Med. J. Cairo Univ., Vol. 86, No. 1, March: 617-622, 2018
www.medicaljournalofcairouniversity.net

Efficacy of Adding Atracurium to Percaruncular Block for High Myopes (A Randomized Controlled Trial)

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Abstract

Background: In the current study, it was hypothesized that adding low dose atracurium to Local Anesthetic (LA) mixture would provide an early onset of akinesia and favorable surgical condition in percaruncular peribulbar anesthesia for high myopes undergoing phacoemulsification.

Methods: 91 ASA-PS I-III high myopes scheduled for phacoemulsification were enrolled in this randomized controlled trial. The enrolled patients were randomly allocated to one of two groups. Group C (n=46) received 2.5ml of lidocaine 2%, 2.5ml of bupivacaine 0.5% with hyaluronidase 15IU/ml and 1ml normal saline, while patients in Group A (n=45) received the same mixture with 5mg atracurium. The onset of globe and eyelid akinesia and duration of akinesia were recorded. The need for supplementation, total LA volume and surgeons' satisfaction were recorded.

Results: Eighty-two patients were analyzed with 41 patient in each group. The onset of globe akinesia was earlier in Group A than Group C [4 (2-9), 4 (4-15) min. respectively, $p<0.001$]. Furthermore, fewer patients in Group A required supplementation compared to Group C, 27% versus 62% respectively, $p=0.002$. The onset of eyelid akinesia, duration of akinesia and the total volume of LA were comparative between the 2 groups.

Conclusion: Adding 5mg atracurium to LA solution reduced the time to onset of globe akinesia and the need for supplementation in the percaruncular block in myopic patients with no effect on duration of akinesia or quality of analgesia.

Key Words: *Atracurium – Percaruncular – Medial canthal – Peribulbar anesthesia – High myopes.*

Introduction

THERE are several regional anesthetic techniques available for phacoemulsification procedures and the choice depends on patient, surgical and operator factors [1]. Patients with axial myopia (axial length more than 26mm) have thin sclera, limited space between globe and orbit and out-pouching of the sclera (staphyloma). Staphylomata are more frequently encountered inferior to the posterior pole (increasing the risk of perforation following an inferotemporal puncture in both peri-and retrobulbar blocks) [2-5].

Single medial canthal peri-bulbar injection (percaruncular) may provide a safer and familiar alternative to inferotemporal peri- and retrobulbar techniques for phacoemulsification procedures in myopic patients. The space between the medial orbital wall and the globe is comparable to that of inferotemporal approach and devoid of blood vessels. Moreover, myopic staphylomata are infrequently located on the nasal side of the globe [2,5-8].

The effect of using non-depolarizing neuromuscular blockers as an adjuvant to the retrobulbar or peri-bulbar block, in developing early akinesia had been demonstrated in several studies [9-14].

The current study aimed to test the efficacy of adding low dose atracurium to lidocaine, bupivacaine and hyaluronidase mixture in providing an early onset of akinesia and favorable surgical condition in percaruncular peri-bulbar anesthesia for high myopes undergoing phacoemulsification.

Material and Methods

The protocol was registered in ClinicalTrials.gov under I.D. number: NCT03243500.

This was a single center parallel randomized controlled trial conducted in Ophthalmology Sur-

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gical Theater, Kasr Al-Ainy Hospital, Cairo, Egypt from May 2015 to May 2016.

After obtaining the Department of Anesthesia, Pain Management and Surgical ICU and Department of Ophthalmology Ethical Committee approbation, Cairo University Medical School approval (July, 2014) and informed consents from the patients, 91 American Society of Anesthesiologists' physical class (ASA-PS) I-III patients scheduled for phacoemulsification with high myopia (axial length ≥26mm) were enrolled in the study.

Patients who were <18 or >75 years old, pregnant, ASA-PS >III, their axial length was <26mm or had contraindication to regional anesthesia (absolute contraindications: Patient refusal to participate in the study, local anesthetic allergy and Infection/marked orbital inflammation or relative contraindications: Unable to lie flat for a sufficient length of time, confusion or psychiatric illness, communication difficulties, bleeding diathesis or taking anticoagulants, previous scleral buckling or space-occupying lesions within the orbit) were excluded from the study.

