SUBTENON BUPIVACAINE INJECTION FOR POSTOPERATIVE PAIN RELIEF FOLLOWING PEDIATRIC STRABISMUS SURGERY: A RANDOMIZED CONTROLLED DOUBLE BLIND TRIAL

RADWA H BAKR** and HESHAM M ABDELAZIZ*

Abstract

Background: Strabismus surgery in children is often associated with undesirable intraoperative and postoperative side effects including pain, postoperative nausea and vomiting (PONV), and oculocardiac reflex (OCR). Systemic analgesics have side effects and are contraindicated in some cases. We hypothesized that the preoperative subtenon injection of bupivacaine would reduce postoperative pain and the incidence of side effects adverse effects.

Methods: Sixty children (2 to 6 years of age, ASA status I to II) were randomized to receive either subtenon bupivacaine 0.5% or a saline injection before the beginning of surgery in a double-blind manner. Pain scores using the Face, Legs, Cry, Activity, and Consolability (FLACC) scale, incidence of OCR and PONV, requirement of additional systemic analgesia, and time to discharge from the recovery room were compared.

Results: The pain scores were significantly lower in the subtenon bupivacaine group at 0 min ($p = 0.0056$) and at 30 min ($p = 0.013$). There was no significant difference between the two groups at the other time intervals. There was a significant reduction in the incidence of oculocardiac reflex and the incidence of vomiting in the subtenon bupivacaine group. Eight of the 27 patients in the subtenon bupivacaine group required additional systemic analgesia compared to 19 of 29 controls. The time to discharge from recovery room was lower in the subtenon bupivacaine group.

Conclusion: These data provide some evidence that a preoperative subtenon block with bupivacaine combined with general anesthesia allows efficient control of postoperative pain as well as a reduction in the incidence of OCR and PONV in young children undergoing strabismus surgery.

Keywords: Bupivacaine, Pain, Pediatrics, Strabismus surgery, Subtenon anesthesia.

Introduction

Following strabismus surgery children often experience severe discomfort and are unable to open the operated eye. The surgical manipulation of the medial rectus muscle causes severe bradycardia because of the oculocardiac reflex. The postoperative period is marked by frequent obvious discomfort, caused by a high frequency of postoperative nausea and vomiting and pain. Pain after strabismus correction is thought to be in the conjunctival area, but Tenon’s capsule, sclera, and stretched muscles may also contribute to its intensity. This pain represents a source of distress to the child and the parents. Different modalities of treatment have been proposed and found to be variably effective. Opioids are helpful but carry the risk of nausea, vomiting, and drowsiness.

* MD.

Department of anesthesia and intensive care, Faculty of Medicine, Ain Shams University, Cairo, Egypt.
Non-steroidal anti-inflammatory drugs (NSAIDs) remain controversial in small children. The side effects of these agents are particularly undesirable in the ambulatory surgery setting or are contraindicated in many children. Regional anesthesia has been proposed for management of postoperative pain following strabismus surgery. Topical amethocaine 1% drops and subconjunctival infiltration with bupivacaine 0.5% administered at the conclusion of strabismus surgery have been shown to be effective in reducing postoperative pain. Retrobulbar and peribulbar block have been explored in children with varying degrees of success. Among the different techniques, the subtenon eye block is widely used for anterior and posterior segment surgery in adults. A small quantity of local anesthetic is injected in the subtenon space by use of a smooth cannula after surgical incision of the conjunctiva. This technique ensures adequate postoperative analgesia in adults although it has not been sufficiently explored when used before the start of surgery in children.

We performed a prospective, randomized, double-blind, controlled study to determine the efficacy of subtenon’s bupivacaine injection at reducing postoperative pain, the incidence of postoperative complications, and the requirements of postoperative analgesics in pediatric patients undergoing strabismus surgery.

