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Safety of Low Dose Atracurium Added to Lidocaine, Bupivacaine and Hyaluronidase Mixture in Percaruncular Peribulbar Anesthesia for High Myopes Undergoing Phacoemulsification (A Randomized Controlled Trial)

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Abstract

Background: The current study explored the safety of adding low dose atracurium to lidocaine, bupivacaine and hyaluronidase mixture in percaruncular peribulbar anesthesia for high myopes undergoing phacoemulsification.

Methods: 82 ASA-PS I-III patients scheduled for phacoemulsification with high myopia were enrolled in this randomized controlled double-blinded trial. The enrolled patients were randomly allocated to one of two groups. Group C (n=41) 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=41) received the same mixture with 5mg atracurium. Patients' hemodynamics, peripheral O_2 saturation, occurrence of intraoperative pain and incidence of were recorded.

Results: There were no major complications in any of the 82 cases. The incidence of minor complications between both groups were comparative. Chemosis occurred in 12.2% of Group A and in 24.3% of Group C. Sub-conjunctival hemorrhage occurred in 4.9% of patients of both groups. Local hyperemia were only observed in Group A (7.3%) with no statistical significance.

Conclusion: Adding 5mg atracurium to LA solution did not increase the incidence of complications in percaruncular block in high myopes.

Key Words: *Lidocaine – Atracurium – Bupivacaine – Hyaluronidase – High myopes – Phacoemulsification.*

Introduction

THERE are several regional anesthetic techniques available for phacoemulsification procedures and the choice depend 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 inferotemporal puncture in both peri- and retro-bulbar blocks) [2-5].

Single medial canthal peri-bulbar injection (percaruncular) may provide a safer alternative to inferotemporal peri-and retro-bulbar 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 Non-Depolarizing Neuromuscular Blockers (ND-NMB) on the inferotemporal peri- and retrobulbar block has been described in many studies. The studied ND-NMB were atracurium, cis atracurium, and vecuronium. According to those studies, the use of ND-NMB as adjuvant to inferotemporal peri-and retrobulbar block provide early onset of akinesia in absence of any adverse effects [9-15].

The current study aimed to explore effect of adding low dose atracurium to local anesthetic mixture on incidence of complications, hemodynamics and peripheral O_2 saturation (SpO_2) in percaruncular peri-bulbar anesthesia for high myopes undergoing phacoemulsification.

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Patients and Methods

This was a single center parallel randomized controlled double-blinded trial conducted in Kasr Al-Ainy Hospital, Ophthalmology Surgical Theater, 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 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), 2.5 ml of bupivacaine 0.5% (Sunnypivacaine 0.5% 20 ml 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 1ml 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.

Pre-operatively, 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% 10ml 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. Blood pressure, heart rate (baseline, 5 minutes after local anesthetic injection, 5 minutes after the beginning of the operation) and peripheral O_2 saturation (SpO_2) (baseline and 5 minutes after local anesthetic injection) were recorded.

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 [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, 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 occurrence of major complications (retrobulbar hemorrhage, globe penetration, optic nerve damage, local anesthetic toxicity) or minor complications (chemosis, subconjunctival hemorrhage, diplopia or/and local hyperemia) was recorded.

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 and range. Categorical variables were presented as numbers and percentages. Wilcoxon Matched-Pair Signed-Rank was used to compare paired non-parametric 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 were needed for the study (MedCalc® version 12.7.1.0-64-bit).

Results

82 patients scheduled for phacoemulsification in Kasr Al-Ainy Hospital were enrolled in the current study and randomly allocated into two groups [Group A (n=41) and Group C (n=41)] from May, 2015 to May, 2016.

As regards the demographic characteristics of both groups, there were no significant statistical difference (Table 1).

Table (1): Demographic 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 (53.7)	22 (53.7)	1
Male	19 (46.3)	19 (46.3)	
Axial length (mm)	29.1±2.12	29 ±2.28	0.677
Need for sedation n (%)	11 (26.8)	12 (29.3)	0.806
Duration of the surgery (min.)	45.5±12.73	47.3±15.69	0.601
Posterior staphyloma n (%)	3 (7.3)	4 (9.7)	0.765
ASA-PS n (%):			
I	19 (46.3)	17 (41.5)	0.656
II	20 (48.8)	18 (43.9)	0.658
III	2 (4.9)	6 (14.6)	0.264

Numerical data were presented as mean ± SD, categorical data were presented as frequency (%), $p<0.05$ considered statistically significant.

There was no statistically significant deference regarding the hemodynamic changes between the two groups, furthermore there was no statistical significant difference between the hemodynamic readings inside each group (Table 2).

Table (2): Hemodynamic changes.

	Group A (N=41)	Group C (N=41)	*p** value
MAP:			
• Base line	90.1±11.07	92.7±12.92	0.219
• 5min. after LA injection	89.7±10.57	92.2±12.52	0.408
• 5min. after procedure onset	89.7±11.30	92.4±12.59	0.503
• At regaining full ocular movement	89.9±10.97	92.6±12.50	0.345
• *p#*	0.276	0.359	
HR:			
• Base line	75.0±8.63	74.6±8.86	0.949
• 5min. after LA injection	74.9±8.14	74.7±8.12	0.896
• 5min. after procedure onset	74.2±7.89	74.2±8.40	0.969
• At regaining full ocular movement	73.6±6.80	73.2±7.40	0.708
• *p#*	0.250	0.195	

Numerical data were presented as mean ± SD.
*p**<0.05 was considered statistically significant when both groups were compared together.
p#<0.05 was considered statistically significant when 5min. after onset of procedure reading compared to baseline reading within the same group.