The enrolled patients were randomly allocated to one of two groups using a computer-generated number and concealed using sequentially numbered, sealed opaque envelopes. Group C (n=46) received 2.5ml of lidocaine 2% (lidocaine hydrochloride 2% pharmacell 20ml, manufactured by Sigmatec Pharmaceutical Industries, 6 October city, Egypt for Pharmacell Company, Egypt), 2.5ml of bupivacaine 0.5% (Sunnypivacaine 0.5% 20ml vial, Sunny Pharmaceutical, Badr City, Cairo, Egypt) with hyaluronidase 15IU/ml (Omnidase 1500iu Injection, Sunways India Pvt Ltd, India. Diluted in 2 vial lidocaine 20ml resulting 37.5IU/ml lidocaine and 93.7/2.5ml lidocaine or 15.6IU/ml of the 6ml solution) and 1 ml normal saline to make total volume of 6ml, while patients in Group A (n=45) received 2.5ml of lidocaine 2%, 2.5ml of bupivacaine 0.5% with hyaluronidase 15IU/ml and 5mg atracurium (Atracurium Hameln 10mg/ml manufactured by Sunny Pharmaceutical, Badr City, Cairo, Egypt under license of Hameln Pharmaceuticals-Germany) in 1ml normal saline to make a total volume of 6ml from which the patient received 5-6ml. Neither the administrator of the block nor the surgeon knew which drug mixture was given.

Preoperatively, the axial length of the enrolled patients was measured by ultrasound biometry and the presence of staphyloma was identified by B-scan.

In the preparation room, the Intravenous (IV) cannula was placed. Anxious patients were given midazolam intravenously (titrated to response according to patient's age and associated medical condition).

In the operating room, standard monitoring of pulse oximetry, Electrocardiography (ECG) and noninvasive arterial blood pressure were commenced. The O_2 was administered at 2ml/minutes by the nasal O_2 cannula.

Benoxinate 0.4% eye drops (BENOX® 0.4% 10 ml Manufactured by Egyptian Int. Pharmaceutical Industries Co. (E.I.P.I.CO.)-Egypt) were instilled in the eye to be operated upon three times separated by a one-minute interval.

While in a supine position, the patient was asked to look directly ahead focusing on a fixed point on the ceiling so that the eyes were in the neutral position. A medial canthus injection was given using a 25G, 25mm needle under complete aseptic condition. The needle insertion point was just medial to the caruncle. While the needle was perpendicular to the face, it was introduced parallel to the medial orbital wall to 15-20mm depth **[5]**.

After negative aspiration, the already chosen local anesthetic mixture was injected slowly. If the tension was felt to rise in the globe during injection (the globe was palpated with one finger and the lids tension was tested frequently) the injection would be stopped. After injection, external compression with Honan balloon inflated to 20-30mm Hg was applied for 10 minutes and was removed every 2 minutes to test akinesia and anesthesia **[5]**.

The data were recorded by the administrator of the block who was blinded to which drug mixture was given.

Ocular Movement Score (OMS) was assessed every 2 minutes by asking the patient to move his/her eye in four directions; up, down, medially and laterally and the movement in each direction is given a score from 0 to 2 as follows: Movement more than 2mm was given a score of 2, 1-2mm movement was given a score of 1 and no movement was given a score of 0. A total score of 2 or less was considered adequate akinesia for surgery. The beginning of motor blockade (OMS ≤6) and onset time of globe akinesia were recorded. Moreover, the OMS was assessed at the end of the surgery and then every 30 minutes post-operative till regaining full ocular movement to determine the duration akinesia **[8]**.

Eyelid movement score was assessed by asking the patient to open his/her eye widely followed by squeezing them maximally. A full movement was given a score of 2, the flickering was given a score of 1 and no movement was given a score of 0. The time to score of ≤ 1 was recorded [8].

If, after 10 minutes, the block was inadequate, a 3-4ml supplementation of lidocaine 2% by the same technique was given. If the block was still inadequate, it was considered a failure and excluded from the study. When the block was considered a failure the patient received either supplemental inferotemporal injection (if ultrasound excluded presence of posterior staphyloma), topical anesthesia, intravascular fentanyl 50mcg or general anesthesia according to the patient's condition. After adequate analgesia (loss of sensation to touch by a small cotton wool) and akinesia (OMS ≤2), the surgeon was allowed to start the surgery.

