Sub-Tenon’s lidocaine injection improves emergence agitation after general anaesthesia in paediatric ocular surgery

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Abstract

Objective: This study aimed to evaluate the effect of a sub-Tenon’s lidocaine injection on emergence agitation in children receiving sevoflurane or halothane anaesthesia for strabismus surgery.

Design: A prospective, randomised study.

Setting: The study setting included a hospital where a surgical team performed strabismus surgery.

Subjects: Our study enrolled 520 children, aged 4-12 years, who were scheduled for strabismus surgery. Patients were randomised into four groups. Group S/S received sevoflurane and an isotonic saline injection, group S/L received sevoflurane and a lidocaine injection, group H/S received halothane anaesthesia and an isotonic saline injection, and group H/L received halothane anaesthesia and a lidocaine injection. Anaesthesia was maintained with sevoflurane (groups S/S and S/L) or halothane (groups H/S and H/L), and at the end of surgery, the surgeon injected 1 ml of isotonic saline (groups S/S and H/S) and topical proxymethocaine 0.5% or 2% lidocaine (groups S/L and H/L) and a topical placebo (balanced salt solution) into the sub-Tenon’s space. Emergence behaviour was assessed in the post-anaesthesia care unit using a five-point scale (1: asleep, 2: awake and calm, 3: irritable behaviour or consolable crying, 4: inconsolable crying, and 5: severe restlessness). We defined a score of 4 or 5 as emergence agitation. The incidence of emergence agitation was analysed using the \( \chi^2 \) test and Fisher’s exact test.

Results: The incidence of emergence agitation in groups S/L and H/L was significantly lower than that in groups S/S and H/S (p-value = 0.022, 0.038). The lidocaine-injected group showed a significantly lower occurrence of emergence agitation (10.4%) than the saline-injected group (27.2%, p-value = 0.002). Emergence agitation was significantly higher following sevoflurane (25%) than halothane anaesthesia (13.1%, p-value = 0.046).

Conclusion: Emergence agitation was significantly reduced by a sub-Tenon’s lidocaine injection, regardless of the modality of anaesthesia used.

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Introduction

For decades, halothane was the predominant anaesthetic that was given to children. With recognition of postoperative pain management in children and the increased use of analgesics, the incidence of emergence agitation was attenuated. However, with the introduction of the short-acting, volatile anaesthetics (sevoflurane and desflurane) into clinical practice, the problem of emergence delirium resurfaced.¹ Some studies suggest that emergence agitation occurs more often after sevoflurane than halothane anaesthesia,¹ ⁴ while others have found no difference between the two anaesthetics.⁵ ⁷

In recent years, numerous cases of emergence agitation and delirium after sevoflurane anaesthesia have been reported,³ ⁶ in which the incidence, associated factors and efficacy of treatment in relation to emergence agitation has been described.³ ⁸ ¹² However, a young age seems to be the
most important factor in various modalities that have been used to treat emergence agitation.\textsuperscript{8,13}

We focused on paediatric ophthalmic patients who commonly display maladaptive behaviour on emergence from anaesthesia in the post-anaesthesia care unit.\textsuperscript{14} with the assumption that postoperative pain and patient characteristics (age and sex) might be the contributory factors. Recently, several investigators reported that an intraoperative local anaesthetic injection into the sub-Tenon's space was associated with a significant reduction in postoperative pain after paediatric strabismus surgery.\textsuperscript{8,15,16}

The purpose of our study was to determine the effect of a sub-Tenon's lidocaine injection on emergence agitation in children who had received sevoflurane or halothane anaesthesia for strabismus surgery.

**Method**

After obtaining approval from the ethics and research committee of the department of anaesthesia and written informed consent from the parents of the study participants, this prospective randomised controlled study was conducted in the ophthalmic surgery department of our university hospital. A total of 520 American Society of Anesthesiologists status I and II boys and girls, ranging in age from 4-12 years, and weighing 13-30 kg, were recruited over a span of 36 months (January 2009 to January 2012). All patients were scheduled for extraocular muscle surgery for strabismus. Children in whom intubation was expected to be difficult, and those with significant cardiac, respiratory, renal, hepatic or neurological disorders, were excluded from the study. All patients fasted for 6-8 hours. Procedures were performed in the early morning after premedication with midazolam 0.5 mg/kg orally ~ 30 minutes before induction, and atropine 0.01 mg/kg intravenously immediately before induction. Children were continuously monitored in the operating room by electrocardiography and pulse oximetry (oxygen saturation), and for blood pressure and end-tidal carbon dioxide. An intravenous cannula was placed. A local anaesthetic solution or isotonic saline was prepared by an anaesthetic technician. The person who performed the injections was blinded to which solution he or she was injecting. All the syringes or eyedrop bottles were identical and contained similar volumes to the test and placebo solutions.

