 13 (50%)</td>
<td>16 (84.8%)</td>
<td></td>
</tr>
<tr>
<td>Operated muscle</td>
<td>Rectal 11 (42.3%)</td>
<td>8 (42.1%)</td>
<td>0.493</td>
</tr>
<tr>
<td></td>
<td>Lateral rectus 8 (30.7%)</td>
<td>9 (47.4%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other 6 (23%)</td>
<td>2 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>Type of surgery</td>
<td>Recession 18 (69.2%)</td>
<td>16 (84.2%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Resection 6 (23%)</td>
<td>2 (10.5%)</td>
<td></td>
</tr>
<tr>
<td>Duration of procedure</td>
<td>36.7 (13.1) (15-60)</td>
<td>41.5 (13.5) (10-55)</td>
<td>0.192</td>
</tr>
</tbody>
</table>

Propofol alone group and in 5 (19.2) patients in the ketofol group. There were no significant differences were found (P=1.000).

IOP was measured at four points: at 1 minute following induction of anesthesia, at 3 minutes following insertion of LMA, and at the end of the surgery. All IOP values were between 5 and 25 mmHg. In both groups, the mean IOP values were between 10 and 13 mmHg at all four measurement times. When comparing the mean IOP values between the two groups, no significant differences were found (P>0.05) (Table 3).

Table 3: The comparison of IOP values between the groups

<table>
<thead>
<tr>
<th>IOP values (mmHg)</th>
<th>Propofol alone (n=26)</th>
<th>Ketofol (n=19)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP of right eye (baseline)</td>
<td>12.9 (3.5) (8-20)</td>
<td>13.6 (5.1) (8-25)</td>
<td>0.899</td>
</tr>
<tr>
<td>IOP of left eye (baseline)</td>
<td>12.1 (3.1) (6-17)</td>
<td>13.3 (4.4) (8-24)</td>
<td>0.494</td>
</tr>
<tr>
<td>IOP of right eye (1st min of induction)</td>
<td>11.1 (2.9) (8-18)</td>
<td>12.1 (5.6) (5-25)</td>
<td>0.945</td>
</tr>
<tr>
<td>IOP of left eye (1st min of induction)</td>
<td>10.7 (3.7) (5-24)</td>
<td>11.4 (4.5) (6-22)</td>
<td>0.676</td>
</tr>
<tr>
<td>IOP of right eye (3rd min of LMA insertion)</td>
<td>11.1 (3.5) (10-19)</td>
<td>10.7 (4.7) (5-25)</td>
<td>0.443</td>
</tr>
<tr>
<td>IOP of left eye (3rd min of LMA insertion)</td>
<td>10.4 (3.7) (5-21)</td>
<td>10.7 (3.9) (5-20)</td>
<td>0.905</td>
</tr>
<tr>
<td>IOP of right eye (end of the surgery)</td>
<td>11.1 (3.7) (5-21)</td>
<td>10.4 (5.5) (2-15)</td>
<td>0.187</td>
</tr>
<tr>
<td>IOP of left eye (end of the surgery)</td>
<td>10 (3.5) (6-19)</td>
<td>10.1 (4.1) (4-19)</td>
<td>0.990</td>
</tr>
</tbody>
</table>

Discussion

The present study showed that, compared with the use of propofol alone, the combination of ketamine and propofol did not cause any significant changes in IOP values in pediatric strabismus surgery. Moreover, the addition of ketamine to propofol reduced the frequency of OCR and provided a positive effect on basic hemodynamic parameters, although these differences were not statistically significant.

