Original Article

Comparison of topical oxybuprocaine and intravenous fentanyl in pediatric strabismus surgery

ABSTRACT

Purpose: To compare the outcomes such as postoperative nausea/vomiting, analgesic requirements, and hospital stay following the use of topical oxybuprocaine hydrochloride 0.4% or intravenous (IV) fentanyl in children undergoing strabismus surgery.

Methods: This was a prospective cohort study. Children operated under general anesthesia for strabismus were given topical oxybuprocaine hydrochloride 0.4% (Group T) and IV fentanyl (Group F) before surgery. The episodes of nausea/vomiting, pain score, requirement of additional analgesia during postoperative period, and duration of hospital stay were compared in two groups.

Results: There were 47 children in Group T and 59 children in Group F. The median pain score in two groups were 2.38 (25% quartile; 2.0) and 3.00 (25% quartile; 3.00), respectively. The difference was significant (K W $P < 0.03$). The episodes of nausea/vomiting in two groups were in 2 and 6 children in Group T and Group F, respectively. The median hospital stay of children of Group T and Group F were 242 and 285 min, respectively. The difference was not statistically significant ($P = 0.22$).

Conclusions: Using intraoperative topical oxybuprocaine drops, one can achieve better analgesic outcomes and reduce risk of nausea and vomiting compared to intravenous opioid analgesics and therefore, the hospital stay could also be marginally reduced.

Key words: Analgesia; pain score; strabismus

Introduction

Strabismus correction in children is more often a "Day care surgery." To prevent postoperative pain, opioids such as fentanyl are used. However, they cause hangover, sedation, nausea and vomiting and thus may prolong stay in the hospital.[1] In contrast, with the use of oxybuprocaine topical drops, systemic side effects are rare. In previous reports, either two different local anesthetic drops/gel[2] or drops versus peribulbar block were assessed to evaluate postoperative analgesic efficacy and incidence of nausea and vomiting in pediatric strabismus surgery.[3,4] To the best of our knowledge, a comparison of oxybuprocaine 0.4% local anesthetic ophthalmic drops to the intravenous (IV) fentanyl in children undergoing strabismus surgery has not been undertaken.

We undertook a study to compare the outcomes such as postoperative nausea/vomiting, analgesic requirements, and hospital stay following the use of topical oxybuprocaine hydrochloride 0.4% or IV fentanyl in children undergoing strabismus surgery.

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Methods

This prospective randomized, double-blind study was conducted during February 2014 to November 2015 at a specialized ophthalmic hospital. Approval from Institutional Review Board was taken, and parental informed consent was obtained. The American Society of Anesthesiologists physical status of children was 1–II.

We assumed that the outcome variable of importance will be postoperative pain at 30 min after surgery. For a randomized control trial having one group of the patient operated under topical oxybuprocaine hydrochloride 0.4% (Group T) and other under IV fentanyl (Group F), we assumed that the acceptable level of pain score in Group F after 30 min of surgery will be in 50% of cases. While in Group T, it will be in 25% of patients only. The minimum required sample size was calculated for each group to achieve 95% confidence interval (CI), 80% power of the study with 1:1 ratio of patients in Group T and Group F.

All children planned for elective unilateral strabismus surgery for correction of 1–2 muscles were selected. Children with a history of previous strabismus surgery, presence of any other anterior segment pathology, previous intraocular surgery, neurological disorders, which might affect the anxiety level and pain threshold and any known allergy to opioid medications or local anesthetic drops were excluded from this study.

Children were randomly assigned to two groups by computer-generated tables either in Group T (topical drops-oxybuprocaine) or Group F (IV injection-fentanyl). The children of both groups received midazolam premedication (0.4 mg per kg up to maximum total dose of 10 mg with paracetamol 15 mg/kg orally 1 h before surgery.

General anesthesia was induced with sevoflurane inhalation mixed in 100% oxygen. IV line was maintained with 5% dextrose in 1/4th normal saline. The usual standard monitoring was applied to all patients. The airway was maintained with a suitable sized laryngeal mask airway to deliver 40% oxygen in air with sevoflurane concentration to achieve minimum alveolar concentration value between 1.5% and 2% depending on the hemodynamic responses to surgical intervention. Nitrous oxide was omitted. Each child received glycopyrrolate 2 mg/kg, ondansetron 0.15 mg/kg, and dexamethasone 0.2 mg/kg during surgery according to standard practice at our institute. Group F children received IV dose of fentanyl 2 mg/kg body weight, 5 min before starting the surgical procedure. For the Group T, topical drops of oxybuprocaine hydrochloride 0.4% were applied over bulbar/palpebral conjunctiva 5 min before starting the procedure and later, over the exposed rectus or superior/inferior oblique muscles after 15 min and at the end of surgery before final dressing.

The intraoperative pain was measured by the evidence of sympathetic stimulation secondary to painful stimuli. Heart rate or blood pressure more than 25% increase from baseline values were considered as a sign of intraoperative pain. In Group T, any such event was managed with supplemental topical oxybuprocaine drops while in Group F supplemental IV fentanyl 0.005 mg/kg was given.