Anaesthetic induction was carried out with propofol (2-2.5 mg/kg) for all children and tracheal intubation with an appropriately sized uncuffed tube was facilitated with atracurium (0.5 mg/kg). Children were assigned to four groups using a computer-derived randomisation list. Group S/S received sevoflurane and an isotonic saline injection and topical proxymethacaine 0.5% as postoperative analgesia. Group S/L received sevoflurane (3-8%) and a lidocaine injection and topical placebo (balanced salt solution). Group H/S received halothane anaesthesia with an isotonic saline injection and topical proxymethacaine 0.5%. Group H/L received halothane anaesthesia (1-5%) and a lidocaine injection and topical placebo (balanced salt solution).

Anaesthesia induction and maintenance were performed with sevoflurane or halothane using a Datum Sevotec\textsuperscript{®} or an Ohmeda Flutec-3\textsuperscript{®} vaporiser. The dose of sevoflurane or halothane was adjusted to maintain heart rate and blood pressure within 20% of baseline values. Controlled ventilation was selected to maintain end-tidal CO\textsubscript{2} values between 30 and 35 mmHg. Immediately prior to conjunctival closure, the surgeon slowly injected 1 ml of a coded solution (isotonic saline or 2% lidocaine) into the sub-Tenon’s space. The sub-Tenon’s block was performed using a 19G metal cannula in the inferonasal quadrant, as described by Stevens.\textsuperscript{17} Following test aspiration, 1 ml of local anaesthetic solution or isotonic saline was injected slowly. Manual compression was performed. Topical randomised solution was applied to produce anaesthesia for conjunctiva and cornea by administering two to three drops of proxymetacaine 0.5% or topical placebo (a balanced salt solution). Anaesthetic administration was discontinued at the end of surgery and the trachea was extubated when the patient resumed adequate spontaneous breathing and a gag reflex. The patient was then transferred to the post-anaesthesia care unit.

On arrival at the post-anaesthesia care unit, two trained observers, blinded to the patient’s treatment group, assessed and rated his or her emergence behaviour using the five-point scoring system for emergence delirium described by Cole et al (1: asleep, 2: awake and calm, 3: irritable behaviour or consolable crying, 4: inconsolable crying and 5: severe restlessness).\textsuperscript{13} Scores were recorded on arrival in the post-anaesthesia care unit and at 15-minute intervals for the first 45 minutes. If delirium was continuous or severe, propofol (1-2 mg/kg) was administered intravenously and antiemetics were prescribed for severe nausea and vomiting. Children were discharged from the post-anaesthesia care unit when they met the discharge criteria, including stable vital signs, being fully awake, oxygen saturation > 95% of room air and the absence of vomiting and agitation.

For statistical purposes, children with an agitation score of 4 or 5 were classified as agitated. The primary end-point of the study was the presence of emergence delirium, as defined by an emergence agitation score of 4 or higher. A group size of 520 was chosen, based on the assumption that the incidence of emergence agitation in the sevoflurane group would be 30%\textsuperscript{13} and that the incidence of emergence agitation in the group receiving pain control would be 10-15%, with an \( \alpha \) of 0.05 and a power of 0.8.
Data were compared using analysis of variance, and continuous data, such as age, weight, the time interval from discontinuation of the anaesthetic to arrival in the post-anaesthesia care unit, and duration of anaesthesia and surgery, were presented as mean ± standard deviation. Data were analysed using SPSS® version 14.0 (SPSS, Chicago, Illinois, USA). P-values less than 0.05 were considered to be statistically significant. The incidence of emergence agitation in the groups was compared using the \( \chi^2 \) test and Fisher's exact test, as appropriate. Kappa statistics assessed interobserver reliability and chance-adjusted percentage agreement was calculated.

