

The Effect of Sub-Tenon's Bupivacaine on Oculocardiac Reflex during Strabismus Surgery and Postoperative Pain: A Randomized Clinical Trial

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Abstract

Purpose: Oculocardiac reflex (OCR), defined as bradycardia induced by manipulation of extraocular muscles, is a serious complication during strabismus surgery for which prevention and proper management is required. In the present study, we investigated the efficacy of sub-Tenon injection of bupivacaine for prevention of OCR and postoperative pain.

Methods: A prospective randomized controlled clinical trial was conducted. Fifty patients who were candidates for strabismus surgery were randomized into case (sub-Tenon's bupivacaine injection) or control (normal saline injection) groups. Standard strabismus surgery was performed for all cases. Occurrence and severity of OCR (primary outcome) and postoperative pain (using the Visual Analog Scale) were compared between the two groups.

Results: Both incidence (32% vs. 100%; $P = 0.002$) and severity of OCR (mean heart rate decrease, 10.1 vs. 38.7 beats/minute; $P < 0.001$) were significantly lower in the study group compared to those in the control group. Postoperative pain scores were significantly lower in the case group than in the control group (mean score, 2.8 vs. 5.9 at 60 minutes after surgery; $P < 0.001$).

Conclusions: Sub-Tenon injection of bupivacaine as a local anesthetic can significantly prevent OCR and decrease the severity of bradycardia. This technique can also diminish postoperative pain in patients who underwent strabismus surgery.

Keywords: Bupivacaine; Oculocardiac Reflex; Pain; Strabismus

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INTRODUCTION

Strabismus surgery is one of the most common ophthalmic operations in children. It can have adverse

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effects during or after surgery. Bradycardia caused by oculocardiac reflex (OCR) is a frequent and serious adverse event during strabismus surgery in children. The reflex is triggered by the manipulation of the globe and extraocular muscles; it may cause bradycardia, arrhythmia, and even cardiac arrest. The afferent limb of this reflex is the ophthalmic division of the trigeminal nerve, from which fibers pass through the gasserian

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ganglion to the main sensory nucleus of the trigeminal nerve; the efferent pathway is the vagus nerve.^[1] OCR was first described by Aschner in 1908, who observed that application of pressure to the eyeball results in a decrease in heart rate. The incidence of this event has been varied due to different definitions. When it is defined as a greater than 10% decrease in heart rate by manipulation of the extraocular muscles, its reported incidence is up to 82%.^[1]

Several studies have been conducted to investigate the efficacy of different modalities of treatment in the prevention or alleviation of bradycardia due to OCR. The findings for these modalities have been conflicting. Anesthetic regimes and local anesthetics have been evaluated since they may influence the occurrence and magnitude of OCR, especially by influencing the afferent limb. Sevoflurane, desflurane, and ketamine have been found to decrease the occurrence of OCR and severity of bradycardia.^[2-5] Sub-Tenon anesthetic injections have also been investigated for their preventive effect on OCR in pediatric strabismus surgery.^[6-8] In 2005, Steib et al studied the efficacy of sub-Tenon injection of bupivacaine in pediatric strabismus surgery, and reported significant decrease in the incidence and severity of OCR, postoperative pain, and nausea/vomiting.^[7] The occurrence of OCR, defined as a decrease in heart rate greater than 20%, in their study was 11% in the bupivacaine group versus 56% in the control group.^[7] This study was repeated by Tuzcu et al in 2014, and they found no significant differences in the occurrence of OCR between saline and bupivacaine injected groups.^[8] In the present study, we primarily investigated the effects of sub-Tenon bupivacaine versus saline injection, combined with intravenous general anesthesia, in decreasing the occurrence and severity of OCR during strabismus surgery. The secondary endpoint was to evaluate the effects of sub-Tenon bupivacaine versus saline injection in prevention of postoperative pain in children undergoing strabismus surgery.