SpO_2 readings were recorded (on nasal O_2 cannula) at baseline and 5 minutes after local anesthetic injection. There was no statistical significant deference in SpO_2 readings between the two groups (Table 3).

Table (3): SpO_2 changes.

	Group A (N=41)	Group C (N=41)	*p*-value
• Base line	98.8±1.17	98.8±1.11	0.755
• 5 minutes after local anesthetic injection.	98.8±1.12	98.7±1.02	0.753

Numerical data were presented as mean ± SD, $p<0.05$ considered statistically significant.

Regarding the incidence of complications, there was no major complications in any of the 82 cases. As regard minor complications, there was no statistical significant difference in the incidence of minor complications between both groups (p= 0.666) (Table 4).

Table (4): Incidence of complications.

	Group A (N=41)	Group C (N=41)	p-value
Total No. of complications n (%).	10 (24)	12 (29)	0.666
Chemosis n (%).	5 (12)	10 (24)	0.153
Subconjunctival Hemorrhage n (%).	2 (5)	2 (5)	1
Local hyperemia n (%).	3 (7)	0 (0)	0.241

Categorical data were presented as frequency (%), p-value <0.05 considered statistically significant.

Chemosis and sub-conjunctival hemorrhage were managed conservatively. Local hyperemia were only observed in Group A (3 cases) and were managed by I.V steroid. Local hyperemia resolved by the time of completion of the surgery.

Discussion

Due to the presence of staphylomas, myopic patients are at increased risk of globe perforation following inferotemporal punctures in both peri- and retro-bulbar blocks **[2-5]**. Because of that, available regional anesthetic techniques for phacoemulsification would be either topical, sub-Tenon's or medial canthal block. The use of topical anesthesia preserved to an experienced surgeon, uncomplicated surgery and cooperative patients **[1]**. It was observed that not many ophthalmic surgeons nor anesthetists (residents and senior registrars) are experienced with sub-Tenon's block in kasr al-ainy hospital. Medial canthal peribulbar (percaruncular) technique provide a good and familiar alternative for myopic patients.

While many studies demonstrated the effect of adding ND-NMB to peri-and retrobulbar regional block on achieving better akinesia, the current study demonstrated the effect of adding low dose atracurium to lidocaine, bupivacaine and hyaluronidase mixture on on incidence of complications, hemodynamics and peripheral O_2 saturation (SpO_2) in percaruncular peri-bulbar anesthesia for high myopes undergoing phacoemulsification.

There were no statistically significant differences in peripheral oxygen saturation, mean blood pressure and heart rate values between Groups A and Group C during the study. This was comparative with Küçü kyavuz et al., **[16]** findings. Also the mean blood pressure and heart rate variability were not significant within each group. While other studies that tested the effect of ND-NMB did not comment on hemodynamic changes nor SpO_2 changes **[10,12-15]**.

Other studies that used ND-NMB as well as the current study did not report any major systemic or local complications related to the drug nor the used technique **[10-15,17]**.

The incidence of chemosis was comparative between the 2 groups (12% (5/41) in Group A and 24% (10/41) in Group C. Chemosis was not reported by other studies that used ND-NMB. This could be due to the use of techniques other than percaruncular injection in those studies **[10-14,17,18]**.

Sub-conjunctival hemorrhage occurred in 4 cases (2 (4.9%) in each group). While A. Abdellatif et al., **[12]** reported Sub-conjunctival hemorrhage in 6 (20%) patients in control and 8 (27%) in rocuronium, this might be due to giving double injections from the start.

While chemosis and subconjunctival hemorrhage could be attributed to the used technique, we observed 3 cases of local hyperemia in Group A which was not reported in studies that used atracurium in ophthalmic regional blocks **[13,15,16]**. Local hyperemia managed by giving I.V steroid and was resolved at the time of completion of the procedure. The occurrence of local hyperemia might be due to local histamine release effect of atracurium **[19]**.

In conclusion, adding 5mg atracurium to LA solution in the percaruncular block in myopic patients did not affect patients' hemodynamics nor SpO_2 with low risk of drug-related complications.

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كفاءة وسلامة إضافة جرعة منخفضة من عقار الآتراكيريم إلى الليدوكاين، البوبيفاكاين والهيالورونيداز فى التخدير محيط باللحيمة فى العين عند مرضى قصر النظر الذين يخضعون إلى إستحلاب العدسة

المرضى الذين يعانون من قصر النظر المحورى (طول محورى أكثر من ٢٦ملم) هم 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 الإتراكيوريم 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.

الهدف من الدراسة الحالية التعرف على تأثير إضافة عقار الإتراكيوريم إلى خليط الليدوكايين والبوبيفاكاين والهيالورنيداز فى التخدير المحيط باللحيمة على ضغط الدم وضربات القلب ونسبة الآكسجين فى الدم ونسبة حدوث المضاعفات الموضعية فى العين.

وجدت الدراسة أن إضافة عقار الإتراكيوريم إلى خليط التخدير المحيط باللحيمة لا يزيد خطر المضاعفات ولا يؤثر على ضغط الدم وضربات القلب ونسبة الآكسجين فى الدم. كما أوضحت أيضا الدراسة الحالية أن الحقن المخدر الموضعى حول اللحيمة آمن وفعال خصوصا لمرضى قصر النظر المحورى لعمل إستحلاب العدسة.