Patients and Methods

Approval to perform the study was granted by the Institutional Review Board. Informed written consent was obtained from the parents prior to their children’s enrollment in the study. Sixty children aged 2-6 years of age with ASA status I to II scheduled for primary surgical correction of unilateral or bilateral strabismus were included in the study. Patients were randomly allocated to one of 2 equal groups. The inclusion criteria were: age 6 years or under, unilateral or bilateral surgery, primary surgery or reoperation, horizontal, vertical, or oblique muscle surgery. Exclusion criteria were: known drug sensitivity or body weight less than 8 kg.

A standard anesthetic protocol was used for all children included in the study. Midazolam (0.3 mg/kg) and atropine (10 μg/kg) were given rectally 30 minutes before anesthesia. EMLA (eutectic mixture of local anesthetics) cream was applied rectally 30 min before anesthesia over two potential venipuncture sites. Induction was by sevoflurane inhalation and maintenance was by spontaneous ventilation of sevoflurane in oxygen and nitrous oxide via laryngeal mask airway. Intraoperative analgesia was in the form of rectal paracetamol 20 mg/kg. Patients were monitored intraoperatively by electrocardiography, pulse oximetry, noninvasive blood pressure, and end-tidal CO₂ measurements. Heart rate and blood pressure were recorded before induction and every 5 minutes during anesthesia and surgery until the end of the procedure. After induction, bupivacaine 0.5% or a placebo saline solution were slowly injected in the subtenon space with a curved, blunt 25-mm 20 gauge cannula introduced through a small conjunctival and subtenon limbal aperture. The dose of bupivacaine was titrated according to the child’s body weight to ensure a subtoxic dose of less than 2.5 mg/kg. The efficacy of the block was judged satisfactory if the pupil was widely dilated and fixed, thus confirming ciliary ganglion blockade.

The anesthesiologist, surgeon, and nurses were blinded to the nature of the injected solution. All operations were performed by the same surgeon. Surgery was started 5 minutes after the subtenon injection. The surgical protocol was standardized; for surgery on the vertical rectus muscles the conjunctiva was opened over the insertion. The inferior oblique was approached via limbal peritomy if surgery on the lateral rectus was also being performed, or via a circumferential conjunctival incision 10 mm from the limbus if not. The conjunctiva was closed with 6-0 or smaller Vicryl®. All patients received 1 drop of amethocaine 1% onto the operated eye at the conclusion of surgery. After emergence from anesthesia patients were transferred to the recovery ward. On arrival in the recovery room, the patient’s behavior was assessed by a nurse who was not aware of the nature of the solution injected in the subtenon space. The pain scale used for assessment was the Face, Legs, Activity, Cry, Consolability scale (FLACC) (Table 1). This behavioral pain assessment scale is widely accepted as a method of assessment for pain in children by direct observation. The scale consists of 5 categories. Each category is scored on a 0-2 scale, which results in a total score of 0-10. A score
Subtenon bupivacaine for pediatric strabismus surgery

of 0 means relaxed and comfortable, 1-3 indicates mild discomfort, 4-6 indicates moderate pain, and 7-10 indicates severe discomfort or pain or both. Pain assessment was performed after the removal of the laryngeal mask, and then at 30 min intervals until discharge from the recovery ward. Children with a FLACC score equal to or higher than 4 were given 20 mg/kg rectal paracetamol. The following parameters were collected in the recovery room: pain scores, at 0 min, 30 min, 1hr, 2hrs, 3hrs, incidence of occurrence of Occulo-cardiac reflex (indicated by a sudden decrease of the heart rate higher than 20% and concomitant with muscular traction), incidence of postoperative nausea and vomiting, number of patients requiring additional systemic analgesia, and the mean time to first analgesia.

Statistical analysis was done using SPSS (version 14.0, SPSS Inc., Chicago, IL, USA). Continuous data, such as age, weight, anesthetic duration, time to discharge from the recovery ward and time to eye opening, were expressed as mean and SD and were analyzed using Student’s t-test. A chi-squared test was performed for the comparison between qualitative variables. A Mann-Whitney U test allowed intergroup comparison between quantitative variables. A P value < 0.05 was considered as significant. Results were expressed as mean ± SD. Confidence intervals of 95% are provided for statistically significant results.