The need for supplementation and the total volume of the local anesthetic mixture were recorded. The pain was assessed by using a 3 point scoring system: (no pain=0, discomfort=1, pain=2) throughout the operation. If the score was ≥1, we started by reassurance. If psychological reassurance failed, 50mcg fentanyl IV was given. Surgeons' satisfaction was assessed at the end of the surgical procedure by using a three-point scale: 0=not satisfied, 1= moderately satisfied, 2=satisfied.

Statistical analysis:

Statistical analysis was carried out using S-Plus Statistical Software (SPSS) for Windows (Version 20.0, SPSS Inc. Chicago, Illinois). All variables were tested for normality using Kolmogorov-Smirnov test; if the test was significant, non-normality was accepted. Otherwise, double-checking using graphs, skewness and kurtosis were required to confirm normality.

Continuous variables were described as mean ± standard deviation when normality of distribution assumptions was satisfied. If not, it was presented as median [IQR]. Categorical variables were presented as numbers and percentages. Wilcoxon Matched-Pair Signed-Rank was used to compare paired nonparametric data. Two-tailed unpaired student *t*-test was used to compare quantitative variables, and Fisher's exact test was used to compare qualitative variables. A p-value of <0.05 was accounted to be significant.

Based on a two-sided alpha of 0.05, 95% power, and a clinically relevant difference in time of onset of akinesia at least 3 minutes, a minimum of 74 patients was needed for the study (MedCalc® version 12.7.1.0-64-bit).

Results

Ninety 0ne patients scheduled for phacoemulsification in Kasr Al-Ainy Hospital were enrolled in the current study and randomly allocated to two groups [Group A (n=45) and Group C (n=46)] from May 2015 to May 2016. Fig. (1) illustrates the enrollment, intervention allocation, follow-up, and data analysis. The nine excluded patients achieved adequate surgical condition after receiving an inferotemporal injection of 2ml lidocaine except for one patient (in Group C) who received superior nasal supplementation.

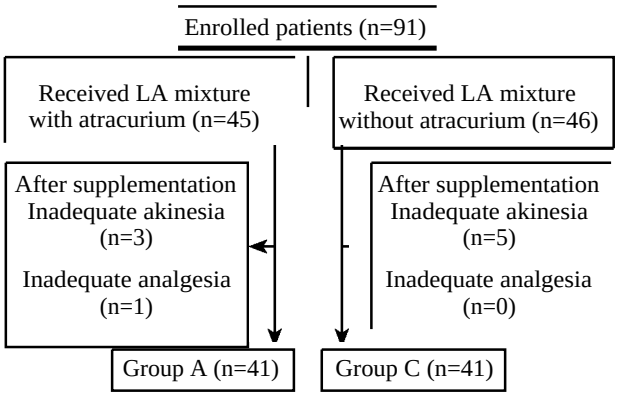

Fig. (1): Flow diagram of enrollment, intervention allocation, follow-up, and data analysis ‡‡.

‡‡ LA: Local Anesthesia.

The baseline demographic and clinical characteristics for the included 82 patients (41 for each group) are shown in Table (1).

Table (1): Demographic and clinical characteristics ‡‡.

	Group A (n=41)	Group C (n=41)	*p*-value
Age (years)	49.2±8.21	52.3±9.32	0.493
Gender n (%):			
Female	22 (54)	22 (54)	1
Male	19 (46)	19 (46)	
Axial length (mm)	29 [27.7-31]	29 [27-30]	0.677
Need for sedation n (%)	11 (26.8)	12 (29.3)	0.806
Duration of the surgery (min.)	45 [35-60]	50 [40-60]	0.601
Posterior staphyloma n (%)	3 (7.3)	4 (9.7)	0.765
ASA-PS n (%):			
I	19 (46)	17 (41)	0.656
II	20 (49)	18 (44)	0.658
III	2 (5)	6 (15)	0.264

‡ ‡: Numerical data were presented as mean ± SD when normality of distribution assumptions was satisfied. If not, it was presented as median [IQR], categorical data were presented as frequency (%), p<0.05 considered statistically significant.
ASA-PS: American Society of Anesthesiologists-Physical Status.

