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Research Article

Adding low dose rocuronium to local anesthetic mixture: Effect on quality of peribulbar blockade for vitreoretinal surgery

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KEYWORDS

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Abstract *Background:* The purpose of this study was to assess the effect of adding low dose rocuronium to local anesthetic solution on the quality of peribulbar blockade for vitreoretinal (VR) surgery.
Methods: 80 consecutive adult patients scheduled for VR surgery were enrolled in this double-blind randomized clinical trial. Patients were categorized randomly into 2 equal groups: group C (control group) received local anesthetic mixture (4 ml lidocaine 2%, 4 ml bupivacaine 0.5%, and hyaluronidase "30 U/ml") plus 0.5 ml normal saline, and group S (study group) received the same local anesthetic mixture plus 5 mg (0.5 ml) rocuronium. Globe and lid akinesia were assessed 15 min after injection, and supplemental peribulbar blockade was done in case of inadequate analgesia and or akinesia. Intraoperatively, supplementary sub-Tenon infiltration was performed in case of inadequate analgesia and/or akinesia. Measurement data included rate of supplementation, analgesic efficacy, time to first sub-Tenon infiltration, and total anesthetic volume. Major complications, and patient's and surgeon's satisfaction were also recorded.
Results: The adequacy of peribulbar blockade 15 min after injection was comparable in both groups. Rate of supplementary sub-Tenon infiltration was lower in the rocuronium group which is statistically significant (15 injections versus 53 injections in the control group). Time to first sub-Tenon infiltration was significantly prolonged in the rocuronium group (90.4 + 11.8 versus 60.2 + 9.2 in the control group). The total anesthetic volume injected was significantly lower in the rocuronium group (13.2 + 0.6 versus 20.6 + 0.8 in the control group). There were no major systemic or local complications in both groups. Patient's and surgeon's satisfaction was significantly higher in the rocuronium group.
Conclusion: Adding low dose rocuronium to local anesthetics prolongs duration of peribulbar anesthesia and offers an optimal surgical condition without serious adverse effects for patients undergoing VR surgery.

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1. Introduction

Peribulbar blockade has been widely performed for anterior segment surgery as it provides the same effect as retrobulbar anesthesia, but with a lower complications rate [1]. On the other hand, the lengthy VR surgery that has un-predictable and uncomfortable nature often necessitates general anesthesia; however, there are many trials proved the safety and efficacy of local anesthesia in this type of surgery [2–4].

Previous studies demonstrated that ophthalmic procedures more than 2 h duration needed an anesthetic adjuvant and cannot be performed using the mere standard anesthetics [5,6]; moreover, it may be necessary to add two adjuvants to prolong the duration of local anesthetics [7]. Extending the duration for LA has been also achieved by supplementary sub-Tenon's infiltration or indwelling catheter technique in other studies [8–10].

The efficacy of adding neuromuscular blockers to the standard LA for anterior segment surgery performed under peribulbar block has been previously studied [11–15]. To the best of our knowledge, there were no trials studied the use of neuromuscular blockers as an adjuvant to the peribulbar blockade for VR surgery. We hypothesis that, for VR surgery, adding low dose neuromuscular blocker to the peribulbar LA solutions may prolong duration, optimize both globe and lid akinesia and analgesia, and may limit intraoperative sub-Tenon supplementation.

2. Patient and methods

After obtaining the approval of the local ethical committee, and Informed written consent from each patient, 80 adult patients scheduled for VR surgery in Zagazig University Hospitals of either sex from the beginning of June 2013 to the end of May 2014 were included in this prospective double-blind randomized clinical trial. Exclusion criteria included patients younger than 18 years, patients who refused local anesthesia, those with single eye, ocular infection, and when the decubitus position was impossible. Patients with communication problems, coagulopathy, impaired consciousness, and mental retardation, were also excluded from the study.

Preoperative investigations in the form of electrocardiography (ECG), complete blood picture (CBC), coagulation profile, liver function, kidney function, and biometry were done for every patient. All patients received no premedications.

In the anesthetic room, an intravenous line was inserted, basic monitors were applied (5-lead ECG, pulse oximeter, automated non-invasive blood pressure "NIBP"), and a nasal cannula 2 L/min was attached. Monitoring and oxygen therapy were continued for all patients throughout the procedure. Topical anesthesia of the conjunctiva and cornea was provided by administering 2–3 drops of Benoxinate hydrochloride 0.4%. Titrated doses of Midazolam 0.5 mg and/or 20 uq fentanyl were administered 5 min before peribulbar injection with a target to keep the patient calm and cooperative.