METHODS

Study Population

In this single center, prospective, double blind randomized controlled trial, we recruited 50 children aged 8–17 years with American Society of Anesthesiologists (ASA) physical status I–II who were scheduled for elective strabismus surgery in our hospital. Patients who fulfilled the following criteria were excluded: Patients with underlying heart disease; had ocular pathologies other than strabismus and paralytic, fibrotic, or restrictive strabismus diseases; required additional anesthetic agents for any reason; had learning disorders, developmental delays, or

communication disabilities; and required revision or second strabismus surgery.

Informed consent was obtained from the parents of all patients before enrollment. This study conformed to the tenets of the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of our university.

Randomizations and Masking

Patients randomly received sub-Tenon's injection of bupivacaine solution or sterile saline, which were previously prepared in similar vials. These were marked with codes that were not revealed to the surgeon and the study executor who evaluated pain and monitored the patient during the operation for measurement of heart rate. Randomization was performed using random number generators. The letters containing the type of injection for each patient were concealed within opaque envelopes, which were then opened at the time of surgical intervention.

Interventions

General anesthesia

For all patients, premedication was given as 0.02–0.03 mg/kg midazolam and 1–2 µg/kg fentanyl intravenously 3–5 minutes prior to induction of anesthesia. General anesthesia was induced with 5 mg/kg thiopental and 0.5 mg/kg atracurium and maintained by infusion of 100–150 µg/kg/minute propofol according to each patient's requirement. Patients were intubated with an endotracheal tube and ventilated at a tidal volume of 7 ml/kg at an age specified rate and 50% FiO₂. End-tidal CO₂ partial pressure was maintained between 35 and 40 mmHg during surgery. During the operation, patients were continuously monitored by electrocardiography, pulse oximetry, capnography, and blood pressure. At the end of the operation, maintenance of anesthesia was discontinued with antagonizing neuromuscular blockade. As soon as the patient was capable of spontaneous respiration, the endotracheal tube was removed and patient was transferred to the recovery section.

Surgical interventions

The sub-Tenon injections [0.1 ml of 0.5% of bupivacaine (Merck®, Lyon, France) or 0.1 ml of normal saline] were performed under general anesthesia just prior to surgery using a curved blunt 19-gauge cannula over the insertion of muscles. Surgical resection or recession of the medial or lateral rectus muscles were performed 5 minutes after sub-Tenon injection through the same conjunctival aperture used for injection. Surgical technique was similar for all patients (recess,

resect, or both) and all operations were performed by the same surgeon. If two muscles in one eye needed surgery, we studied only the first muscle.

Outcome Measures

The baseline heart rate was recorded from the real-time electrocardiography monitoring device just before sub-Tenon injections. Heart rate was monitored during manipulation of the rectus muscles and the lowest recorded heart rate was used for measurement. The incidence of OCR was regarded as the primary outcome measure and was defined as a greater than 10% decrease in the baseline heart rate during manipulation of the muscle. Considering a study power of 90% and a two-sided alpha level of 0.05, 23 patients were required in each group to detect a 50% decrease in the incidence of OCR. We enrolled 25 patients in each group to compensate for a possible 10% patient loss after enrollment due to surgical or anesthesia complications.

The magnitude of heart rate deceleration was calculated in all cases using the formula: *baseline heart rate – minimal recorded heart rate during manipulation*. Postoperative pain scores were assessed using the visual analog scale (VAS) in which the patient reports pain according to a 0–10 scale. A score of 10 is indicative of the most severe pain imaginable and zero represents no feeling of pain. Pain scores were recorded at 30 and 60 minutes, postoperatively. Patients with pain scores higher than 4 at 60 minutes received 10–15 mg/kg intravenous acetaminophen.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics software version 21 (SPSS Inc., Chicago, IL). The incidence of OCR was compared between groups using the Chi-square test. The magnitude of heart rate deceleration and the scores for postoperative pain were assessed using the independent samples *t*-test. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

The data of 50 patients (25 per group) were recorded and analyzed. The case and control groups were similar in age and sex distribution. The mean age was 12.5 (95% CI: 10.8–14.3) and 11.5 (95% CI: 10.1–13) years in the case and control groups, respectively ($P = 0.388$). In the case and control groups, 11 (44%) and 13 (52%) male patients were included, respectively ($P = 0.571$).