Table (2) presents block criteria in each group. The onset of motor blockade and full akinesia were earlier in Group A compared to Group C. Furthermore, fewer patients in the Group A required supplementation compared to Group C. On the other hand, the onset of eyelid akinesia, the total volume of LA and the duration of akinesia were comparable between the two groups.

Table (2): Block criteria ‡‡.

	Group A (n=41)	Group C (n=41)	*p*-value
Onset time of:			
OMS ≤6 (min.)	2 [2-3]	4 [2-4]	<0.001
OMS ≤2 (min.)	4 [2-9]	12 [4-15]	<0.001
Eyelid akinesia (min.)	4 [2-4]	4 [2-6]	0.319
Total volume of LA (ml)	6 [5-8.5]	8 [5.5-9]	0.061
Duration of akinesia (min)	190 [180-240]	180 [180-210]	0.621
• The incidence of supplementation n (%)	11 (27)	25 (62)	0.002

‡‡: Numerical data were presented as median [IQR], categorical data were presented as frequency (%), $p<0.05$ considered statistically significant.
OMS: Ocular Movement Score.

In Group A, 5 (12%) patients experienced pain compared to 6 (14%) patients in Group C with no statistically significant difference. The experienced pain occurred toward the end of the surgery during Intraocular Lens (IOL) insertion except for one case in Group C, the pain occurred during irrigation and aspiration. Furthermore, the pain was mild that required only reassurance except for one patient in Group A and 2 in Group C who required 50mcg fentanyl intravenously.

Surgeons' satisfaction at the end of the surgery was comparable between the two groups. The current study surgeons found the operative conditions to be satisfactory (90% in Group A and 83% in Group C) with 4 surgeons (10%) in Group A and 7 surgeons (17%) in Group C were less satisfied.

Discussion

The current study demonstrated the effect of adding low dose atracurium to lidocaine, bupivacaine and hyaluronidase mixture on providing an early onset of globe akinesia and favorable surgical condition in percaruncular peribulbar (PB) anesthesia for high myopes undergoing phacoemulsification.

In the current study, it was observed that onset of the motor blockade (OMS ≤6) and full akinesia (OMS ≤2) was earlier in Group A than in Group C [4 (2-9), 4 (4-15) min. respectively].

The current study results were consistent with those reported by Küçü Kyavuz et al., **[10]** who have demonstrated that the addition of atracurium 5mg to a mixture of lidocaine 2% and bupivacaine 0.5% with volume of 8.5ml injected in inferotemporal quadrant and lateral to the supratrochlear notch, improve orbital akinesia and hasten block (onset time of akinesia was 10 ± 3 minutes in the control and 7 ± 2 minutes in the atracurium group, $p<0.05$).

Furthermore, Eghbal et al., **[14]** noticed that adding 5mg atracurium to 2mL of 2% lidocaine in retrobulbar anesthesia significantly decreased the onset time of akinesia (4.7 ± 1.1 minutes in the atracurium group and 6.9 ± 0.96 minutes in the control group).

Rocuronium is another non-depolarizing neuromuscular blockers that had been studied in the peribulbar anesthesia **[11,13]**. Abdellatif et al., **[11]** reported that the addition of rocuronium (5mg) to a local anesthetic mixture of lidocaine 2% and bupivacaine 0.5% (4.25ml inferotemporal quadrant and 4.25ml percaruncular) significantly improved the time to adequate akinesia compared to control group (6.9 ± 4.1 and 9.8 ± 2.9 minutes respectively, $p=0.01$). Aissaoui et al., **[13]** added rocuronium 0.06mg/kg to the bupivacaine lidocaine mixture without hyaluronidase in a single inferotemporal injection. The authors found that rocuronium improved akinesia scores at 2, 5 and 10min after the injection.

On the otherhand, Godarzi et al., **[12]** compared the effect of adding 0.5ml Atracurium (5mg) and 0.5ml cis-Atracurium (1mg) to bupivacaine 0.5%, Lidocaine 2% and Hyaluronidase 90IU with the volume of 8.5ml in inferotemporal PB anesthesia. The study found that after 10 minutes, the percentage of akinesia was comparative among the 3 groups (92.6% in the Atracurium group; 85.2% in the cis-Atracurium and the control group).

As regards to the need for supplementation, significantly fewer patients in the Group A required supplementation (due to the failure of the first injection to achieve adequate surgical condition after 10 minutes) compared to Group C, 27% and 62% respectively. Aissaoui et al., **[13]** also demonstrated that Supplementary injections were lower in rocuronium group (13%) than in control group (40%).