Participants were randomly allocated using a closed envelope into two equal groups according to the type of the test drug: group C (control group) received a local anesthetic mixture (4 ml lidocaine 2%, 4 ml bupivacaine 0.5%, and hyaluronidase "30 U/ml") plus 0.5 ml normal saline, and group S (study group) received the same standard local anesthetic mixture (4 ml lidocaine 2%, 4 ml bupivacaine 0.5%, and hyaluronidase "30 U/ml") plus 5 mg (0.5 ml) rocuronium.

The LA solution used for each patient was revealed by opening sealing envelopes, and then prepared by the same nurse anesthetist who drew up the LA mixture and provided an unlabelled syringe to the same anesthetist who performed all blocks and were unaware of the LA nature.

After sterilization, the solution study was injected after negative aspiration using a 27 G 16 mm needle according to the injection site described by Rizzo et al. [16], percutaneous and limited superiorly from the inferior lacrimal canaliculus, median from lateral margin of the nose, laterally from imaginary perpendicular line that joins the inferior lacrimal papilla to the inferior margin of the orbit and inferiorly from the inferior margin of the orbit. The needle was advanced percutaneously in an anteroposterior direction for half of its length (never more than 10 ml) and later obliquely in the direction of the orbital foramen. End points of injection were proptosis, fullness of the upper eyelid, or when the globe became subjectively tense. As soon as the globe became soft, the injection was started again until the globe becomes tense again. A gentle digital massage of the eyeball was done for one minute followed by application of a Hanon balloon inflated to 30 mmH_2O for 15 min.

After removing the balloon, analgesia, ocular and eyelid movements were evaluated by the same surgeon who was also blinded to the LA solution used. Analgesia was considered to be perfect when the patient did not notice any pain on holding bulbar conjunctiva and lateral rectus muscle insertion. Eyelid and globe akinesia were assessed by the scoring system described by Brahama et al. [17] (Table 1); Patients were asked to squeeze the eye while it is opened in by the surgeon's hand (score of 2 if eyelid moves freely, score of 1 if it is flickering only, and score of 0 if there is no movement). Globe movement was scored for each direction of gaze with a total sum of 12 (score of 3 = full movement, score of 2 = moderate movement, score of 1 = flicker movement, and score of 0 = no movement). If the block was inadequate (presence of any sensation, total inability to squeeze the eyelid, or globe movement score of 2 or more in any direction), a supplementary injection was performed via the same approach, using 3–6 ml of lidocaine 2%, and then, the Hanon balloon was reapplied again for 10 min. If eyelid or globe movements score still more than 2 in any direction, the block was considered to be failed.

If the patient experienced considerable pain and/or the eyelid and or globe akinesia was inadequate to a degree that disturbs the operating surgeon, a supplemental lidocaine 2%

Table 1 Scoring system for degree of akinesia.

Ocular movement	
Full movement	3
Moderate movement	2
Flicker	1
No movement	0
Eyelid movement	
Full movement	2
Flicker	1
No movement	0

(5–8 ml) was administered by sub-Tenon infiltration by the surgeon as described by Calenda et al. [8]; A buttonhole was fashioned through the conjunctiva and the Tenon's capsule 10 mm posterior to the limbus in the temporal superior quadrant, then, the anesthetics delivered using a blunt cannula.

The study parameters were recorded using a data collecting form by the same anesthetist, who performed all blocks and as said before, were unaware of the anesthetic mixture administered.

Measurement parameters included patient's characteristics, duration and type of surgery, efficacy of analgesia, supplementation rate, time to first sub-Tenon injection, total anesthetic volume, major complications, patient and surgeon's satisfaction. The efficacy of analgesia was graded as follows: grade 1-adequate analgesia throughout surgery without any supplementation; grade 2-adequate analgesia with sub-Tenon injection; and grade 3-inadequate analgesia despite the sub-Tenon injection [5].

Postoperatively, surgeons assessed the quality of anesthesia either it was satisfactory or not. Patients were questioned about their experience intraoperatively either it was comfortable, mildly uncomfortable or intensely uncomfortable.

2.1. Statistical analysis

Before carrying out statistical inferential tests, variables were tested for normal distribution. Normal distribution was assumed based on graphical presentation of bar charts and values of skewness and kurtosis – according to descriptive data feature in SPSS program – between (+1) and (−1) for all variables.

