Evaluation of minimal dose of atracurium for cataract surgery in children: A prospective randomized double-blind study

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ABSTRACT

Background: Cataract surgery when performed under general anesthesia, especially without neuromuscular blocking agents, eccentric position of the eye has been reported. However, no evidence exists for the need and optimal dose of neuromuscular blocking agents for surgical reasons when the anesthetic management may be done without its need. We hypothesize that the minimal dose atracurium may accomplish the surgical requirement of cataract surgery in children. Materials and Methods: After ethical committee approval, this double-blind, prospective, randomized study was conducted in children scheduled for cataract surgery under general anesthesia. Anesthesia was induced in a standardized manner and using laryngeal mask airway. The patients were randomized into four groups of 55 patients each and atracurium was administered as per group allocation: Group 0: No atracurium was administered; Group 50: Received atracurium at 50% dose of ED₉₅; Group 75: Received atracurium at 75% dose of ED₉₅; Group 100: Received atracurium of 100% dose of ED₉₅. Surgeon was asked to grade surgical condition just after the stab incision in the cornea. The primary outcome variable included the need of atracurium supplementation based on grading of surgical conditions by the operating surgeon who was blinded to the randomized group. Results: The need of atracurium due to unacceptable surgical conditions based on surgeon satisfaction score was statistically significant when compared among the groups being maximum in Group 0 (P < 0.001). Also, the surgeon satisfaction score was statistically significant among the groups (P < 0.0001) with the least satisfaction in Group 0. The laryngeal mask airway (LMA) insertion score was statistically significant in the four groups (P = 0.001). However, number of attempts for LMA placement was comparable among the four groups (P = 0.766). Conclusion: We conclude that a balanced anesthetic technique including atracurium provided better surgical condition for cataract procedures in children. The surgical condition improved with increasing dose of atracurium from 25% to 100% ED₉₅ dose.

Key words: Anesthesia, atracurium, cataract, children, dose, eye position

INTRODUCTION

Cataract surgery in adults is usually performed with topical and local anesthetics. However, children usually do not cooperate during placement of blocks and require general anesthesia for cataract extraction and placement of intraocular lens. Optimal surgical conditions require a still, motionless eye with a central gaze.

Cataract surgery when performed under general anesthesia, especially without neuromuscular blocking agents, eccentric position of the eye has been reported. In earlier days, tracheal intubation was the standard airway device for eye surgeries and thus required the use of neuromuscular blocking drugs. This also fulfilled the surgical need of quite still eye. However with the advent of the supraglottic airway devices (SAD), the need of neuromuscular blocking drugs has been almost abolished as there is enough evidence to show that they are not essential when securing airways with supraglottic devices. In view of these, there is a dilemma whether neuromuscular blocking agents are still necessary.
to be used, particularly in short surgical procedures like cataract surgery. There is no published data to support or refute them. On the other hand, there are studies reported that have evaluated the dose-response/need of neuromuscular blocking agents for the placement of the SAD. However, no evidence exists for the need and optimal dose of neuromuscular blocking agents for surgical reasons when the anesthetic management may be done without its need.

To the best of our knowledge and belief, there is no literature published with regard to the need and optimal dose of muscle relaxant used for providing a still and relaxed eye under general anesthesia in children. We hypothesize that the lesser dose atracurium may accomplish the surgical requirement of cataract surgery in children without compromising the anesthetic quality. In view of this, we planned to conduct this randomized study to evaluate the need and optimal dose of muscle relaxant (atracurium) for cataract surgery in children.

MATERIALS AND METHODS

After taking institutional ethical committee approval, this double-blind, prospective, randomized study was conducted in this tertiary care referral center. All the children aged 6 months to 10 years of age scheduled for cataract surgery under general anesthesia were recruited in the study. Children with upper respiratory tract infection, refusal to participate in the study, traumatic cataract, any neuromuscular disease, craniofacial anomalies and significant cardiac anomalies were excluded from the study. A thorough preanesthetic assessment was done for all children. Parents of the children were explained about study protocol and written informed was taken for participation in the study.