**Results**

Initially, 520 children were enrolled in the study. Final analyses of emergence behaviour included 500 children. Twenty (10 from the SS group and 10 from the SL group) were excluded in the preoperative holding area or during induction of anaesthesia. Children who became agitated with intense preanaesthetic anxiety or crying were also excluded from the study because of the higher correlation between preoperative anxiety and the development of adverse postoperative phenomena. Enrolment data are summarised in Figure 1. There were no differences between the groups for age, sex, weight, time from discontinuation of anaesthetic administration to arrival in the post-anaesthesia care unit and duration of anaesthesia or operation (Table I).

Of the 500 analysed children, 94 developed emergence agitation. The incidence was 35% in the S/S group, 15% in the S/L group, 20% in the H/S group and 6.2% in the H/L group. There was significantly lower emergence agitation in the S/L and H/L groups, compared with the S/S and H/S groups (\( p \)-value = 0.022 and \( p \)-value = 0.038, respectively). However, there were no significant differences between the S/S and H/S groups, or between the S/L and H/L groups (\( p \)-value = 0.144, 0.212 respectively) (Table II).

Two thousand observations were made in 500 children. A score of 4 or 5 for agitation was recorded in 126 of 2 000 observations (20/480 in the S/S group, 30/480 in the S/L group, 36/520 in the H/S group and 8/520 in the H/L group) in 94 different children. Sixty-eight of the 94 agitated children (72.3%) developed emergence agitation within 15 minutes of arrival in the post-anaesthesia care unit. Eighty-six of the 126 episodes (68.2%) were observed within 15 minutes (46 in the S/S group, 20 in the S/L group, 12 in the H/S group and eight in the H/L group). The other 40 episodes (16 in the S/S group and 24 in the H/S group) were observed at a later stage. In the groups that

![Flow diagram of participant progress through the phases of a randomised trial](image-url)
Received sevoflurane anaesthesia (p-value = 0.017), and in the combined H/S and H/L group that received halothane anaesthesia (p-value = 0.004) (Table IV).

Most of the emergence agitation tended to be relapsing in nature, rather than continuous. We administered a sedative in cases of continuous, severe emergence agitation. Twenty-six (14 in the S/S group, two in the S/L group, 10 in the H/S group and no patients in the H/L group) of the 94 agitated children required pharmacological intervention for emergence agitation. In the other 68 children, the agitation episodes were self-limiting and did not require pharmacological intervention. No adverse effects were associated with a sub-Tenon’s injection, except mild petechia of the lower eyelid. Petechia was observed in 9.2% of the children. There was no difference among the groups.

### Discussion

The aim of the present study was to estimate the effect of a sub-Tenon’s lidocaine injection on emergence agitation in children who had received sevoflurane or halothane anaesthesia for strabismus surgery. In our study, the occurrence of emergence agitation with sevoflurane anaesthesia (the S/S and S/L groups) was more frequent than that with halothane anaesthesia (the H/S and H/L groups). However, there was no significant difference between the S/S and H/S groups, and the S/L and H/L groups, suggesting that the analgesia provided by the lidocaine block reduced the incidence of emergence agitation regardless of the inhalation agent used. A study by Voepel-Lewis et al in 2003 showed that 96 of 521 children (18%) experienced emergence agitation and that several factors were found to be associated with this: age, previous surgery, adaptability, ophthalmology and otolaryngology procedures, sevoflurane, isoflurane, sevoflurane/isofoflurane, analgesics and time to awakening.

Sevoflurane is associated with emergence agitation. Occurrence rates range from 10-80%.2,6,14 Emergence agitation is less frequent with halothane anaesthesia.6,7

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**Table II: Incidence of emergence agitation**

<table>
<thead>
<tr>
<th></th>
<th>S/S group (n = 120)</th>
<th>S/L group (n = 120)</th>
<th>H/S group (n = 130)</th>
<th>H/L group (n = 130)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 6 years</td>
<td>20 (70%)</td>
<td>6 (78%)</td>
<td>10 (88%)</td>
<td>2 (84%)</td>
</tr>
<tr>
<td>≤ 6 years</td>
<td>22 (50%)</td>
<td>12 (42%)</td>
<td>16 (42%)</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.022</td>
<td>0.144</td>
<td>0.038</td>
<td>0.212</td>
</tr>
<tr>
<td>Total</td>
<td>42 (35%)</td>
<td>18 (15%)</td>
<td>26 (20%)</td>
<td>8 (6.2%)</td>
</tr>
</tbody>
</table>

Values are numbers of patients.

