A Comparison of 1% Ropivacaine and 1% Ropivacaine with Clonidine for Retrobulbar Block

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Citation
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Abstract
Background and Objectives: To compare the efficacy of 1% ropivacaine as a sole agent and ropivacaine with additional clonidine for retrobulbar (intraconal) anesthesia in cataract surgery.

Methods: Sixty patients undergoing retrobulbar anesthesia for elective cataract phacoemulsification were prospectively studied and randomly assigned to 1 of 2 groups according to the local anesthetic used. Patients were randomized to receive 1% ropivacaine (ropivacaine group) or 1% ropivacaine with additional clonidine 1 µg/kg (ropivacaine plus clonidine group). Retrobulbar anesthesia was always accomplished by the same physician who was blind to the anesthetic used. Evaluation included assessment of pain on local anesthetic injection, ocular and eyelid akinesia, intraocular pressure (IOP), the duration of anesthesia, hemodynamic parameters, and incidence of perioperative complications.

Results: No difference between the groups was found regarding the ocular movement. There was no difference in terms of IOP. Retrobulbar injection caused a significant drop of IOP in both of the groups (p<0.05). There was no significant difference among the study groups in terms of visual analog scale (VAS) for retrobulbar injection (p>0.05). Lid injection was less painful in the ropivacaine plus clonidine group (p<0.05). Lid injection was more painful than the retrobulbar injection for both of the groups (p<0.05). Mean arterial pressure (MAP) was not significantly different between the study groups. Heart rate (HR) was significantly lower in the ropivacaine plus clonidine group (p<0.05).

Conclusion: 1% ropivacaine is effective as a sole agent for retrobulbar anesthesia with a long recovery time. Additional clonidine to 1% ropivacaine for retrobulbar injection had no clinically significant benefit.

INTRODUCTION
Ropivacaine is an aminoamide local anesthetic agent with a greater margin of safety than bupivacaine for cardiotoxicity and central nervous system toxicity \cite{1,2}. The efficacy and safety of ropivacaine for anesthesia during cataract surgery is well studied, \cite{3,4,5,6,7,8} with most of the studies using a peribulbar technique and hyaluronidase to facilitate the onset of anesthesia and akinesia. Topical anesthesia is a much more preferred technique than regional anesthesia as revealed by a survey \cite{9}. However, topical anesthesia may not be appropriate for all and regional anesthesia should be performed for certain cases \cite{9}.

There is a reduced risk of globe perforation and optic nerve damage with peribulbar (extraconal) than retrobulbar (intraconal) injections however, a greater volume of anesthetic solution must be used and peribulbar anesthesia may be associated with postoperative diplopia, transient intraocular pressure (IOP) elevation, and a shorter duration of anesthesia \cite{10,11,12,13,14}. Retrobulbar injection is still a common procedure at many institutions especially when hyaluronidase is not available and a fast and reliable akinesia is needed for teaching purposes. Intraconal injections are also useful to provide reliable sensory and motor blocks which needed for corneal transplantations and for vitreoretinal surgery.

Uy et al. \cite{15} have shown the combination of 2% ropivacaine and 2% lidocaine is equal to a mixture of 0.5% bupivacaine and 2% lidocaine in producing ocular analgesia and akinesia for extracapsular cataract extraction (ECCE) anesthesia using a retrobulbar technique. However, they did not study the duration of akinesia, therefore we aimed to investigate the duration of akinesia obtained with retrobulbar injection.
A Comparison of 1% Ropivacaine and 1% Ropivacaine with Clonidine for Retrobulbar Block

There are very few studies using an alpha-2 adrenoreceptor agonist clonidine in ophthalmic blocks, and these have shown contradictory results. Mjahed et al. [16] used 2 µg/kg clonidine with 2% lidocaine for retrobulbar block and found increased duration of analgesia and akinesia with a decrease in intraocular pressure and recommended its use. However, Connelly et al. [17] did not find any significant effect of 100 µg clonidine added to 1% lidocaine on the onset time and postoperative analgesic requirement after peribulbar block.

We aimed to evaluate the duration and quality of anesthesia obtained with 1% ropivacaine via intraconal injection in a prospective double-blind study. We also assessed the effects of additional clonidine 1 µg/kg on cardiovascular system, IOP, and quality of block.