On the day of surgery after shifting the child in the operating room, monitors like electrocardiogram, noninvasive blood pressure, pulse oximeter ($\text{SpO}_2$) were attached. General anesthesia was induced with incremental concentrations of sevoflurane (2.8%) in 100% oxygen till there was a loss of eyelash reflex. Capnography was also initiated. An intravenous line was secured followed by intravenous administration of fentanyl 1 µg/kg. The patients were randomized into four groups of 55 patients each using computer generated random number table with randomized group sealed in an opaque envelope.

The neuromuscular blocking drugs (atracurium) were administered as per group allocation:

- **Group 0**: No atracurium was administered.
- **Group 50**: Received atracurium at 50% dose of ED$_{95}$.
- **Group 75**: Received atracurium at 75% dose of ED$_{95}$.
- **Group 100**: Received atracurium of 100% dose of ED$_{95}$.

The dose of atracurium was calculated for each child based on age and weight and was diluted in normal saline to a total volume of 5 mL by an independent anesthesiologist not involved in clinical management or observation of the child in perioperative care. After 3 min, appropriate size reusable flexometalic laryngeal mask airway (LMA) was inserted, and the LMA insertion score was noted [Table 1] and accordingly considered as excellent, satisfactory or poor.$^{13}$ Total score of 18 was considered as excellent, 16-17 as satisfactory, <16 as poor. Thereafter, lungs were ventilated with sevoflurane (1.0-2%) in nitrous oxide and oxygen (50:50) to keep a minimum alveolar concentration between 1.2 and 1.5. The ventilator setting was adjusted to achieve an Et$\text{CO}_2$ of 35-40 mmHg. The mode of ventilation (controlled vs. support) was adjudged as per child requirement. In case of presence of respiratory efforts, the breath was assisted to achieve normocapnia.

All the surgery was performed by the same surgeon. Surgeon was asked to grade surgical condition [Table 2] just after the stab incision in the cornea. Supplementation of atracurium was administered in the dose of 50% of ED$_{95}$ in children with surgeon assessment grade of 2 or 3. Vitals were monitored continuously and noted every 5 min. Inhalational agents were stopped at completion of the surgery. The residual neuromuscular blockade was reversed using neostigmine (0.05 mg/kg) and glycopyrrolate (0.01 mg/kg). The reversal agents were prepared by the same anesthesiologist who prepared...

| Table 1: LMA insertion score |
|-----------------------------|
| Variables | Scoring |
| Mouth opening | Nil (1) | Partial (2) | Full (3) |
| Ease of insertion | Impossible (1) | Difficult (2) | Easy (3) |
| Swallowing | Gross (1) | Slight (2) | Nil (3) |
| Coughing/gagging | Severe (1) | Mild (2) | Nil (3) |
| Patients movement | Vigorous (1) | Moderate (2) | Nil (3) |
| Laryngospasm | Severe (1) | Mild (2) | Nil (3) |

LMA: Laryngeal mask airway

| Table 2: Surgeon’s satisfaction score |
|--------------------------------------|
| Grade | Parameter for grading surgical condition |
| 0 | Excellent surgical condition, eye center, no movement |
| 1 | Good manageable surgical condition with slight upward or downward deviation of the eyeball can proceed with surgery |
| 2 | Difficult to operate with major upward or downward deviation of the eyeball, cannot proceed, needs definite anesthetic management |
| 3 | Extremely difficult to operate with extreme deviation of the eyeball requiring urgent anesthetic intervention |
the study drugs. Patients in Group 0 were given normal saline, and rest of the groups received full dose of reversal agents. The drugs were mixed in a syringe to a total volume of 5 mL. The anesthesiologist involved in the case management was not aware of the reversal drugs. Supraglottic device was removed once the patient was fully awake with adequate respiratory efforts. Postoperative analgesia was maintained with 0.5 mcg/kg fentanyl for first 2 h and then with syrup ibuprofen and paracetamol combination as per need.

The primary outcome variable included the need of atracurium supplementation based on grading of surgical conditions by the operating surgeon who was blinded to the randomized group. The secondary outcome variables included surgeon satisfaction score, LMA insertion score, number of attempts required for LMA placement. Any complications during the procedure were also noted.

**Statistical analysis**

Based on the pilot study on 40 patients, and assuming that the supplementation of atracurium required is 90%, 70%, 40%, 10% in Group 0 (no atracurium), Group 50 (50% of ED$_{95}$ atracurium), Group 75 (75% of ED$_{95}$ atracurium) and Group 100 (100% of ED$_{95}$ atracurium) respectively. With $\alpha = 5\%$ and power of 80%, we required to enroll 212 cases in four groups that are, 53 cases in each group. So we randomized 220 cases (55 in each group) to accommodate any drop out using computer-generated random number table.