Results

Fifty six children completed the study. One child in the control group and three in the treatment group were excluded after recruitment due to incomplete data. 46 (82.0%) underwent unilateral and 10 (18.0%) underwent bilateral surgery. 45 operations (81.1%) were primary procedures and 11 (18.9%) were reoperations. 27 children (48.6%) were randomized to the treatment group and 29 (51.4%) were randomized to the control group. The groups were similar with regards to age, weight, sex, proportions having bilateral surgery or reoperations, and number of muscles operated upon (Table 2).

The pain scores at each time interval are summarized in Table (3). The treatment group experienced significantly less pain than the control at the 0-h observation (P = 0.005) and at 30 min (P = 0.013). There was no significant difference between the two groups at the other time intervals. There was a significant reduction in the incidence of occurrence of occulocardiac reflex that required a temporary interruption of traction on the muscles and the injection of atropine in the study group (5 patients) compared to (11 patients) in the control group. The incidence of nausea was not significantly decreased in the study group (3 patients compared to 4 patients in

Table 1

<table>
<thead>
<tr>
<th>FLACC (face, legs, activity, cry, consolability) scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face 0 1 2</td>
</tr>
<tr>
<td>Legs 0 1 2</td>
</tr>
<tr>
<td>Activity 0 1 2</td>
</tr>
<tr>
<td>Cry 0 1 2</td>
</tr>
<tr>
<td>Consolability 0 1 2</td>
</tr>
</tbody>
</table>

The FLACC scale can be used in children up to 7 years and in children with cognitive impairment. Each of the five categories (faces, legs, activity, cry, consolability) is scored 0-2, and the scores are added to yield a total from 0 to 10. Each section above is scored and a total obtained.
the control group); however, the incidence of vomiting was significantly lower in the study group (6 patients) than the control group (10 patients) (Table 4). Eight of the 27 patients in the subtenons group required additional systemic analgesia (30%) compared to 19 of 29 controls (65%). This difference was borderline with regards to statistical significance ($P = 0.052$). The median time to first analgesia was 2hrs 45min in the control group compared to 1 hour in the study group (Table 5). The length of stay in the recovery room was reduced to a significant degree in the bupivacaine group; two hours after the removal of the LMA, 22 of 29 children recruited in the control group were still present in the recovery room in contrast to 4 of the 27 children in the study group.

**Discussion**

Strabismus surgery in children is frequently performed as an outpatient procedure. A large proportion of children experience clinically significant pain after strabismus surgery. Additionally, Pediatric strabismus surgery often leads to postoperative behavioral problems during the recovery period as a result of pain, visual disturbances, nausea and vomiting, and separation from parents. A study demonstrated that altered behavior was encountered on emergence in 44% of operated children, and that 20% of them exhibited complex symptoms simulating delirium.

Symptoms such as PONV and pain are the main cause of delayed discharge, contact with the hospital after discharge, and hospital readmission after outpatient surgery for these children.

Pain after strabismus surgery may be caused by sectioning and traction exerted on the extraocular muscles. Many strategies have been proposed for treatment of the pain experienced by these children. Topical analgesia using drops containing a NSAID was efficient in some studies, but not effective in others.

