ORIGINAL RESEARCH

REGIONAL ANESTHESIA

Comparative efficacy of mepivacaine vs. bupivacaine added to lignocaine plus hyaluronidase for percutaneous peribulbar injection in cataract surgery

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ABSTRACT

Background: Peribulbar anesthesia had been developed as a safer, easier, and effective alternative to retrobulbar anesthesia that provides ocular akinesia and anesthesia.

Objective: This study aimed to compare the efficacy of mepivacaine 3% – lidocaine 2% hyaluronidase mixture with that of bupivacaine 0.5% – lidocaine 2% - hyaluronidase to produce optimal operative and post-operative conditions in patients receiving single peribulbar injection for cataract surgery.

Patients and Methods: In this randomized, double-blind study, 90 adult patients were assigned to one of two groups (M and B), each comprising 45 patients. Study participants received 6-8 ml combination of equal parts of either mepivacaine 3% (Group M) or bupivacaine 0.5% (Group B) both with lidocaine 2% and hyaluronidase 25 IU/ml. Akinesia was assessed with a 12-point scale at 2, 5, 10 and 15 min after injection. Onset of sensory block, time to start surgery, pain and requirement for supplemental injection were also assessed.

Results: Group M showed better akinesia scores than Group B and the onset of globe akinesia and sensory block were significantly faster in Group M. The duration of globe and lid akinesia was longer in Group B (159.16 ± 5.71 min and 150.02 ± 4.42 min, respectively) than in Group M (142.89 ± 6.52 min and 135.69 ± 4.81 min, respectively) and this showed statistical significance (P < 0.001). The percentage of patients who required supplementary injection was significantly higher in Group B (7 patients) compared to that in Group M (2 patients).

Conclusion: Using a mixture of mepivacaine and lidocaine gives perfect globe akinesia and quicker establishment of appropriate conditions to start cataract surgery and shortens the block onset time with faster recovery compared with the addition of bupivacaine to lidocaine in peribulbar anesthesia.


Abbreviations: ASA PS - American Society of Anesthesiologists Physical Status; PACU - Post Anesthesia Care Unit; VRS - Verbal Rating Scale; PBA - Peribulbar Anesthesia

Key words: Peribulbar block, Cataract extraction, Mepivacaine, Lidocaine, Bupivacaine.

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1. INTRODUCTION

Some ophthalmic procedures, such as cataract extraction with phacoemulsification and intraocular lens implantation, can be performed with either topical or regional anesthesia, especially when total akinesia of the eyeball and eyelids are required. In such procedures, rapid recovery from the block is always desirable.

Peribulbar anesthesia has been developed as a safe, easier, and effective alternative to retrobulbar anesthesia that provides ocular akinesia and anesthesia. Single injection technique is a simple technique that provides efficient regional ocular anesthesia with less complications as compared to classic technique. The addition of hyaluronidase as an adjuvant to local anesthesia has been well established in eye surgery to enhance the local anesthetic spread and overcome the slow onset of orbital akinesia associated with peribulbar anesthesia.

The most commonly used agent in ocular surgeries is lidocaine. Mepivacaine has an equivalent pharmacologic profile to lidocaine and bupivacaine, a homologue of mepivacaine (used either as a single agent or in combination with lidocaine). Bupivacaine is more potent and more toxic when compared to mepivacaine.

Lidocaine has a limited duration of action as compared to bupivacaine, which is characterized by its slow onset which makes it not an ideal agent for use as a sole agent. Mepivacaine provides rapid onset of sensory block and elevated levels of motor block. However, these characteristics rely on the concentration of the solution and the anesthetic technique employed. No previous studies have evaluated the efficacy of the combined mixture of mepivacaine and lidocaine in peribulbar block for ophthalmic surgery.

We aimed to compare the efficacy of mepivacaine 3% added to lidocaine 2% plus hyaluronidase with that of bupivacaine 0.5% added to lidocaine 2% plus hyaluronidase to produce optimal operative and postoperative conditions in patients receiving single peribulbar injection for cataract surgery.

2. METHODOLOGY

This randomized double-blinded study was conducted in Ain Shams University Hospitals from March 2018 to March 2019. The study was approved by the hospital ethical committee and was run in accordance with the ethical guidelines of the Declaration of Helsinki, 1975.

The study included 90 adult patients of either gender, ASA I to III, scheduled for phacoemulsification and posterior chamber artificial lens implantation with an expected duration of less than 60 min. The benefits and risks of the employed technique were explained to the patients, and informed consent obtained.