All surgeries were performed by one consultant surgeon (member, pediatric division). All postoperative data were recorded by a research assistant who was masked to the type of the drug used during surgery.

Intraoperative data were collected for heart rate, noninvasive blood pressure, need for supplemental topical or IV analgesics, signs of sympathetic stimulation such as lacrimation, salivation, upward rolling of the eyeballs, and duration of surgery (measured from eyelid retractor application to its removal). Any surgical procedure which extended beyond 90 min were excluded from the study group. At the end of surgery, Surgeon satisfaction for the ease of surgical procedure in relation to quality of analgesia was also obtained with score 0 as not satisfied to score 10 as maximum satisfaction.

In postoperative period to assess pain, an effective communication was maintained between the child whenever feasible, their family, and the multidisciplinary team members. Face pain rating scale was used with the assistance of the parents at 1, 2, 3, and 4 h after surgery.[5-7] In addition, 0–10 numeric pain rating scale was also used by the observer.[8] According to the good practice in postoperative and procedural pain management guidelines from the association of pediatric anesthetists of Great Britain and Ireland, an observational measure was used in conjunction with self-report by the young children to increase the reliability and validity of pain intensity[9] Any episode of nausea/vomiting and the time of discharge were recorded for each group. Any additional treatment of vomiting or pain was also recorded.

The average pain scores in both groups were compared with an unpaired *t*-test. A Chi-square test was used to compare the proportions of children requiring additional intra- and post-operative analgesia. Statistical Package for Social Studies (SPSS 22) (IBM Corp., New York, NY, USA) was used for statistical analysis.

Results

In our study, we included 47 children in Group T and 59 in Group F. There were 22 (46.8%) boys and 25 (53.2%) girls in Group T. There were 23 (39%) boys and 36 (61%) girls in Group F. The gender difference in two groups was not statistically significant ($P = 0.4$). The median age of children in Group T was 84 months (25% quartile 59). Whereas children of Group F group had median age of 60 months (25% quartile 60 months). The demography of children of two groups was not significantly different.

The postoperative pain score 20 min after surgery was evaluated and compared in two groups [Table 1 and Figure 1]. The median pain score in Group T was 2.38 (25% quartile; 2.0) and in Grup F it was 3.00 (25% quartile 3.00). The difference in pain score was significantly more in Group F. (K W $P < 0.03$). Four (8.5%) children in Group T and 9 (15%) in Group F were given additional analgesic medication postoperatively.

The episodes of nausea and vomiting were 2 and 6 children in Group T and Group F, respectively.

Two children of Group T and three children of Group F having residence at far places had to stay overnight and were excluded from the calculation of recovery room stay. The median hospital stay in Group T and Group F were 242 (25% quartile 125) and 285 (25% quartile 200) min, respectively. The difference was not statistically significant ($P = 0.22$).

Table 1: Maximum pain score after strabismus surgery in children given analgesia by topical Oxybuprocaine Hydrochloride compared to Intravenous Fentanyl

Variables	Topical Oxybuprocaine 0.4% (n=47)		Intravenous Fentanyl (n=59)	
	Number	Percentage	Number	Percentage
No-mild (0-3)	45	95.7	48	81.3
Moderate (4-6)	2	4.3	11	18.7
Severe (7-10)	0	0.0	0	0.0

Validation: Relative Risk=3.1 95% Confidence interval 1.1-24.5, P=0.03

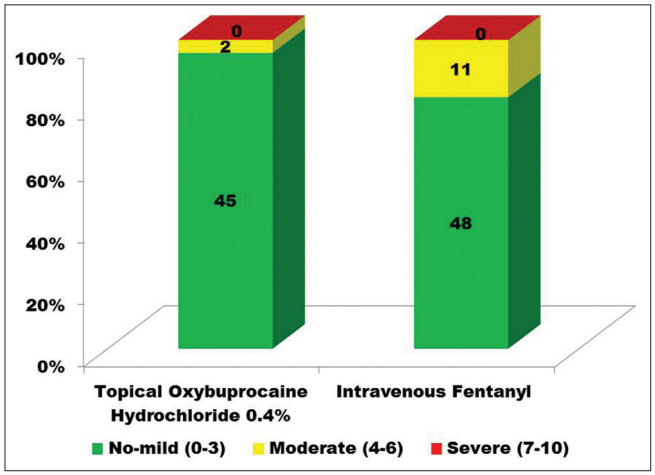

Figure 1: Comparison of pain score of children operated for strabismus using topical oxybuprocaine hydrochloride 0.4% or intravenous fentanyl. X axis: Children of two groups of analgesia method. Y axis: Percentage proportions of children in three grades of pain score

Discussion

Our results demonstrate that topical use of 0.4% oxybuprocaine is comparable to IV fentanyl administration to achieve desirable analgesia during the intra- and post-operative period and help in early discharge from hospital.