METHODS

We obtained approval from the Celal Bayar University Medical Faculty Research Ethics Committee. Patients who will have unilateral ECCE with phacoemulsification under local anesthesia without sedation were eligible for the study and all of the patients who took part in the study provided informed consent. Patients were excluded if they had a history of allergy to amide-type anesthetic agents, or if they were unwilling to take part.

Computer generated numbers equal to the number of patients who were scheduled for the study was put into sealed envelopes. Before surgery an envelope containing the random number was drawn for each patient. If the number was even, a solution of 8 mL ropivacaine 1% was prepared (n = 30). If the number was odd, a solution of 8 mL ropivacaine 1% plus 1 µg/kg was prepared (n = 30) by one of the authors, he was no further involved in data collection, and surgery. The patient, anesthesiologist, and surgeon were masked to which anesthetic agent would be used.

A baseline intraocular pressure (IOP) measurement was provided after instilling proparacaine 0.5% with Schiotz tonometer. A single surgeon did all the blocks. A 23-gauge, 38 mm needle was introduced through the skin at the area of the infraorbital notch. The needle is passed posteriorly parallel to the plane of orbital floor at angle of 10° to the horizontal until the tip passes the equator of the globe. Then the needle is directed slightly upward and medially when the hub of the needle reached the plane of the iris, the anesthetic was slowly injected after aspiration. This was followed by van Lint injection to the upper eyelid only of the mixture to block the orbicularis muscles and obtain lid anesthesia.

Patients graded eye pain using a visual analog scale system (VAS) from 0 (no pain) to 10 (worst imaginable pain). VAS was obtained for retrobulbar injection and lid injection separately.

The IOP was measured with Schiotz tonometer at the 5 min, 10 min, and 15 min after the injection. We did not elect to use a pressure lowering device such as a Honan balloon as frequent readjustments in between the measurements would render the procedure inconvenient. Gentle globe massage was applied between the measurements. The total amount of globe excursion in the superior, inferior, medial and lateral directions of gaze was measured with a ruler using the limbus as a reference point. The movement of the globe was measured at the 1 min, 5 min, 10 min, and 15 min.

Sedation scores were obtained by a blinded observer at baseline, 1, 5, 10, and 15 min following retrobulbar block, intraoperatively and postoperatively. The level of sedation was assessed using Ramsay sedation scale (0, anxious or agitated or both, 6, no response to a light glabellar tap) [18]. Nausea was monitored on a four-point scale (0, no nausea or vomiting; 1, mild nausea; 2, severe nausea, 3, retching or vomiting) [19]. When nausea and vomiting was score 2 and more, patients were given i.v. metoclopramide 10 mg.

Blood pressure (BP) was monitored noninvasively every 5 minutes throughout surgery, and heart rate (HR) and peripheral oxygen saturation (SpO2) were continuously monitored throughout surgery. A decrease in mean arterial pressure (MAP) greater than 15% below preanesthetic baseline was treated by incremental doses of ephedrine, 5 mg IV. Decreases in HR below 50 bpm were treated with incremental doses of atropine 0.25 mg IV. Intraoperative adverse effects were assessed by the anesthesiologist who was unaware of the groups.

The parametric data such as age, the sum of the movement of the eye in millimeters to four cardinal positions, mean arterial pressure, heart rate, are expressed as mean ± SD and compared using the unpaired Student's t-tests. Within group comparisons was made by analysis of variance (ANOVA) test. We used Pearson $\chi^2$ test and Fisher's exact test to compare the number of reinjections between the two groups and the percentages of patients who were ready for surgery at the 10 th minute. All comparisons were two-tailed, and p values of <0.05 were considered significant.
RESULTS

The groups were comparable in terms of demographic data including age, male: female ratio, weight and ASA status and duration of surgery and no significant difference was detected (p>0.05) (Table 1).

Figure 1

Table 1: Demographic data of patients.

<table>
<thead>
<tr>
<th></th>
<th>Ropivacaine (n=30)</th>
<th>Ropivacaine plus clonidine (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>65.6±10.6</td>
<td>70.3±8.3</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>180.0±3.9</td>
<td>171.5±4.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.6±10.9</td>
<td>70.4±9.1</td>
</tr>
<tr>
<td>ASA Grade (I/II)</td>
<td>22/5/3</td>
<td>20/6/4</td>
</tr>
<tr>
<td>Gender (m/f)</td>
<td>12/18</td>
<td>17/13</td>
</tr>
<tr>
<td>Duration of surgery</td>
<td>49.5±8.6</td>
<td>50.0±12.7</td>
</tr>
</tbody>
</table>

There were no statistically significant differences in total globe movement in the 4 directions of gaze between the 2 groups at 1 min, 5 min, 10 min, 15 min after infiltration and at 2 h, and 8 h postoperatively (Table 2). There was not any significant difference between the groups regarding the lid movement at 1 min, 5 min, 10 min, and 15 min after infiltration and at 2 h, and 8 h postoperatively.

