ISSN: 1607-8322, e-ISSN: 2220-5799 Anaesthesia, Pain & Intensive Care
Vol 27(5); October 2023 DOI: 10.35975/apic.v27i5.2167

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.

Trial registration: Registered at http:// www.pactr.org; No. PACTR201810828658359. Dated: October8, 2018.

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.

Citation: Saleh AN, Haiba Ali Ibrahim DM, Zekry MR. Comparative efficacy of mepivacaine vs. bupivacaine added to lignocaine plus hyaluronidase for percutaneous peribulbar injection in cataract surgery. Anaesth. pain intensive care 2023;27(5):464–470; DOI: 10.35975/apic.v27i5.2167

Received: April 09, 2023; **Reviewed:** August 08, 2023; **Accepted:** August 18, 2023

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.[1] In such procedures, rapid recovery from the block is always desirable.[2]

Peribulbar anesthesia has been developed as a safe, easier, and effective alternative to retrobulbar anesthesia that provides ocular akinesia and anesthesia.[3] Single injection technique is a simple technique that provides efficient regional ocular anesthesia with less complications as compared to classic technique.[3] 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.[4,5]

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.[4,6,7,8]

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.[9] 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.[10] 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 post-operative 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.[3]

All the procedures were done by the same anesthesiologist.

The following parameters were recorded:

Table 1: Demographic and clinical data of the study participants (n=90)

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

Data presented as mean ± standard deviation or numbers (percentage)

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.[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 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.

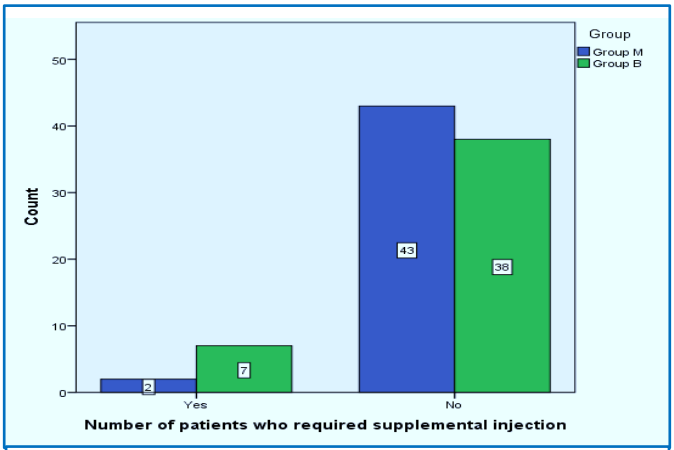

Figure 1: Comparison between the two groups as regards supplemental injection requirement

Table 2: Comparison between the 2 studied groups as regards block parameters

Variables	Group M (n = 45)	Group B (n = 45)	P value	95% Confidence Interval of the Difference
Onset of globe akinesia (min)	3.67 ± 0.15	3.82 ± 0.41	0.022	0.02 - 0.28
Duration of globe akinesia (min)	142.89 ± 6.52	159.16 ± 5.71	< 0.001	13.69 - 18.84
Duration of lid akinesia (min)	135.69 ± 4.81	150.02 ± 4.42	< 0.001	12.39 - 16.27
Onset of sensory block (min)	2.62 ± 0.24	2.79 ± 0.17	< 0.001	0.08 - 0.26
Time to start surgery (min)	8.05 ± 0.34	8.29 ± 0.29	0.001	0.11 - 0.37

*Data presented as mean ± standard deviation or number (percent); *Measured by Chi-square test; °Measured by independent t-test*

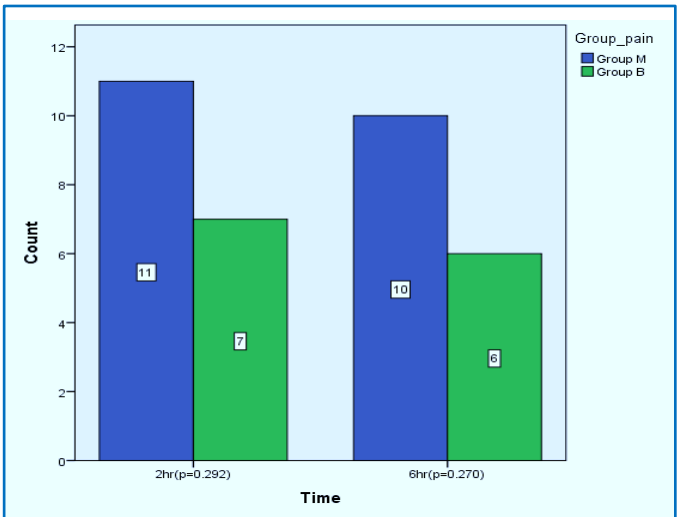

Figure 2: Number of patients with pain at 2 and 6 h postoperatively.