In our study, baseline characteristic such as age and weight were compared among the four groups using one-way analysis of variance by the operating surgeon who was blinded to the randomized group. The secondary outcome variables included surgeon satisfaction score, LMA insertion score, number of attempts required for LMA placement. Any complications during the procedure were also noted.

The LMA insertion score was statistically significant in the four groups ($P < 0.001$) [Table 3]. The score progressively improved with the increasing dose of the atracurium. On further analysis using Bonferroni correction for multiple comparisons, LMA insertion score was statistically significant when compared between Group 0 and Group 100 ($P < 0.001$); while rest of the comparison between the groups were statistically comparable ($P > 0.05$). However, number of attempts for LMA placement was comparable among the four groups ($P = 0.766$) [Table 3].

No untoward complication was observed during the perioperative period.

**DISCUSSION**

We observed from our study that atracurium is required during the cataract surgical procedures for achieving optimal surgical conditions. The surgical conditions based on surgeon satisfaction score improved with the increasing dose of the atracurium from no dose to 100% of ED$_{95}$.
dose. The LMA could be placed successfully irrespective of the use and dose of the atracurium. However, the LMA insertion score improved with the increasing dose of atracurium.

The deviation of the eye under general anesthesia has been reported. Under anesthesia without the use of muscle relaxant, eye is eccentrically deviated usually in extreme upward gaze. This eccentric position of the eye has been attributed to unopposed actions of different ocular muscles. The position of the eye is more divergent if the eyes are rotated up and more convergent if the eyes are rotated down. This eccentric location of eye leads to unsatisfactory surgical field leading to difficulty in surgical intervention and also increases the risk of surgical complications like loss of the capsulorhexis, difficult off-axis views and hindering the maneuverability of instruments within the eye. The incomplete capsulorhexis may increase the risk posterior capsule rupture and its associated sequelae leading to ocular morbidity. Also, problems such as extraocular muscle contraction and intraocular pressure rise resulting in radialization of a continuous curvilinear capsulorhexis, activation of Bell’s phenomenon or problematic intraocular lens implantation occurs if eye is not still and centralized.

The various options to prevent deviation of the eye for optimal ocular intervention has been reported. These include both ophthalmic and anesthetic interventions. The ophthalmic intervention includes the use of superior rectus stay suture. The anesthetic interventions include the use of local anesthetic for sub-Tenons or peribulbar blocks, deepening the anesthesia by volatile agents and use of neuromuscular blocking agents along with controlled ventilation. Also, it appears agents like opioids, propofol, dexmedetomidine may also serve the purpose of centralization of eye by deepening of anesthesia in addition to the use of volatile anesthetic agents. The use of regional blocks or stay suture is not desirable in children as it increases surgical morbidity by increasing the intraocular pressure. Moreover, akinesia is variable after peribulbar blocks or sub-Tenon’s block for ocular surgery.

In recent years, supraglottic devices have emerged as the main airway management devices for ocular procedures under general anesthesia and has replaced the conventional endotracheal intubation for airway management even with positive pressure ventilation. The need of neuromuscular blockade for placement of supraglottic devices has been studied with variable results. However, the preference tilts toward avoiding neuromuscular blockade for general anesthesia when SAD is used. In view of the short surgical duration, there is also concern to anesthesiologist whether neuromuscular blocking agents should be used or not. As per our experience of over 3000 pediatric cataract cases, it has been observed that there is upward rolling of the eye ball usually in cases where neuromuscular blockade is not used. This hinders the provision of optimal surgical condition and may affect the outcome. At our center, the neuromuscular blocking drugs are administered for surgical reasons for pediatric cataract surgery.