Figure 2

Table 2: Ocular movement measurements. There was no difference between the groups (p>0.05).

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Ropivacaine (n=30)</th>
<th>Ropivacaine plus clonidine (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.4±4.7</td>
<td>5.7±5.9</td>
</tr>
<tr>
<td>5</td>
<td>8.5±4.6</td>
<td>9.8±7.9</td>
</tr>
<tr>
<td>10</td>
<td>6.3±4.2</td>
<td>13.1±4.8</td>
</tr>
<tr>
<td>15</td>
<td>4.3±3.8</td>
<td>9.4±5.3</td>
</tr>
<tr>
<td>180</td>
<td>4.9±4.4</td>
<td>7.1±5.7</td>
</tr>
<tr>
<td>480</td>
<td>7.9±6.9</td>
<td>4.0±3.8</td>
</tr>
</tbody>
</table>

Mean pain on intraconal injection was 4.4±2.3 for the ropivacaine group and 5.3±3.1 for the ropivacaine plus clonidine group. There was no significant difference between the two groups (p>0.05).

Mean pain on lid injection was 7.5 for the ropivacaine group and 6.5 for the ropivacaine group. Lid injection was more painful in the ropivacaine group (p=0.025). Patients regarded lid injections significantly more painful than retrobulbar injections within both of the study groups (p<0.0001, and p=0.0346 respectively). Mean pain was 0.9 at the 3 h and 0.6 at the 9 h for the ropivacaine group. Mean pain was 0.4 at the postoperative 3 h and 0.9 at the 9 h for the ropivacaine plus clonidine group. Postoperative pain scores at 3 h and 9 h were not significant between the two groups (p>0.05).

There was not any significant difference between the study groups in terms of IOP before injection, at 5 min, 10 min, and 15 min after injection (p>0.05). The IOP at 5 min and 10 min after injection was significantly lower than it was before the injection for the ropivacaine group. The IOP at 5 min and 10 min after injection was significantly lower than it was before the injection for the ropivacaine plus clonidine group also (Figure 1).

Figure 3

Figure 1: Intraocular pressure (IOP) measured at baseline and after the retrobulbar anesthesia. There was no significant difference between groups (p<0.05). There was a significant difference within the ropivacaine group (p=0.026). Baseline versus 10 min *, p<0.05. There was a significant difference within the clonidine group (p=0.012). Baseline versus 15 min †, p<0.05; Baseline versus 15 min ‡, p<0.01.

There was no significant difference in terms of MAP between the study groups (Fig 2). There was no statistically significant difference of MAP from baseline for both of the study groups (Figure 2). HR was significantly lower in the ropivacaine plus clonidine group compared to ropivacaine group at the baseline and 1 min, 5 min, 10 min, and 15 min after the injection, at the start of surgery, at the 3 h, and 8 h postoperatively (Figure 3). There was no statistically significant difference of HR from the baseline for both of the study groups.
Figure 4
Figure 2: Mean arterial pressure (MAP) measured at baseline and after the retrobulbar anesthesia. There was no significant difference between the groups (p>0.05).

There was not a significant difference of sedation scores of the patients between the groups at any the start and at the conclusion of the surgery (p>0.05). Two patients had some degree of nausea during the injection period in the ropivacaine group. This was not statistically significant (p>0.05). No SpO2 lower than 94% was noted.

The groups were comparable in terms of reinjection rates. Four (13.3%) patients in the ropivacaine group and 3 (10.0%) patients in the ropivacaine plus clonidine group had reinjections (p>0.05). We have encountered no adverse events related to retrobulbar (intraconal) anesthesia, other than periorbital ecchymosis in one patient in the ropivacaine group.