Most of the strabismus surgeries are done under day care setting. Improved pain management is utmost important to avoid postoperative unwanted events specially in children after general anesthesia. The use of opioid analgesic during strabismus surgery may pose a higher risk of postoperative nausea and vomiting (PONV) along with hangover sedation leading to delay in hospital discharge.[10] Fentanyl acts on opioid receptors in the brain and spinal cord producing an analgesic effect while its adverse effects lead to respiratory depression, drowsiness, lightheadedness, weakness, fatigue, nausea and vomiting after surgery. It has a relatively shorter duration of action (30–60 min) with up to 4 h of elimination half–life.[11] Therefore, fentanyl is considered a suitable analgesic agent for day care patients. In our study, six children required additional doses of fentanyl. It is known that shorter duration of action for fentanyl may be secondary to its redistribution effect, and additional doses may be needed after 1 h of initial drug administration. This may result in drug accumulation due to high lipophilicity. Clinical effects may last longer until the drug is metabolized.[12] Therefore, fentanyl should be used at the beginning of surgery, and the supplemental dose is better to be avoided.

Oxybuprocaine (benoxinate), is an ester-type preservative-free local anesthetic. Anesthetic activity is ten times that of cocaine and twice that of tetracaine (amethocaine). Surface anesthesia occurs in approximately 1 min with 0.4% intraocular solution, and peak response is between 1 and 15 min. Anesthesia persists for about 20–30 min, with full corneal sensitivity taking up to 40 min or more to return. The sensation of pain is locally and reversibly reduced, along with temperature and pressure sensitivity.[13] In our study, the use of topical oxybuprocaine hydrochloride 0.4% provided similar analgesic efficacy as with IV fentanyl with improved margin of safety to patients undergoing strabismus surgery. Systemic absorption may be reduced by compressing the lacrimal sac at the medial canthus for a minute during and following the instillation of the drops. We used three doses of topical oxybuprocaine drops in each patient as per our study protocol. A systematic review found no reports of serious complications.[14]

Strabismus surgery in children has been identified as an independent risk factor for PONV.[15] We maintained standard antiemetic protocol in both groups using ondansetron and dexamethasone. The incidence of PONV is variable in children. The combination of ondansetron 0.1 mg/kg IV and dexamethasone 0.1–0.2 mg/kg IV have been proven effective in reduction[16] of this complication. It is known that there is increase in PONV risk at the age of 3 years, with a 0.2–0.8% annual increase in risk thereafter.[17] The incidence of vomiting is 2.5-fold higher when surgery is performed on both eyes compared with one eye.[1] It is well known that the use of intraoperative opioids cause PONV. Fentanyl is commonly used for strabismus day care surgery but causes PONV.[18,19] This matched with our study findings. Opioid should be avoided in strabismus surgeries due to its effect on chemoreceptor trigger zone, vestibular center, and gastric emptying time.[20] Oh *et al*.[21] reported 17.9% incidence of PONV with sevoflurane anesthesia using remifentanil as opioid analgesic. Our results are consistent with the study by Wennström and Reinsfelt[10] where IV morphine administration was associated with more postoperative nausea or vomiting in comparison to rectally administered diclofenac.

The use of topical anesthesia in strabismus surgery has been found to be useful.[22] Anninger *et al*.[23] used 1% of tetraciane topical eye drops before and after surgery with improvement in postoperative strabismus surgery pain. The use of topical 1% tetracaine has also provided significantly better postoperative analgesia after strabismus surgery,[24,25]. el Kasaby[26] used subconjunctival bupivacaine following strabismus surgery with improvement in postoperative comfort and early discharge. Sheard *et al*.[27] administered 2% of lidocaine in subtenon space after strabismus surgery in children and noted a significant reduction in postoperative pain during the 1st h. In contrary to above studies, no improvement in postoperative pain score was noted after intraoperative administration of topical 0.5% ketorolac or 0.5% tetracaine when compared to placebo in children undergoing strabismus surgery.[28,29]

The operated eye is usually not dressed after strabismus surgery. The use of long-acting local anesthetic may result in trauma to the operated eye if the eye is numb and the child could scratch it. Oxybuprocaine 0.4% local anesthetic drops have a relatively shorter duration of action. The corneal sensitivity returns to normal after about an hour. We did not encounter any physical injury of the operated eye by the child in the postoperative period. However, the review of literature is revealing that use of shorter duration of topical anesthetic drops does not cause postsurgical complications following pediatric ophthalmic surgery.[23]

In our study, topical oxybuprocaine hydrochloride 0.4% produced local preemptive analgesia in the operating eye before surgical incision, and later, additional supplemental drops over surgical site abolished further analgesic requirement for intra- and post-operative period without any hangover sedation or episodes of significant nausea and vomiting as occurs with IV fentanyl administration. This strategy was beneficial in avoiding PONV and delays in hospital discharge.

Conclusions

The pain of strabismus surgery can be easily managed using topical local anesthetic drops before surgical incision, intraoperatively over the exposed muscles, and before final dressing. Intraoperative opioids may be avoided to decrease the incidence of postoperative nausea vomiting and ensure an early discharge from day care unit. Any subsequent postoperative pain can be satisfactorily controlled using regular doses of paracetamol and a nonsteroidal anti-inflammatory analgesic. Early discharge reduces the hospital cost and increases patients' satisfaction level.

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Conflicts of interest

There are no conflicts of interest.

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