Exclusion criteria included patients younger than 21 y, patients refusing local anesthesia, those with single eye, ocular infections, and in cases when the decubitus position was difficult. Patients with communication problems, impaired consciousness, coagulopathy, and mental retardation, were also excluded from the study.

Relevant clinical and demographic data were collected for participating patients using a standardized data collection form. Patients were kept fasting 8 h for solids, and 2 h for clear fluids. No sedative premedication was administered in the preoperative period. The patients were randomly assigned to one of two groups, Group M and Group B, each comprising 45 patients. Randomization was achieved using a computer-generated list of random numbers and opaque sealed envelopes.

An anesthesia technician / nurse was responsible for preparing the intravenous (IV) solution to be administered (based on the patient’s assigned group) and handing it to the anesthesiologist. The patients, investigating anesthesiologist, the surgeon, and the Post Anesthesia Care Unit (PACU) nurse remained blinded to the groups.

2.1. Intraoperative Interventions and Management

In the operating room, an IV line was inserted and standard monitoring (heart rate, electrocardiography, oxygen saturation, and noninvasive blood pressure) was applied to all patients.

Patients in Group M received 8 ml mixture of equal parts of either mepivacaine 3% (Alexandria Company for Pharmaceuticals) and lidocaine 2% (Sigma-Tec Pharmaceutical Industrial) and those of Group B received bupivacaine 0.5% (Sigma-Tec Pharmaceutical Industrial Company.) and lidocaine 2%; both with hyaluronidase 25 IU/ml.

The injections were performed with a 25-gauge, 16-mm bevel disposable needle. The injection site was percutaneous and bounded superiorly by inferior lacrimal canaliculus, medially by lateral border of nose, laterally by imaginary perpendicular line that joined inferior lacrimal papilla to inferior border of orbit and inferiorly by inferior border of the orbit. The single peribulbar injection technique was performed as previously described by El Said et al.

All the procedures were done by the same anesthesiologist.

The following parameters were recorded:
1. Onset and duration of globe akinesia and duration of eyelid akinesia from the time of injection till complete recovery of ocular and eyelid movements. Globe and eyelid akinesia were assessed using a 12-point scale at 2, 5, 10, and 15 min after the end of the injection as previously described by Ngwu et al.\textsuperscript{11}

2. Onset of sensory block: from the time of injection of the anesthetic solution until complete disappearance of sensation. It was assessed by mild sensory touch to the conjunctiva with a cotton swab. The return of sensation to the globe was assessed by cotton swab test as mentioned previously (Globe anesthesia (feeling pain on touch) was assessed on a 0–2 scale where 0 = no anesthesia, 1 = partial but acceptable anesthesia and 2 = complete anesthesia).

3. Time to start surgery was determined based on detection of corneal anesthesia and ocular movement score of ≤1 in each direction and eyelid akinesia score of 0.

4. Pain was assessed by verbal rating scale (VRS) on a scale of 0–10 (0 refers to no pain, and 10 refers to the worst imaginable pain) at 2 and 6 h post operatively.

5. Requirement for supplemental injection: If adequate condition to start surgery was not obtained at the end of 20 min after performing the block, supplemental injection of 4 ml of a mixture of equal parts of either mepivacaine 3% and lidocaine 2% (Group M) or bupivacaine 0.5% and lidocaine 2% (Group B) was done inferotemporally.

2.2. Sample size determination

The primary outcome to be used in the sample size calculation is the time (in min) required to the onset of motor akinesia. A sample size of 90 cases (45 cases per group) was calculated to be satisfactory to detect an effect size of 0.6 (a medium effect size) using independent t-test with level of significance of 0.05 and power of 0.80.

2.3. Statistical analysis

Data were analyzed using Statistical Package for Social Science (SPSS version 21.0. Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation. Qualitative data were expressed as count. The independent-samples t-test was used to compare between means in the two groups. Skewed numerical data are presented as median (range) and independent samples median test was used to compare between medians in both groups. Chi square test was used to compare proportions between two qualitative parameters. P < 0.05 was considered significant and P < 0.01 was considered highly significant.