DISCUSSION
We have shown that intraconal injections of 1% ropivacaine alone or a combination of 1% ropivacaine with 1µg/kg clonidine are effective to provide adequate motor and sensory block for cataract surgery. There have been concerns about the efficacy of ropivacaine as a sole agent for ocular anesthesia and in most of the studies ropivacaine has been combined with lidocaine to provide a quick onset of anesthesia [13,14]. We were able to achieve adequate anesthesia for cataract surgery in 15 min after the injection for all of our patients without using additional lidocaine. Nicholson et al. [13] have shown that peribulbar injection of 1% ropivacaine as the sole agent was comparable to a mixture of 0.75% bupivacaine and 2% lidocaine, although ocular motor scores were higher at 2, 4 and 6 min, for ropivacaine group than the bupivacaine and lidocaine group, both groups were similar at 8 min in terms of anesthesia. In a study comparing 0.5%, 0.75% and 1% ropivacaine, more than 80% of patients receiving peribulbar injections of 0.75 or 1% ropivacaine reported complete akinesia of the operated eye within the first 10 to 15 minutes after injection [15]. Huha et al. [4] have shown that 1% ropivacaine was faster than 0.75% bupivacaine in the onset of globe and lid akinesia. Perello et al. [8] have shown that the onset of action found to be slower for 0.5% ropivacaine than mixtures of 0.375% bupivacaine – 1% lidocaine and 0.5% ropivacaine – 1% lidocaine thus it seems that the onset of action for ropivacaine being concentration dependent.

A shorter duration of motor block is advantageous as prolonged paralysis from local anesthesia leaves the vulnerable to trauma and drying. Recently Uy et al. [15] have shown that a retrobulbar anesthesia with a combination of 1% ropivacaine and 2% lidocaine is effective as a combination of 0.5% bupivacaine and 2% lidocaine for cataract surgery, they have stated that retrobulbar injection of 1% ropivacaine resulted persistence of akinesia for 1 h after the injection, however they did not study the duration of akinesia. Epidural ropivacaine has been reported to be less potent than bupivacaine at the same concentrations in terms of motor blockade [13]. The reduced potency in terms of motor blockade thus seems to be advantageous for ropivacaine. There are few studies assessing the duration of ocular motor block obtained by ropivacaine and all of them are for peribulbar block. Huha et al. [4] have shown that 15 of 50 patients had partial recovery of eye movements at 6 h postoperatively, and all of the patients had complete recovery of ocular movement at 24 h. Giaoa et al. [13] have reported that 100% of patients had complete recovery at 7 h postoperatively who had received a peribulbar injection of 0.5% or 0.75% ropivacaine and 90% percent had complete recovery of motor function who had received 1%
ropivacaine. Most of the studies report a similar onset of duration of ropivacaine and bupivacaine with peribulbar injection \[1\,\text{to}\,3\]. To our knowledge this the first study, evaluating the duration of motor block obtained by retrobulbar ropivacaine. We have not used a scoring system but when considering at least 3 mm of eye movement to 4 directions of gaze, totaling 12 mm, and patients who had a total of 12 mm or more movement as had partial recovery. Six (20.0%) and 12 (39.6%) of our patients had partial recovery at 3 h and 8 h respectively in ropivacaine group. None of the patients had partial recovery of at 3 h and 11 (%36.3) had partial recovery at 8 h in the ropivacaine plus clonidine group. Sixteen (52.8%) and 26 (85.8%) of the patients had some eyelid movement at 3 h and 8 h respectively in the ropivacaine group. Eighteen (58.4%) and 27 (89.1%) of patients had some eyelid movement at 3 h and 8 h respectively in the ropivacaine plus clonidine. All of the patients were evaluated in the morning the day after the surgery which is a minimum of 18 h after; all of the patients had complete recovery of ocular and eyelid movement at that time. Although we have not systematically evaluated the extent of the sensory block, some of the patients complained of an ongoing numbness around the area of their operated eye which had resolved in the morning after the surgery.

Clonidine has been shown to prolong anesthesia via a mechanism involving direct action on nerve fibers \[3,25\]. This action might involve a drug interaction as it has been shown that very low dose clonidine increases the C-fiber blockade from lidocaine in an isolated nerve model \[3\]. Furthermore, the effect could be a result of direct action of clonidine on peripheral alpha-2 receptors \[23\]. Barioni et al. \[35\] have shown that prolonged anesthesia and analgesia were evident only in patients receiving peribulbar injections of clonidine whereas per oral clonidine did not show the same effect thus favoring a local action. In accordance with these, we have observed that lid injections were less painful in the ropivacaine plus clonidine group than the clonidine group.