**Table 2**

*Patient characteristics: Data is presented as mean ± SD*

<table>
<thead>
<tr>
<th></th>
<th>Subtenon Group (N = 27) Mean (SD)</th>
<th>Control Group (N = 29) Mean (SD)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>3.27 ± 1.69</td>
<td>3.37 ± 1.71</td>
<td>0.38</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>17.6 ± 3.6</td>
<td>17.9 ± 3.9</td>
<td>0.54</td>
</tr>
<tr>
<td>Sex ratio (male: female)</td>
<td>12:15</td>
<td>11:18</td>
<td>0.62</td>
</tr>
<tr>
<td>ASA I:II</td>
<td>18:1</td>
<td>18:1</td>
<td>1</td>
</tr>
<tr>
<td>Unilateral: Bilateral surgery</td>
<td>22:5</td>
<td>24:5</td>
<td>0.9</td>
</tr>
<tr>
<td>Primary surgery: reoperations</td>
<td>21:6</td>
<td>22:8</td>
<td>0.69</td>
</tr>
<tr>
<td>Number of operated muscles</td>
<td>2.2 ± 0.8</td>
<td>2.2 ± 0.8</td>
<td>1</td>
</tr>
<tr>
<td>Length of the operation</td>
<td>35.5 ± 10</td>
<td>36 ± 10.2</td>
<td>0.63</td>
</tr>
</tbody>
</table>

**Table 3**

*Summary of pain scores, Mean ± SD*

<table>
<thead>
<tr>
<th></th>
<th>Subtenon Group (N = 27)</th>
<th>Control Group (N = 29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 min</td>
<td>1.77 ± 1.12</td>
<td>3.41 ± 1.12</td>
<td>0.005</td>
</tr>
<tr>
<td>30 min</td>
<td>1.66 ± 1</td>
<td>3.17 ± 1.04</td>
<td>0.013</td>
</tr>
<tr>
<td>1 hr.</td>
<td>2.11 ± 0.89</td>
<td>2.14 ± 0.1</td>
<td>0.91</td>
</tr>
<tr>
<td>2 hrs.</td>
<td>2.55 ± 0.89</td>
<td>2.86 ± 1.41</td>
<td>0.57</td>
</tr>
<tr>
<td>3 hrs.</td>
<td>3.04 ± 1.4</td>
<td>2.72 ± 1.47</td>
<td>0.38</td>
</tr>
</tbody>
</table>
Opioid analgesia is frequently used to reduce postoperative pain after strabismus surgery; however, these drugs often cause nausea, vomiting, and drowsiness. A study showed that opioid analgesia is associated with more prolonged recovery times after anesthesia, a longer stay in hospital, and delayed return to normal activity when compared to other analgesics. Intravenous NSAID such as ketorolac have been shown to be as effective as morphine and pethidine for the relief of pain after strabismus surgery in children, and with a lower incidence of postoperative nausea and vomiting. Other studies showed that systemic NSAIDs such as ketoprofen were efficient in reducing pain after strabismus surgery in children when compared to placebo.

On the other hand certain NSAIDs such as ibuprofen and simple analgesics such as paracetamol were shown to be less effective.

Asthma occurs in 30% to 40% of children, 20% of those are sensitive to aspirin and other NSAIDs. In addition, reactions to NSAIDs include urticaria, angioedema, rhinitis, and exacerbation of asthma or bronchospasm, which may be fatal. These side effects occur after administration in common ophthalmic procedures and have been shown to occur with NSAIDs such as ibuprofen, diclofenac, and ketorolac. Therefore the use of NSAIDs may not be appropriate for many children undergoing strabismus surgery.

Different techniques of regional anesthesia combined with general anesthesia have been proposed for the young child undergoing strabismus surgery. In addition to controlling postoperative pain, it has been suggested that suppression of the trigeminal reflex by regional anesthesia may correlate with a decrease in the incidence of vomiting.

These techniques have yielded conflicting reports. Postoperative topical tetracaine compared with topical saline in pediatric strabismus surgery was shown to provide a short-lived but significantly better pain relief as judged by both pain score and analgesic requirement.

Topical amethocaine 1% drops and subconjunctival infiltration with bupivacaine 0.5% administered at the conclusion of strabismus surgery have been shown to be equally effective in reducing postoperative pain, although another study did not show any additional analgesic effect of either of these interventions when compared to placebo. Similarly, a study showed that the subconjunctival injection of bupivacaine 0.5% as compared with a placebo decreased postoperative pain scores in 36 young children. Another study compared subconjunctival bupivacaine to topical tetracaine in children undergoing squint surgery, with both giving effective analgesia.