4. RESULTS

The study included 90 patients, 34 females (37.8 %) and 56 males (62.2 %) of ASA physical status I–III.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group M (n=45)</th>
<th>Group B (n=45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28 (62.2)</td>
<td>27 (60)</td>
<td>0.664*</td>
</tr>
<tr>
<td>Female</td>
<td>17 (37.8)</td>
<td>18 (40)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>51.16 ± 14.24</td>
<td>50.82 ± 10.01</td>
<td>0.898*</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>22 (48.9)</td>
<td>17 (37.8)</td>
<td>0.568*</td>
</tr>
<tr>
<td>II</td>
<td>14 (31.1)</td>
<td>17 (37.8)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>9 (20)</td>
<td>11 (24.4)</td>
<td></td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>73.71 ± 0.77</td>
<td>74.84 ± 0.79</td>
<td>0.409*</td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td>23.71 ± 0.73</td>
<td>23.84 ± 0.79</td>
<td>0.109*</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>31.11 ± 1.48</td>
<td>30.80 ± 1.50</td>
<td>0.325*</td>
</tr>
<tr>
<td>Surgical side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>20 (44.4)</td>
<td>29 (64.4)</td>
<td>0.067*</td>
</tr>
<tr>
<td>Left</td>
<td>25 (55.6)</td>
<td>16 (35.6)</td>
<td></td>
</tr>
</tbody>
</table>

Data presented as mean ± standard deviation or numbers (percentage)
Relevant clinical and demographic data are shown in Table 1. There was no statistically significant difference between the two study groups with respect to age, sex, weight, ASA physical status, duration of surgery, axial length, or surgery side (right/lef) as shown in Table 1.

Table 2 shows that the onset of globe akinesia was significantly faster in Group M in comparison with Group B (3.67 ± 0.15 vs. 3.82 ± 0.41 min; P = 0.022). The duration of globe and lid akinesia was longer in Group B, 159.16 ± 5.71 and 150.02 ± 4.42 min, respectively, than in Group M (142.89 ± 6.52 and 135.69 ± 4.81 min, respectively) and this was statistically significant (P < 0.001). The onset of sensory block was also faster in Group M in comparison with Group B (2.62 ± 0.24 vs. 2.79 ± 0.17 min) with significant difference (P < 0.001). Time to start surgery was significantly shorter in Group M as compared to Group B (8.05 ± 0.34 vs. 8.29 ± 0.29 min; P = 0.001).

Group M showed generally better akinesia scores at 2, 5 and 10 min after injection than Group B (Table 3). The percentage of patients who required supplementary injection before the operation was significantly higher in Group B (7 patients) compared to that in Group M (2 patients) (Figure 1).

Number of patients experiencing pain was more in Group M at 2, 6 h postoperatively, in comparison with Group B indicating shorter recovery time in the Group M. However, this was statistically non-significant (P = 292, P = 270 respectively) (Figure 2). Three patients in Group M complained of mild pain (pricking sensation) within 6 h after surgery, which was easily relieved by IV paracetamol.

Comparison between both groups regarding the surgeon’s and patients’ satisfaction, which was higher in the Group M but without significant differences as denoted by the P values represented in the annotations (Figure 3). Both groups provided similar analgesia during the operation and similar rates of incidence of chemosis. Drawbacks included one...
case of inferior lid hematoma, and two cases of chemosis that did not interfere with surgery. There was no incidence of perforation of the globe, retinal or optic nerve injury.

4. DISCUSSION
Combining local anesthetics for regional anesthesia has been practiced as early as 1952 and is still common in recent clinical practice. Moore et al. described the safety and value of combining tetracaine (a long-acting local anesthetic) with several intermediate-acting local anesthetics, such as lidocaine and mepivacaine in more than 10,000 regional anesthetic procedures in their publication that included a varied series of nerve blocks. The authors recommended that the mixtures of local anesthetics compensated for the side effects of each drug.

Mepivacaine is an intermediate-acting local anesthetic that may be an alternative to the standard lidocaine-bupivacaine mixture. It offers a more dense block, with shorter onset, and no need for supplemental injection, and shorter recovery time. Although both are classified as intermediate acting local anesthetics of the amide group, mepivacaine’s duration of block lasts longer than lidocaine by 50%. Tagariello et al. showed average duration of action of mepivacaine to be 192 to 234 min. Mepivacaine has some advantages over the classical lidocaine-bupivacaine mixture in offering sufficient episcleral anesthesia for ophthalmic surgery, especially because of the reliability of the blocks. A superior efficacy of blocks with mepivacaine was anticipated because of its pharmacological and physicochemical characteristics: it has a low pKa responsible for a quick onset of block, and it spreads readily through tissues. It does not produce irritation or tissue damage.

The result of our study concerning the rapid onset of mepivacaine group agrees with Ripart et al. who compared the classic mixture of lidocaine 2% plus bupivacaine 0.5% to mepivacaine 2% for caruncle episcleral (sub-Tenon) anesthesia for cataract surgery. Mepivacaine gives a more efficient block with a quicker onset and a quicker recovery. However, these differences were very small and were of little clinical concern. Sheng et al. assessed the efficacy of mepivacaine 3% for oral local anesthesia over 68 non-hypertensive patients and 36 hypertensive patients and concluded that 3% mepivacaine has quick onset, ideal anesthetic effect and little side effect on cardiovascular system. In our study, we used inj. mepivacaine 3% which could have explained significant difference as regards rapid onset of efficient akinesia.