OCR occurred in eight patients (32%) in the case group and in all patients (100%) in the control group. Statistical analysis showed a statistically significant difference in the occurrence of OCR between groups ($P = 0.002$; Figure 1). The mean value of heart rate deceleration was 10.2 (95% CI: 7.9–12.4) and 38.7 (95% CI: 34.3–43.1) beats per

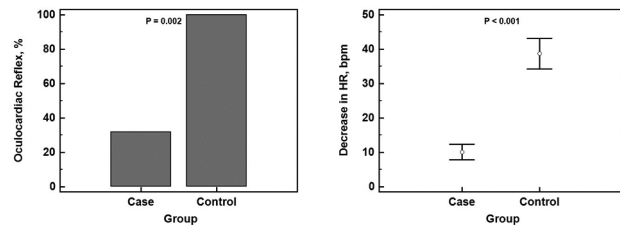


Figure 1. The comparative incidence and severity of oculocardiac reflex during strabismus surgery in patients who received sub-Tenon's bupivacaine injection versus those who received normal saline.

minute (bpm) in the case and control groups, respectively. These indicate the significant effect of sub-Tenon bupivacaine injection in decreasing the magnitude of heart rate deceleration ($P < 0.001$; Figure 1).

The mean postoperative pain scores at 30 minutes were 2.6 (95% CI: 1.8–3.4) in the case group and 4.9 (95% CI: 3.9–5.8) in the control group ($P < 0.001$). At 60 minutes postoperatively, the mean pain scores were 2.8 (95% CI: 2.1–3.5) and 5.9 (95% CI: 5.0–6.7) in the case and control groups, respectively ($P < 0.001$). Overall, the VAS scores were significantly lower in the case group than in the control group at both occasions [Figure 2].

DISCUSSION

The results of the present study on 50 children who underwent elective strabismus surgery demonstrated that sub-Tenon injection of bupivacaine as a local anesthetic could significantly prevent OCR and decrease the magnitude of bradycardia during surgery. This technique could also prevent postoperative pain in patients undergoing strabismus surgery.

Several anesthetic regimens, including retrobulbar and sub-Tenon injections of anesthetics, have been studied for decreasing OCR, which is an important and frequent complication during strabismus surgery. Although OCR may manifest as life threatening complications such as cardiac arrhythmias and hypotension, a safe and effective method to eliminate or reduce it is yet to be identified. Finding such a method is an important subject of research. General anesthetics have been compared for their efficacy in the prevention of OCR.^[2,5,6] In the study by Deb et al, peribulbar block was found to reduce the incidence of OCR.^[9] Compared to retrobulbar or peribulbar blocks, sub-Tenon anesthesia seems to offer some advantages in pediatric strabismus surgery. Sub-Tenon injection is less invasive because it could be performed through the same incision for the rest of the extraocular surgery. Cooperation of the patient is also less important than in retrobulbar or peribulbar injection, which requires full attention and cooperation of patient to avoid complications such as globe rupture and nerve injury. In addition, complications attributed

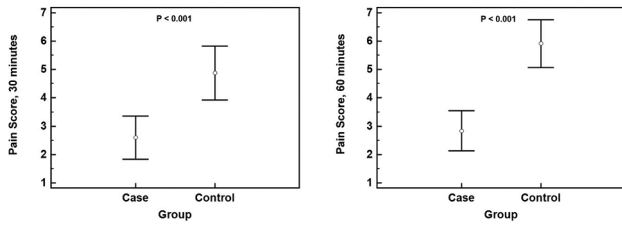


Figure 2. Comparison of the pain score results at 30 and 60 minutes after strabismus surgery between patients who received sub-Tenon's bupivacaine injection versus those who received normal saline.