*p-value = 0.022 vs. S/S group, **p-value = 0.038 vs. H/S group
H/L group: Halothane anaesthesia with a lidocaine injection and topical saline
H/S group: Halothane anaesthesia with a saline injection and a topical local anaesthetic
S/L group: Sevoflurane anaesthesia with a sub-Tenon’s lidocaine injection and topical saline
S/S group: Sevoflurane anaesthesia with a saline injection and a topical local anaesthetic

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**Table III: Occurrence of emergence agitation over time (postoperative)**

<table>
<thead>
<tr>
<th></th>
<th>S/S group (n = 120)</th>
<th>S/L group (n = 120)</th>
<th>H/S group (n = 120)</th>
<th>H/L group (n = 120)</th>
</tr>
</thead>
<tbody>
<tr>
<td>On arrival</td>
<td>54 (28.3%)</td>
<td>18 (15%)</td>
<td>4 (3.1%)</td>
<td>6 (4.6%)</td>
</tr>
<tr>
<td>≤ 15 minutes</td>
<td>12 (10%)</td>
<td>2 (17.6%)</td>
<td>8 (6.2%)</td>
<td>2 (1.5%)</td>
</tr>
<tr>
<td>≤ 20 minutes</td>
<td>8 (6.7%)</td>
<td>0</td>
<td>12 (9.2%)</td>
<td>0</td>
</tr>
<tr>
<td>≤ 45 minutes</td>
<td>8 (6.7%)</td>
<td>0</td>
<td>12 (9.2%)</td>
<td>0</td>
</tr>
<tr>
<td>p-value</td>
<td>0.217</td>
<td>0.031</td>
<td>0.012</td>
<td>0.087</td>
</tr>
<tr>
<td>Total</td>
<td>62 (50%)</td>
<td>40 (48%)</td>
<td>36 (52%)</td>
<td>8 (520)</td>
</tr>
</tbody>
</table>

Values are numbers of patients except for the bottom line, which expresses episodes/periods
H/L group: Halothane anaesthesia with a lidocaine injection and topical saline
H/S group: Halothane anaesthesia with a saline injection and a topical local anaesthetic
S/L group: Sevoflurane anaesthesia with a sub-Tenon’s lidocaine injection and topical saline
S/S group: Sevoflurane anaesthesia with a saline injection

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**Table IV: Incidence of emergence agitation in the combined groups**

<table>
<thead>
<tr>
<th></th>
<th>S/S and H/S group (n = 250)</th>
<th>S/S and H/L group (n = 250)</th>
<th>S/S and S/L group (n = 240)</th>
<th>H/S and H/L group (n = 260)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 6 years</td>
<td>30/158</td>
<td>6/162</td>
<td>26/148</td>
<td>12/172</td>
</tr>
<tr>
<td>≤ 6 years</td>
<td>38/92</td>
<td>18/88</td>
<td>34/92</td>
<td>22/88</td>
</tr>
<tr>
<td>p-value</td>
<td>0.007</td>
<td>0.007</td>
<td>0.017</td>
<td>0.004</td>
</tr>
<tr>
<td>Total</td>
<td>68 (27.2%)</td>
<td>26 (10.4%)</td>
<td>60 (25%)</td>
<td>34 (13%)</td>
</tr>
</tbody>
</table>

Values are number of patients

*: p-value = 0.001 vs. S/S-HS group, **: p-value = 0.023 vs. S/S-SL group
H/S-H/L group: Halothane anaesthesia with an isotonic saline or a lidocaine injection
S/L-H/L group: Sevoflurane or halothane anaesthesia with a lidocaine injection
S/S-H/S group: Sevoflurane or halothane anaesthesia with an isotonic saline injection
S/S-S/L group: Sevoflurane anaesthesia with an isotonic saline or a lidocaine injection

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The mean age of agitated children was 74.46 months (6.2 years). Emergence agitation occurred more frequently in children under 6.2 years of age in all groups. However, the difference was only significant in the H/S group (p-value = 0.019) (Table II). In the combined S/S-H/S group that did not receive a lidocaine injection, children who were younger than 6.2 years of age showed more frequent emergence agitation (41.3%) than children who were older than 6.2 years (18.9%, p-value = 0.007). In the group that was injected with lidocaine (the S/L and H/L groups), 20.4% of the children who were younger than 6.2 years of age showed emergence agitation. This was a significantly higher rate compared to that of the children who were older than 6.2 years (4.9%, p-value = 0.007). Similarly, there were significant differences in the incidence of emergence agitation between children who were younger than 6.2 years and those who were older than 6.2 years in the combined S/S and S/L group that received sevoflurane anaesthesia (p-value = 0.017), and in the combined H/S and H/L group that received halothane anaesthesia (p-value = 0.004) (Table IV).
However, we did not observe this difference in our study. We think such disparity is owing to the paucity of data, or the fact that data were collected every 15 minutes, rather than every five minutes, during recovery.