### Table 4

<table>
<thead>
<tr>
<th></th>
<th>Subtenon Group (N = 27)</th>
<th>Control Group (N = 29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>OCR</td>
<td>5 (18%)</td>
<td>11 (38%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Incidence of nausea</td>
<td>3 (11%)</td>
<td>4 (14%)</td>
<td>0.575</td>
</tr>
<tr>
<td>Incidence of vomiting</td>
<td>6 (22%)</td>
<td>10 (34%)</td>
<td>0.048</td>
</tr>
</tbody>
</table>

### Table 5

<table>
<thead>
<tr>
<th></th>
<th>Subtenon Group (N = 27)</th>
<th>Control Group (N = 29)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients requiring additional systemic analgesia n (%)</td>
<td>8 (30%)</td>
<td>19 (65%)</td>
<td>0.052</td>
</tr>
<tr>
<td>Median time to first analgesia</td>
<td>2 hours 45 minutes</td>
<td>1 hour</td>
<td>0.05</td>
</tr>
</tbody>
</table>
However, some investigators found no difference in pain score after pediatric squint surgery using postoperative topical saline, topical tetracaine or subconjunctival bupivacaine. Although subconjunctival local anesthetics have had some success in the relief of postoperative pain, the source of pain after strabismus surgery is believed to be receptors in tenon’s fascia and muscle tendons as well as conjunctival receptors.

Regional blocks have also been explored in children. Retrobulbar anesthesia by the administration of 2 mL of bupivacaine 0.5% before surgery was as effective as a subconjunctival injection given after the operation in 10 children. However the block reduced the incidence of OCR from 60% (control group) to 4% in children. Similarly, a study proved that peribulbar block (0.3 mL/kg of a bupivacaine 0.5% and lidocaine 2% mixture) reduced postoperative pain in 25 children 5 to 14 years of age to a significant degree; two thirds of these children were operated on for strabismus. The authors also reported a major reduction in the incidence of occulocardiac reflex and postoperative nausea and vomiting compared with the control group treated with pethidine.

However, when comparing different eye blocks in children, subtenon anesthesia seems to offer some advantages over retrobulbar or peribulbar blocks in pediatric strabismus surgery; All these techniques require the cooperation of patients by asking them to move their eyes laterally to exclude perforation of the globe or nerve injury during the procedure. Small children are unable to cooperate in this way, which leads to performance of the block under general anesthesia, with poor clinical control.

Thus, in the current study, we elected to perform subtenon anesthesia in pediatric patients undergoing squint surgery. Subtenon’s anesthesia results in excellent anesthesia and akinesia and is widely used for adult anterior and posterior segment surgery. The anesthetic agent is delivered into the subtenon’s space posterior to the globe’s equator using a blunt cannula inserted through a conjunctival incision, usually located in the inferonasal quadrant. The drug spreads rapidly through the subtenon’s space and anesthetizes the long and short ciliary nerves as they pierce Tenon’s capsule around the optic nerve.

These nerves carry sensory fibers from the sclera, cornea, and uveal tract. Spread of the drug into the muscle sheaths and eyelids results in anesthesia of these structures.

The surgery is then started through the same conjunctival incision which allows access to extraocular muscles. Therefore, application of anesthetics is no more invasive than the operation itself. Moreover, the required volume of local anesthetics to provide adequate analgesia is less important and limits the risks of damage caused by rapid injection or myotoxicity from the anesthetic solution.

Complications after subtenons anesthesia are uncommon but orbital hemorrhage, extraocular muscle injury, and globe perforation with scissors during dissection of the subtenons space have all been reported. There is also a risk of damage to structures crossing the subtenons space during rapid or high volume injection, and of myotoxicity from the anesthetic agent, but neither of these has yet been reported after subtenons administration. This was fully explained to parents at the time of consent. There were no complications resulting from subtenon injection in this study.

We chose to administer the block preoperatively rather than postoperatively since regional blocks are associated with fewer episodes of bradycardia and hypertension intraoperatively caused by the occulocardiac reflex which results from the traction on the extraocular muscles, this was evident in our study where a significant difference in the occurrence of occulocardiac reflex was observed.