to injection such as retrobulbar hemorrhage, globe rupture, muscle injury, and nerve injury are less common after sub-Tenon injection. Moreover, as demonstrated by Ripart et al, compared to peribulbar anesthesia, sub-Tenon anesthesia provides better akinesia, with a quicker onset and higher effectiveness.^[10]

In the study by Ghai et al, sub-Tenon block with a mixture of lidocaine and bupivacaine was found to be superior to intravenous fentanyl in inhibition of OCR during pediatric cataract surgery.^[11] These results were validated for strabismus surgery in 2014 by Ramachandran et al who reported that the incidence of OCR was significantly lower in the sub-Tenon block group than in the fentanyl group.^[12] However, in the study by Sethi et al on 63 infants who underwent cataract surgery, the incidence of OCR was comparable in both sub-Tenon block and intravenous fentanyl groups.^[13] Steib et al conducted a double blind study to evaluate the efficacy of sub-Tenon injection of bupivacaine versus saline injection before the beginning of surgery in prevention of OCR. The results showed a significantly lower occurrence of OCR and postoperative pain in the bupivacaine treated group.^[7] This study was repeated by Tuzcu et al in 2014 and they found no significant difference in the occurrence of OCR between normal saline and bupivacaine injected groups.^[8] Contrary to Tuzcu et al and in agreement with Steib et al, our results clearly demonstrated that compared to the normal saline group who received the same anesthetic regimen and underwent a similar procedure performed by the same surgeon, the sub-Tenon bupivacaine injected group had a significantly lower incidence of OCR.

For postoperative analgesia, our results demonstrated that compared to the normal saline group, postoperative pain scores were significantly lower in the bupivacaine treated group. This result is in agreement with many previous studies. Sheard et al in a pilot study and in another prospective, randomized controlled trial showed that a sub-Tenon's lidocaine injection was associated with a significant reduction in postoperative pain during all types of childhood strabismus surgery.^[14,15] Ghai et al reported that sub-Tenon block using lidocaine and bupivacaine was found superior to intravenous fentanyl

in inducing postoperative analgesia after pediatric cataract surgery.^[11] The same result was reported by Sethi et al regarding higher efficacy and safety of sub-Tenon block versus intravenous fentanyl in infants who underwent cataract surgery.^[13] Steib et al reported that sub-Tenon's block with bupivacaine decreased postoperative pain when compared to a saline injected control group.^[7] Tuzcu et al also reported that pain scores at 30 minutes after surgery and additional analgesic treatment needed during the postoperative period were significantly lower in the sub-Tenon bupivacaine group than in the control group.^[8] Contrary to these studies, in the study performed by Ates et al, there was no significant difference in terms of postoperative analgesia in the retrobulbar block or subconjunctival local anesthetic infiltration groups compared to the control group.^[16] This study was performed with only 10 patients in each group.^[16] Morris et al compared the postoperative pain scores in children who underwent strabismus surgery with preoperative sub-Tenon levobupivacaine versus controls. The pain score in the sub-Tenon levobupivacaine group was not lower than that in the control group. This study used levobupivacaine (not bupivacaine) and has some limitations that the authors have mentioned.^[17]

In conclusion, the results of the present study provide more robust evidence that a sub-Tenon block can significantly reduce the incidence of OCR during strabismus surgery. Compared to the control group, who received the same anesthetic regimen and underwent a similar procedure performed by the same surgeon, the sub-Tenon bupivacaine injected group had significantly less postoperative pain. This indicates that sub-Tenon block alone can safely and effectively reduce the incidence of OCR and the risk of further complications such as hypotension, bradycardia, and cardiac arrest.

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Conflicts of Interest

There are no conflicts of interest.

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