Ripart et al. demonstrated that a small volume of local anesthetic (5-6.5 mL) injected in Peribulbar anesthesia (PBA) is adequate to envelop the eyeball and produce analgesia. The circumferential distribution of the local anesthetic with the addition of hyaluronidase from extraconal to the intraconal space, where the sensory and motor nerves of the eye are located, explains the more adequate akinesia achieved with this technique.

Fanelli et al. compared mepivacaine, ropivacaine and bupivacaine in femoral and sciatic nerve blocks showing faster onset of mepivacaine. Darwish et al. also showed a successful block by a single peribulbar injection of mepivacaine in high axial length cataract patients.

Loots et al. tried mixing bupivacaine 0.5% and lidocaine 2% in peribulbar blocks with unsatisfactory results. He suggested mixing bupivacaine 0.75% with lidocaine 2% to get better results, but still believed the success rate will not reach 90%.

On the contrary to our results, Gadsden et al. found a similar onset of block between mepivacaine 1.5% and bupivacaine 0.5% used in ultrasound guided interscalene block. Also, Jaichandran et al. found no advantage in mixing lidocaine and bupivacaine in vitreoretinal surgeries compared to bupivacaine alone as regards the onset of the blocks.

Another study by Lammers et al. showed no superiority of mixing mepivacaine 3% with lidocaine 2% and epinephrine over lidocaine 2% alone with epinephrine as regard the onset of the block.

The other finding in our results is the rapid recovery with mepivacaine compared with bupivacaine group. This goes in agreement with Mahan et al. who compared mepivacaine to bupivacaine in spinal anesthesia in total knee arthroplasty operations. Mepivacaine showed faster recovery with less length of stay and urinary retention. Also, mepivacaine group did not experience more pain. Borel et al. also recommended using mepivacaine and lidocaine rather than bupivacaine in day case cataract surgeries due to good block and short duration.

Table 3: Comparison between the 2 groups regarding akinesia score at specified time points

<table>
<thead>
<tr>
<th>Time to measure</th>
<th>Group M (n = 45)</th>
<th>Group B (n = 45)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 min after injection</td>
<td>10 (9-11)</td>
<td>11 (9-12)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>5 min after injection</td>
<td>5 (4-7)</td>
<td>6 (5-7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>10 min after injection</td>
<td>1 (1-4)</td>
<td>2 (2-4)</td>
<td>0.006</td>
</tr>
<tr>
<td>15 min after injection</td>
<td>1 (0-2)</td>
<td>1 (0-2)</td>
<td>0.352</td>
</tr>
</tbody>
</table>

Data presented as median (range); All P value measured by independent samples-median test.

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et al. also demonstrated the rapid recovery of mepivacaine compared to bupivacaine in sciatic and femoral nerve blocks.19

The shorter duration of the block with mepivacaine was likewise expected from its pharmacology. In day case surgery this is of curiosity because recovery of blinking allows the occlusive patch to be removed earlier and the patient to be benefited from the early result of surgery before going home.

Ripart et al. found no favor with lidocaine over mepivacaine in episcleral (sub-Tenon’s) eye block, especially in terms of motor-block duration.2

Neuromuscular blocking drugs, such as atracurium27 and vecuronium,28 have also been added to the local anesthetic mixtures and have been shown to enhance the quality of PBA

5. LIMITATIONS

The study has several limitations. First, we only tested mepivacaine 3%. Comparing groups with different concentrations of mepivacaine would have revealed more data. Second, measuring the effect of local anesthetics on intraocular pressure would have been beneficial.

6. CONCLUSION

Peribulbar anesthesia (PBA) using a mixture of mepivacaine, and lidocaine provides optimal globe akinesia and rapid achievement of proper conditions to start eye surgery and shortens the block

7. Data availability

The numerical data generated during this research is available with the authors.

8. Ethical issues

The work was approved by the research ethics committee of Ain Shams University Hospital (FMASU R21/ 2018). The study was prospectively registered with the Pan African Clinical Trial Registry (PACTR) with registration number PACTR201810828658359.

9. Conflict of interest

The study utilized the hospital resources only, and no external or industry funding was involved.

10. Authors’ contribution

ANS: Concept, Manuscript writing, Data collection, Data analysis
DMH: Concept; Literature search, Manuscript writing, Data collection, Statistical analysis
MRZ: Concept, Data collection, Manuscript writing

11. REFERENCES


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