All the data collected were fed into Statistical Package for Social Sciences (SPSS version 19). Data were compared by using the *t*-test and expressed as mean ± standard deviation (Mean ± SD). Scores were presented as median (range). Comparison of percentages was performed using the Fisher's exact method. *P*-value of <0.05 was considered as significant, and *P*-value of <0001 was considered as highly significant.

3. Results

It was found that there were no significant differences between the study groups as regards the age, sex and ASA physical status distribution, duration and type of surgery and axial length (Table 2).

Analgesia and eyelid akinesia were completed at 15 min after injection for all patients in the study groups. Movement's score for globe and lid akinesia was comparable in both groups. Only one patient in the Rocuronium group and 2 patients in the control group needed a supplementary peribulbar injection. Primary and supplementary LA volumes were also comparable in both groups. No reported cases of failed peribulbar block in both groups (Table 3).

Efficacy of analgesia is shown in Table 4; Supplementary sub-Tenon infiltration was significantly lower in the rocuronium group (15 injections versus 53 injections in the control group). Time to first sub-Tenon supplementation was significantly longer in the rocuronium group (90.4 ± 11.8 min. versus 60.2 ± 9.2 min. in the control group) (*P*-value $<$ 0.001). 27 patients in the rocuronium group versus 9 patients in the control group needed no supplementations, while 13 patients needed a variable supplementation rate in the rocuronium group versus 31 patients in the control group (*P*-value $<$ 0.001). There were no reported cases of inadequate analgesia in both groups.

Table 2 Patient's characteristics.

	Study group (n = 40)	Control group (n = 40)
Age (years)	54 ± 8	52 ± 9
Sex (Male/female)	28/12	26/14
ASA (number)		
I	13	15
II	25	22
III	2	3
Duration of surgery (min.)	144.4 ± 14.4	148.6 ± 15.8
Type of surgery (number)		
Vitrectomy	16	14
Retinopexy + vitrectomy	11	12
Scleral buckling	13	14
Axial length	24.4 ± 0.8	23.3 ± 0.7

Data presented as mean ± SD or numbers.

Table 3 Adequacy of peribulbar block 15 min post-injection.

	Study group (n = 40)	Control group (n = 40)
Complete analgesia	40 (100%)	40 (100%)
Globe akinesia score	2 (4)	2 (4)
Eyelid akinesia score	0	0
Primary LA volume (ml)	7.6 ± 0.6	7.8 ± 0.7
Supplementation rate	1	2
LA supplementation volume (ml)	5	8
Block failure	0 (0%)	0 (0%)

Data presented as mean ± SD, median (range), numbers or percentage.

Table 4 Sub-Tenon infiltration, and total anesthetic volume.

	Study group (n = 40)	Control group (n = 40)
Sub-Tenon infiltration injections	15	53†
Time to first sub-Tenon infiltration (min)	90.4 ± 11.8	60.2 ± 9.2†
Analgesia adequacy		
Grade I	27	9
Grade II	13	31†
Grade III	0	0†
Total volume injected	13.2 ± 0.6	20.6 ± 0.8*

Data presented as mean ± SD or numbers.
*p value $<$ 0.05 = statistical difference.
†p value $<$ 0.001 = high statistical difference.

Total LA volume injected (primary peribulbar injection, peribulbar supplementation, and the subsequent sub-Tenon infiltration) was 13.2 ± 0.6 in the rocuronium group versus 20.6 ± 0.8 in the control group (p value $<$ 0.001).

None of the patients required conversion to general anesthesia. Major local or systemic complications were not encountered in this series. Patients' and surgeon's satisfaction was statistically higher in the rocuronium group (p value < 0.001) (Table 5).

4. Discussion

We found that adding rocuronium 5 mg to LA solutions optimized block and prolonged duration of peribulbar anesthesia for patients undergoing VR surgery.

Adding small dose of neuromuscular blocker has been shown to improve efficacy and prolonged duration of neural blockade that cannot be achieved by the standard local anesthetic solution [18,19]. For ophthalmic anesthesia, the exact mechanism through which non-depolarizing muscle relaxant improves orbital and eyelid akinesia is not clear; however, it was explained by the local effects at the muscles motor endplate [13]. Moreover, the extra-ocular muscles are so sensitive to the effect of neuro-muscular blockers as the number of muscle fibers innervated by a single motor neuron is very small [12].