On the otherhand, the need for supplementation was not reduced as reported in Küçü kyavuz et al., 10 (none in atracurium group and 2 cases in the control), and Abdellatif et al., **[11]** (20% in rocuro-

nium group and 30% in control group) while no supplementation was given in Eghbal et al. [14].

The reported higher rate of supplementations in the current study compared to the previously mentioned studies could be due to the use of techniques other than a single percaruncular injection in those studies [10-13,15]. Furthermore in Küçü kyavuz et al., [10], supplementation was given after waiting 20 minutes (10 minutes in the current study). A larger initial volume of LA was used in Abdellatif et al., [11] and Aissaoui et al., [13].

Regarding the duration of akinesia in the current study, it was comparative between the 2 groups which was consistent with Küçü kyavuz et al., [10] results. On the other hand, adding atracurium to retrobulbar prolonged the duration of akinesia as reported by Eghbal et al., [14]. Other mentioned studies did not report the duration of akinesia [11,12].

In contrary to early onset of globe akinesia in Group A in the current study, it was observed that the onset of eyelid akinesia was not significantly earlier in Group A. This might be due to early spread of LA mixture to the eyelid through the percaruncular block which provides good orbicularis akinesia [16,17]. Our results were comparable with Abdellatif et al., [11]. On the other hand, Küçü kyavuz et al., [10] observed that adding atracurium significantly hasten the onset of eyelid akinesia in inferotemporal PB. Also, Aissaoui et al., [13] noticed the earlier onset of eyelid akinesia in rocuronium when given in inferotemporal PB. Eghbal et al., [14] and Godarzi et al., [12] did not record the onset time of the eyelid akinesia.

Adding atracurium to LA solution in percaruncular block did not significantly lowered the total injected volume which was consistent with the observations of the previously mentioned studies [10-14].

The exact mechanism through which the local administration of a nondepolarizing muscle relaxant improves ocular akinesia is not known but is believed to be due to local effects at the muscle's motor end-plate [10,11,14].

In conclusion, adding 5mg atracurium significantly reduced the time of onset of globe akinesia and reduced the need for the second injection when added to LA solution in the percaruncular block in myopic patients. Furthermore, it did not affect the quality of analgesia or the duration of the akinesia with low risk of drug-related complications.

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كفاءة إضافة عقار الآتراكيريم إلى التخدير محيط باللحيمة فى العين عند مرضى قصر النظر

المرضى الذين يعانون من قصر النظر المحورى (طول محورى أكثر من ٢٦ملم) هو معرضون لثقب العين بدون قصد أثناء حقن العين بالمخدر الموضعى من خلال الجزء السفلى الصدغى حول العين.

منطقة حول الحيمى خالية نسبيا من الأوعية الدموية، مما يقلل من الناحية النظرية خطر تكون تجمع دموى خلف العين. وجدت بعض الدراسات أن الحقن المخدر الموضعى حول اللحيمة آمن وفعال خصوصا لمرضى قصر النظر المحورى.

أوضحت عدد من الدراسات أن إضافة عقار الآتراكيوريم إلى خليط المخدر الموضعى يقلل من الوقت اللازم لحدوث شلل تام لعضلات العين عند حقن العين بالمخدر الموضعى من خلال الجزء السفلى الصدغى حول العين.

أوضحت الدراسة الحالية أن إضافة عقار الآتراكيوريم إلى خليط الليدوكايين والبوبيفاكاين والهيالورنيداز فى التخدير المحيط باللحيمة فى العين عند مرضى قصر النظر يقلل من الوقت اللازم لحدوث شلل تام لعضلات العين وقللت من الحاجة إلى الحقن الثانى فى حالة فشل الحقن الأول من تحقيق شلل تام.

ولقد أوضحت الدراسة أيضا أن إضافة عقار الآتراكيوريم إلى خليط المخدر الموضعى لم تؤثر على بداية فقدان الشعور بالألم ولا مدة شلل عضلات العين. كما أوضحت أيضا الدراسة الحالية أن الحقن المخدر الموضعى حول اللحيمة أم وفعال خصوصا لمرضى قصر النظر المحورى لعمل إستحلاب العدسة.