As is well known, keeping IOP within normal limits is of great importance in eye surgery, especially in pediatric cases. IOP can be affected by various factors such as tracheal intubation, MAP, hypercapnia, coughing, vomiting, and patient position on the operating table [12]. In fact, most anesthetic drugs can help to decrease IOP via mechanisms such as decreasing choroidal blood volume and the formation of aqueous humor [12,13]. On the other hand, there is a concern among anesthesiologists regarding the use of ketamine, especially in patients undergoing ophthalmic surgery, due to the general belief that this agent may increase IOP [10]. In daily practice, ketamine is considered a safe and reliable anesthetic agent, with limited cardiorespiratory suppression and few adverse outcomes. In addition, some previous studies have found that ketamine had no significant effect on IOP [14,15]. However, in a study conducted on 60 children with healthy eyes, the authors reported mild yet clinically important increases in IOP [1].

Although the criteria used to define normal IOP values vary between clinical studies, the largest work on this topic reported a mean value of 15.5 mmHg and a normal range of diurnal variations from 5 to 25 mmHg [16]. The baseline mean IOP value of 12–13 mmHg in our cohort was consistent with that value. It should be noted that mean IOP values at other times decreased according to the baseline mean IOP values in both the propofol alone group and the ketofol group. Statistically, the two groups were similar in terms of IOP values measured at the four time points during the procedure. These results are important because they demonstrate that ketofol anesthesia does not cause significant increases in IOP.
At this point, it is necessary to mention the doses of ketamine and propofol used in the ketofol protocol, as the primary goal of the present study was to obtain a smooth anesthesia induction with favorable hemodynamic parameters and to decrease adverse effects of both propofol and ketamine. It is known that cardiorespiratory suppression is related to the increased use of propofol, whereas insufficient doses may lead to difficult LMA insertion. As for ketamine, higher doses are associated with excessive secretions and inadequate suppression of airway reflexes. The doses of propofol and ketamine used in the ketofol protocol vary due to the type of procedure and anesthesia. Here, ketamine was used at the dose of 1.5 mg/kg since the study was conducted on patients under LMA anesthesia. In addition, we aimed to observe the effects of ketamine on IOP and hemodynamic parameters. Ketamine is a sympathomimetic and can theoretically elevate IOP as it causes an increase in HR and blood pressure. However, the present study showed that the combined use of ketamine and propofol at the mentioned doses did not affect IOP.

Hemodynamic indicators such as MAP and HR were found to be statistically similar between the ketofol and propofol alone groups, which is consistent with previous studies. In a study conducted by Yousef et al. [6], ketofol was found to improve hemodynamic stability compared to propofol in children. In another study, ketofol was found to be an alternative induction agent to propofol for LMA insertion in pediatric patients and to provide better hemodynamic parameters [9].

In the present study, another positive contribution of ketamine to hemodynamic stability was in terms of OCR occurrence. Although the difference was not statistically significant, the OCR rate was observed less in patients in the ketofol group. OCR is defined as at least a 20% decrease in HR or a new dysrhythmia after compression of eyeball or traction of extraocular muscles, and is often encountered during strabismus surgery, with a reported rate of up to 90% [17,18]. This complication is more often seen in children than in adults. Pediatric patients are also more susceptible to the dangerous effects of OCR, due to a higher dependence on HR to maintain cardiac output. In a study investigating the effect of four anesthetic regimens—propofol plus alfentanil, sevoflurane, ketamine plus midazolam, and halothane—on OCR during pediatric strabismus surgery, ketamine anesthesia was found to be associated with the least hemodynamic changes induced by OCR [19]. In another study conducted on patients undergoing strabismus surgery, it was shown that ketamine obviates OCR and prevents the unwanted effects of dysrhythmias [20].

Limitations
This study had several limitations. The fact that it was conducted in a single center may limit the generalizability of the results. The relatively small number of patient groups may also lead to difficulty in interpreting subgroup findings. However, the prospective design, the lack of any premedication that may affect the hemodynamic parameters and OCR, and the standardized IOP measurement may be considered the strengths of the study.

Conclusion
The findings demonstrated that, compared to propofol anesthesia, ketofol anesthesia provided similar results in terms of IOP values, occurrence of OCR, and basic hemodynamic parameters such as MAP and HR. Therefore, ketofol can be considered a safe induction agent in pediatric patients undergoing strabismus surgery with LMA anesthesia.

References

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