Airway has been secured with supraglottic devices without muscle management with a high concentration of volatile agents like sevoflurane successfully. However, muscle relaxant effect of sevoflurane is weaker and achieve only at high concentration. Propofol has been used to facilitate tracheal intubation of sevoflurane induction without a muscle relaxant in children. Propofol 2 mg/kg during 8% sevoflurane induction resulted in a higher proportion of excellent intubating conditions compared with propofol 1 mg/kg alone. The addition of opioids to induction agent has been used for tracheal intubation without muscle relaxant in children. Such high concentration of sevoflurane or high dose of propofol or opioids may not be acceptable for maintenance of anesthesia to achieve its muscle relaxant effect for optimal surgical condition because of hemodynamic effects, recovery profile and unpredictable response to these agents specially in infants and younger age children. The potential for worrying acute rises in intraocular pressure postoperatively from nausea and vomiting limits the use of opiate premedication in ocular surgery. Power et al. examined the depth of anesthesia achieved by the administration of sevoflurane through induction by comparing clinical eye signs with electroencephalography polysomnography. They showed that in young adults, the deepest level of sleep was reached on average 3 min prior to the onset of eccentric ocular positioning. This shows that although a patient may appear satisfactorily anesthetized, eccentric eye positioning may still occur. Also, if due to some reasons, lighter plane of anesthesia occurs, an eccentric position of the eye may occur leading to difficulty in surgical intervention. The other adjuvant like dexmedetomidine has been used for airway management without using muscle relaxants. However, its maintenance infusion for surgical conditions and its effects on eye has not been studied and thus cannot be recommended. The most important point to be emphasized here is that there is no literature evaluating this adjuvant like opioids, propofol, dexmedetomidine for preventing the occurrence of eccentric eye position.

Thus, it appears the use of balanced anesthesia using neuromuscular blocking agents should provide acceptable conditions without increasing any adverse effects in pediatric cataract surgeries. It was revealed from a study on horse that the use of atracurium provided better surgical ocular condition as compared to deep levels of
isoflurane under general anesthesia.

To achieve central eye position, the concentration of isoflurane required was high to the extent of leading to hemodynamic instability requiring dobutamine. The effect of neuromuscular blocking agent on position of eye was reported in an animal study wherein, with the use of atracurium (0.2 mg/kg), the eye rotated from a ventromedial position to a central position and remained centrally positioned until 100% recovery of a train-of-four twitch response. In another study, intravenous administration of succinylcholine (2 mg/kg) returned the eyes of 15 anesthetized volunteers to positions comparable with their conscious horizontal basic deviations in the primary position. Also with regards to airway management, some authors have used lower doses of neuromuscular blocking agents to achieve optimal condition like rocuronium dose of 0.2 mg/kg instead of 0.6 mg/kg to achieve adequate intubating conditions. These shorten the onset time and prolong the duration of akinesia without known complications.

In our clinical practice at our center, neuromuscular blocking agents are mostly given to provide a still surgical field to the surgeon and avoid uprolling of the eyeball. However, data are scarce regarding the optimal dose of neuromuscular blocking agents for providing optimal surgical condition during the cataract procedure in children. The dilemma of lesser doses may not serve its purpose, and too much of neuromuscular blocking agents agent can delay the recovery of the patient. We conducted this study to evaluate the need and to find the optimal dose of neuromuscular blockade for achieving optimal surgical condition with a secondary objective of its effect on supragnatic device placement. In our study, we found a positive correlation between the atracurium dose and surgeon satisfaction for surgical condition. The surgical conditions improved with the increasing dose of the atracurium. We observed from our study that the number of attempts to insert supragnatic devices was comparable in all the four groups. The LMA insertion score improved with the increasing dose of the atracurium (P < 0.001). However, on further analysis, we observed that LMA insertion score was statistically significant when compared between Group 0 and Group 100 (P < 0.001); while rest of the comparison between the groups were statistically comparable.

We used atracurium in our study as atracurium is a commonly used nondepolarizing neuromuscular blocking agent whose disposition depends on Hofmann elimination and nonspecific esterase hydrolyses, and is independent of liver and kidney function. In addition, due to organ-independent degradation of atracurium through Hofmann’s elimination, clearance is also expected to remain unchanged in such children who may have associated metabolism issues and thus may prolong the recovery time. The synergism between the anesthetic agents like intravenous induction agents, volatile agents and neuromuscular blocking agents exists. So to get the beneficial effect of this synergism, the muscle relaxant may be used in appropriate doses without undue prolongation of the anesthesia.

We conclude that a balanced anesthetic technique including atracurium provided better surgical condition for cataract procedures in children. The surgical condition improved with increasing dose of atracurium from 25% to 100% ED95 dose.

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