Preoperative administration also offered the advantage of facilitation of surgical dissection and delivery of a controlled volume. The administration of local anesthetic, postoperatively is usually associated with protrusion of Tenon fascia and leakage of anesthetic through the incision. The administration of a preoperative subtenon block did not result in any surgical difficulty from tissue distortion.

In this study we looked at the administration of a long acting anesthetic; bupivacaine has an onset of action of approximately 20 min, preoperative administration ensures analgesic effectiveness as the general anesthetic wears off. We, found significant reduction in postoperative pain score as measured by
Subtenon bupivacaine for pediatric strabismus surgery

Similar results have been obtained in a randomized controlled trial that investigated the postoperative use of sub-Tenon lignocaine in 111 children undergoing squint surgery. Pain was reduced significantly in the first hour after surgery, but thereafter there was no effect. Lignocaine is a shorter-acting anesthetic with a duration of 1-2h when given as a sub-Tenon block, while the effect of bupivacaine lasts for 3-3.5h.

Our findings are also similar to those obtained by Steib et al. who explored the preoperative administration of bupivacaine in 40 children the authors found a significant reduction in pain scores in the study group. The incidence of oculocardiac reflex and postoperative nausea and vomiting were also reduced in the study group.

On the other hand, in a study by Morris et al the authors used preoperative levobupivacaine to perform subtenon block in 27 children undergoing strabismus surgery and found no significant reduction in pain scores in the study group. However, their study had several limitations; a placebo was not used in the control group, and not all patients received exactly the same general anesthetic agents or additional analgesia these two factors may have influenced the results obtained by these investigators. These factors were avoided in our study which may explain our favorable results. However, the results obtained by these authors matched previous results obtained by Carden et al.

No data in the literature suggests the optimal volume to inject in the pediatric population. Use of a large volume to produce akinesia is not essential, as general anesthesia is always used with young children, which allows satisfactory operating conditions by itself.

A significant reduction in PONV was observed in our study during the recovery period. This undesirable effect after strabismus surgery is caused by pain, traction of the muscles, and perioperative use of opioids. A similar reduction in PONV was also encountered in the study conducted by Steib et al.

In conclusion, a preoperative subtenon block with bupivacaine combined with general anesthesia allowed efficient control of postoperative pain as well as a reduction in the incidence of OCR and PONV in young children undergoing strabismus surgery. We recommend that further studies be conducted to determine the optimal volume to inject in the subtenon space and to compare different local anesthetics.

Acknowledgements

The authors sincerely acknowledge the support of the Ain Shams University Ophthalmology Department in supporting this anesthesiology research. The authors also acknowledge the efforts of Mr. Deepak Gupta in the statistical calculations and analysis.
References


The key to

Lock-up

Postoperative Pain

STEP I

Initial bolus
Inject 1 ampoule Tramal® 100 mg
i.v. or i.m. slowly over 2-3 minutes

STEP II

Ways of administration after initial bolus

Infusion
Inject 2 ampoules Tramal®, each 100 mg,
in 500mL of infusion solution.
Infusion rate 12-24 mg Tramal®/h (16-
20 u/h per kg or 30-60mL/h).

PCA
Subsequent increments of 25 mg
with a lock-out time of 5 minutes.

Injection
Usual dose is 50 mg or 100 mg
4-6 hourly up to a total
daily dose of 400 mg except in special clinical
indications which might meritable daily dose up to 600 mg.
Further treatment with Tramal® bolus on demand.