There were many clinical trials that studied the efficacy of adding neuromuscular blockers as adjuvant to the LA solution on the adequacy of peribulbar blockade. Two of these studies used a two injection technique (inferotemporal and medial injections); Reah et al. [12] who compared 5 ml of 2% lignocaine with 1:200,000 adrenaline, 5 ml 0.75 bupivacaine and 150 IU hyaluronidase with either 0.9% saline 0.25, or vecuronium bromide 0.25 ml (5 mg) found that vecuronium improves the quality of globe and lid akinesia without side effects. Moreover, Kucukyavuz et al. [11], compared 8 mL of a lidocaine–bupivacaine mixture plus 0.5 mL (5 mg) atracurium without hyaluronidase and the same amount of the same local anesthetic mixture plus 0.5 mL 0.9% NaCL. The time to the onset of akinesia in minutes was better in the atracurium group; moreover, they also demonstrated an adequate globe and lid akinesia. In our study, a single infero-medial injection was used as it has been established to be more safe and effective than the two injection technique [20]. This finding was demonstrated in our study, as the ocular movement sore was comparable, and only three peribulbar supplementations were recorded in both groups. Also, there were no recorded cases of failed block.

In another study, the authors used a single inferotemporal technique. They added rocuronium 0.06 mg/kg to the bupivacaine–lidocaine mixture without hyaluronidase. Rocuronium improved akinesia scores at 2, 5 and 10 min postinjection with a lower supplementation rate [13].

In the previous 3 studies, neuromuscular blockers were used as an adjuvant for peribulbar anesthesia for patients undergoing cataract surgery. On the other hand, adding atracurium to the standard LA shortened the onset time and prolonged the duration, and provided excellent surgical conditions without known complications of retrobulbar block in one study [21], and sub-Tenon in the other [22]. In the current study, we report the akinesia score only after 15 min peribulbar injection, so unfortunately we did not study the onset of block in the study population.

The rate of sub-Tenon infiltration was highly significant in the Control group (53 injections versus 15 injections in the Rocuronium group). Calenda et al. [8] reported 15% reinjection rates (2–3 ml lidocaine 2%) in a series of 300 patients with 1% failure rate; Supplementary sub-Tenon injection (5–8 ml lidocaine 2%) was 20% in another series that included 141 cases with a 3% failure rate [1]. These two studies had a lower supplementation rate than our study which may be explained by the difference in the type and volume of LA and more importantly the duration of surgery.

As was reported in previous studies [1,15], we did not encounter cases of retinal ischemia or ischemic optic neuropathy despite the relatively larger volume of injected anesthetic than used for peribulbar injection for cataract surgery. The precaution of avoiding anesthetics injection while the globe was tense was responsible for avoiding these life-threatening complications. Also, we did not report any major cardiac, respiratory, or neurologic adverse effects as was observed in previous trials [1,2,14].

There were two important limitations in the present study. The first limitation is the relatively small number of patients; the second one is that the neuro-muscular tracing was not monitored in the study populations. The systemic reabsorption of neuromuscular blocker from peribulbar injection with its potential risk of muscular weakness as was reported by Allan [23] still considered an important issue; however, the relatively large dose of neuromuscular blocker (four times the normal dose) was responsible for the systemic absorption in his report. On the other hand, Aissaoui et al. [13] who used a dose of rocuronium comparable to the present study (0.06 mg/kg) reported no alteration in the neuromuscular function with train of four (TOF) monitoring.

So, further study is recommended on a large number of patients with a close neuromuscular monitoring to confirm the efficacy and safety of adding neuromuscular blocker to the standard peribulbar anesthetic solution for patients undergoing VR surgery.

Table 5 Postoperative questionnaire and complications.

	Study group ($n = 40$)	Control group ($n = 40$)
Surgeon satisfaction		
Good	11	28†
Satisfactory	13	9*
Unsatisfactory	16	3†
Patient satisfaction		
Comfortable	10	35†
Mildly uncomfortable	22	5†
Intensely uncomfortable	8	0†
Complications		
Local and systemic	0 (%)	0 (%)

Data presented as numbers or percentage.
*p value < 0.05 = statistical difference.
†p value < 0.001 = high statistical difference.

5. Conclusion

It can be concluded that, adding low dose rocuronium to local anesthetic mixture prolongs peribulbar block and provides optimal surgical conditions for patients undergoing VR surgery.

Conflict of interest

The authors showed no conflict of interest.

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