Although some authors suggest that emergence agitation occurs despite adequate pain relief,18 or even in the absence of any painful stimulus,8,24 pain should be regarded as a major contributing factor. In preschool-aged children, behaviour that is associated with emergence agitation is often clinically indistinguishable from pain. Other studies have reported a significant reduction in postoperative pain following a sub-Tenon’s local anaesthetic injection.15,16 The oculocardiac reflex and postoperative nausea and vomiting are also reduced in children undergoing strabismus surgery.16 Sub-Tenon’s anaesthesia has become a popular technique for infiltrative anaesthesia in adult ophthalmic surgery8,18 and for adequate postoperative analgesia.20

We designed this study to determine whether a sub-Tenon’s lidocaine injection reduced the incidence of emergence agitation after paediatric general anaesthesia. Although the Pediatric Anaesthesia Emergence Delirium (PAED) scale has proved to be useful and reliable,21 certain limitations have been identified. Bajwa et al22 compared the PAED, Watcha, and Cravero scales in assessing the presence of emergence delirium in children. They reported that all three scales correlated reasonably well with each other, but displayed individual limitations in their potential to identify emergence delirium. They also showed that the Watcha scale was a simpler tool to use in clinical practice and might have a higher overall sensitivity and specificity than the other scales.8,22

We used a five-point scoring scale (described by Cole et al)8 because we thought that it was the most expedient and practical scale, especially in the early postoperative period. It is clear that our observations indicated more quantitative than qualitative estimates of emergence agitation. In our study, most episodes of emergence agitation lasted no more than a minute and agitation rarely recurred after stabilisation. Moreover, medication for emergence agitation was based on clinical findings. Although quantification of agitation was not seriously considered in our study, this will be addressed in future research.

Usually, emergence agitation is a self-limiting phenomenon and the incidence is the greatest during the first 45 minutes after anaesthesia.8,13 In our study, 72.3% of the agitated patients showed emergence agitation within 15 minutes of arrival in the post-anaesthesia care unit. Moreover, none of the group that received a sub-Tenon’s lidocaine injection were agitated 15 minutes after arrival. Based on this result and Sae et al’s9 research results, we assume that the cause of early-stage emergence agitation is likely to be a combination of variables, including pain and some other factors. However, when emergence agitation occurs after 15 minutes, pain is the primary relevant factor. Other contributing factors may relate to metabolic disturbances, bladder distension, hypoxaemia, pre-existing psychosocial pathology, physiological abnormalities (double vision), rapid emergence, a hostile or unfamiliar environment, low adaptability, preoperative anxiety, an increase in the use of specific inhalational agents and residual drug effects.9,23 This hypothesis warrants further evaluation.

Negative behavioural changes following sevoflurane anaesthesia occur more frequently with decreasing age and the incidence peaks in preschool-aged patients.8,24 Our results agreed with those of a study by Seo et al as we divided the patient group into children who were younger than, and who were older than, 6.2 years of age, based on the mean age of agitated children. Unexpectedly, no statistically significant differences were found, despite the fact that emergence agitation occurred in only one of 84 children who were older than 6.2 years of age, compared to three of 46 children who were younger than 6.2 years of age in the H/L group. We suspected that such a statistical result was owing to the paucity of data, so we regrouped the patients into two combined groups based on the use of lidocaine or saline (the S/S and H/S and the S/L and H/L groups) and the modality of anaesthesia (the S/S and S/L and the H/S and H/L groups). We found that the incidence of emergence agitation was significantly higher in children who were younger than 6.2 years of age in all the combined groups.

In summary, the frequency of emergence agitation is significantly reduced by a sub-Tenon’s lidocaine injection, regardless of the modality of anaesthesia used. Additionally, our results agree with those of other investigators who found that emergence agitation was significantly higher in younger children and that emergence agitation tended to decrease with time after strabismus surgery in the children who received a sub-Tenon’s lidocaine injection.

References