STEP III

Follow-up
- 50 mg every 4-6 hours
- 100 mg
- 20-40 drops every 4-6 hours
- 1 suppository every 4-6 hours
- 1 tablet every 12 hours

Intra-Operative

Loading Dose
2.5 - 3 mg/kg at wound closure

Post-Anaesthesia Care Unit

If intra-operative dose not given then:

BOLUS I.V.
100 mg over 2-3 mins

An intra-operative loading dose of Tramal® will reduce
PONV rates


Grunenthal

PATENTED BY GRUNENTHAL
For patients with localized BURNING, SHOOTING, STABBING, Neuropathic pain

versatis®
5% lidocaine medicated plaster
WORKS WHERE IT HURTS

GRUNENTHAL
BRIDION—optimal neuromuscular blockade management and improved recovery

Predictable and complete reversal

- 98% of BRIDION patients recovered to a TOF⁴ ratio of 0.9 from reappearance of T₂ in 5 minutes²
- 97% of BRIDION patients recovered to a TOF⁴ ratio of 0.9 from 1 to 2 PTCs in 5 minutes³

Rapid reversal

- BRIDION rapidly reversed patients from reappearance of T₂ in 1.4 minutes¹
- BRIDION rapidly reversed patients from 1 to 2 PTCs in 2.7 minutes³

BRIDION is indicated for the reversal of neuromuscular blockade induced by rocuronium or vecuronium. In children and adolescents (aged 2-17 years), BRIDION is only recommended for routine reversal of moderate rocuronium-induced neuromuscular blockade.¹

Important safety information

BRIDION is not recommended in patients with severe renal impairment. Studies in patients with hepatic impairment have not been conducted and, therefore, patients with severe hepatic impairment should be treated with great caution. Caution should be exercised when administering BRIDION to pregnant women as no clinical data on exposed pregnancies are available.

BRIDION has not been investigated in patients receiving rocuronium or vecuronium in the Intensive Care Unit (ICU) setting.

If neuromuscular blockade is required within 24 hours of BRIDION administration, a nonpulsatile neuromuscular blocking agent should be used instead of rocuronium or vecuronium. The most commonly reported adverse reactions were dysgeusa (metal or bitter taste) and anesthetic complications (movement, coughing, gagging, or sucking on the endotracheal tube). In patients treated with BRIDION, a few cases of awareness were reported. The relation to BRIDION was uncertain. In a few individuals, allergic-like reactions (ie, flushing, erythematous rash) following BRIDION were reported. Clinicians should be prepared for the possibility of allergic reactions and take the necessary precautions. In a trial of patients with a history of pulmonary complications, bronchospasm was reported in 2 patients and a causal relationship could not be fully excluded.

Volunteer studies have demonstrated a slight (12%-22%) and transient (<30 minutes) prolongation of the prothrombin time/activated partial thromboplastin time (PT/aPTT) with BRIDION; however, clinical studies have demonstrated no clinically relevant effect on peri- or postoperative bleeding complications with BRIDION alone or in combination with anticoagulants. As BRIDION has demonstrated an in vitro pharmacodynamic interaction with anticoagulants, caution should be exercised in patients on anticoagulation for a pre-existing or coronary condition. This pharmacodynamic interaction is not clinically relevant for patients receiving routine postoperative prophylactic anticoagulation. Although formal interaction studies have not been conducted, no drug interactions were observed in clinical trials. Preclinical data suggest that clinically significant drug interactions are unlikely with the possible exceptions of toremifene, fuxidic acid, and hormonal contraceptives.

¹ Train-of-four
² Post-tetanic counts
³ Second twitch


Please see summary of product characteristics for full prescribing information.

MSD Be Well

Copyright © 2010 Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, NJ, USA. All rights reserved. 05-2013-BRID-2011-LEVANT-1196-J
PAJUNK® Pioneering Medical Technology

**TAP Block And InfiltraLong**
For Effective Treatment Of Long And Deep Incisions

**Sono Cannulas**
For Single Shot UltraSound Guided Nerve Blocks

**SonoSystem And SonoLong Curl**
For UltraSound Guided Nerve Blocks

**Sprotte® 2.G**
The New Generation Dura Punctre In Minimum Time

**SonoEye Ophtalmic Block**
For Peribulbar And Retrobulbar Blocks Under Ultrasonic Monitoring

www.mediline-lb.com  Tel:+961 1 697500