Madan et al. \[17\] have shown that clonidine with 2% lidocaine and hyaluronidase mixture produces a dose-dependent prolongation of anesthesia and analgesia after peribulbar block. They have found prolonged globe akinesia and analgesia with doses of 1 µg/kg and 1.5 µg/kg clonidine but not with 0.5 µg/kg clonidine \[17\]. However, in a study for peribulbar block Connelly et al. \[17\] did not find any significant effect of 100 µg clonidine added to 1% lidocaine on the onset of akinesia, sedation, perioperative analgesic requirement, and satisfaction score, they did not study the duration of block. Although ocular movement was less at the postoperative 3 and 8 hours in the ropivacaine plus clonidine group, this was not statistically significant in the current study. The deep anesthesia obtained with ropivacaine may have blunted the effect of clonidine, and we have not observed a prolonged motor block with the addition of clonidine.

The ocular movement measurements of the two study groups were similar at 1 min, 5 min, 10 min, and 15 min after the injection. Some of the studies report a decrease in time to anesthesia with peribulbar or retrobulbar injection of clonidine \[16,23\]. Whereas some other studies report similar times to onset of anesthesia with or without the addition of clonidine to periorcular injectate \[7,23\]. Hutschala et al. \[3\] have also shown similar onset of anesthesia with or without clonidine in healthy volunteers undergoing a brachial plexus block. These studies differ in clonidine concentration and anesthetic agents that have been used and a direct comparison between them is difficult. We have not measured the time to adequate anesthesia in the current study, however ocular movement was similar between the study groups at fixed time intervals that we have measured. This the first study evaluating the effect of addition of clonidine to ropivacaine in retrobulbar injection, further studies measuring the time to onset of anesthesia will further clarify this issue.

A previous report revealed a lowering of IOP with retrobulbar and facial nerve block using clonidine \[16\]. However, Connelly et al. \[17\] did not find any significant effect of clonidine added to lidocaine on IOP. We did not observe a significant drop of IOP with the addition of 1 µg/kg clonidine to 1% ropivacaine. Ropivacaine have been reported to decrease IOP when used in peribulbar blocks \[20,24\]. We had observed a significant decrease of IOP after retrobulbar injection in both of the groups. In our patients, there was a decrease in IOP 5 min after the injection which became significantly less than basal IOP in the following 10 and 15 minutes. It is has been hypothesized that the initial effect on IOP is largely caused by muscle relaxation; and the lower IOP later on could be largely caused by vasoconstriction induced by ropivacaine \[3\]. This drop of IOP obtained by ropivacaine may have overshadowed the IOP lowering effect of clonidine in the current study.

A dose dependent incidence of adverse events such as bradycardia, sedation and hypotension has been observed with the addition of clonidine to the local analgesic \[3\]. In

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accordance with these we have observed a significantly lower HR with the addition of clonidine 1.0 µg/kg to the local anesthetic. MAP in the ropivacaine plus clonidine group was lower than the ropivacaine group, however this was not statistically significant. None of the patients required treatment for bradycardia or hypotension. We have used clonidine in a concentration of 1.0 µg/kg. Madan et al. have reported that addition of 1.0 µg/kg of clonidine to the local anesthetic for peribulbar block produced a decrease in the MAP and HR which was not clinically significant. The proximity of intraconal injection to the optic nerve, and the effect of clonidine centrally through the optic nerve sheath might be responsible for decreased HR we have observed.

Our results have shown that intraconal injection of 1% ropivacaine as a single agent produced a reliable and dense anesthesia with a very long recovery time. 1% ropivacaine might be appropriate for rather long procedures such as complex cataract surgery, or vitreoretinal surgery. The prolonged duration of akinesia may be disadvantageous as it will render the eye susceptible to trauma and drying. We have observed that clonidine eased the pain of lid injection to some degree and decreased the HR, other than this, the surgical and postoperative periods were similar between two study groups. We have not observed any other benefit or adverse effect of clonidine 1 µg/kg. We may conclude that 1% ropivacaine is an effective anesthetic as a sole agent for retrobulbar anesthesia, however it has a long recovery period, and the addition of clonidine 1 µg/kg is not necessary as a supplement to 1% ropivacaine.

References
8. Perello A, George J, Skelton V, Pateman J (2000) A double-blind randomized comparison of ropivacaine 0.5%, bupivacaine 0.375% - lidocaine 1% and ropivacaine 0.5% - lidocaine 1% mixtures for cataract surgery. Anesthesia 55:1003-1024.
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