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/left) 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 Pvalues represented in the annotations (Figure 3). Both groups provided similar analgesia during the operation and similar rates of incidence of chemosis. Drawbacks included one

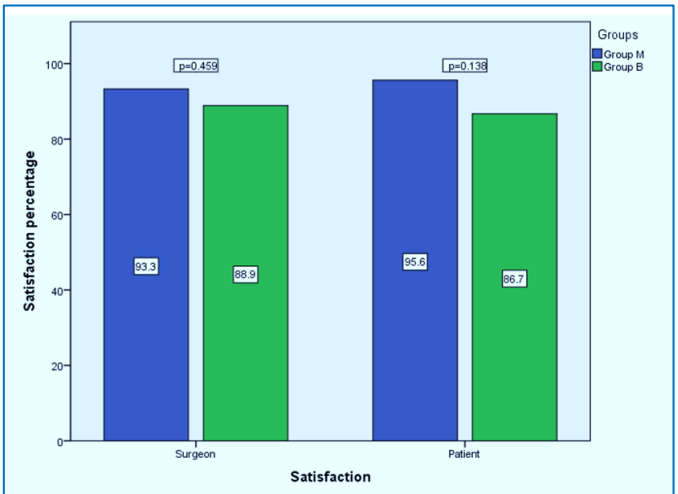

Figure 3: Comparison between both groups regarding surgeon and patient satisfaction.

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

Time to measure	Group M (n = 45)	Group B (n = 45)	P-value
2 min after injection	10 (9-11)	11 (9-12)	< 0.001
5 min after injection	5 (4-7)	6 (5-7)	< 0.001
10 min after injection	1 (1-4)	2 (2-4)	0.006
15 min after injection	1 (0-2)	1 (0-2)	0.352

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

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.[12] 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.[13]

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%.[14] Tagariello et al. showed average duration of action of mepivacaine to be 192 to 234 min.[15] 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.[16] 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.[16] 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.[17] 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.[18]

Fanelli et al. compared mepivacaine, ropivacaine and bupivacaine in femoral and sciatic nerve blocks showing faster onset of mepivacaine.[19] Darwish et al. also showed a successful block by a single peribulbar injection of mepivacaine in high axial length cataract patients.[20]

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%.[21]

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.[22] Also, Jaichandran et al. found no advantage in mixing lidocaine and bupivacaine in vitroretinal surgeries compared to bupivacaine alone as regards the onset of the blocks.[23]

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.[24]

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.[2] Borel et al. also recommended using mepivacaine and lidocaine rather than bupivacaine in day case cataract surgeries due to good block and short duration.[26] Fanelli

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 atracurium[27] 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

1. Crandall AS. Anesthesia modalities for cataract surgery. Curr Opin Ophthalmol. 2001 Feb;12(1):9-11. [PubMed] DOI: 10.1097/00055735-200102000-00003
2. Ripart J, Nouvellon E, Chaumeron A, Chanial-Bourgaux C, Mahamat A. A comparison of mepivacaine versus lidocaine for episcleral (sub-tenon's) block for cataract surgery in an ambulatory setting. Reg Anesth Pain Med. 2006 May-Jun;31(3):206-10. [PubMed] DOI: 10.1016/j.rapm.2006.03.002
3. El Said TM, Kabeel MM. Comparison of classic peribulbar anesthesia and new entry point (single percutaneous injection technique) in vitroretinal surgery. Saudi J Anaesth. 2010 May;4(2):80-5. [PubMed] DOI: 10.4103/1658-354X.65130
4. Adams L. Adjuvants to local anaesthesia in ophthalmic surgery. Br J Ophthalmol. 2011 Oct;95(10):1345-9. [PubMed] DOI: 10.1136/bjo.2010.188789
5. Hamawy T, Bestarous J. Rocuronium versus magnesium as an adjuvant to local anesthetics in peribulbar block. Ain-Shams J Anesthesiol. 2013 Sep 1;6(3):317-21. DOI: 10.7123/01.ASJA.0000433031.32476.a3
6. Ozcan AA, Ozdemir N, Günes Y, Bozkurt A, Yagmur M, Alparslan ZN. Intraocular pressure, quality of block, and degree of pain associated with ropivacaine in peribulbar block: a comparative randomized study with bupivacaine-lidocaine mixture. Eur J Ophthalmol. 2003 Nov-Dec;13(9-10):794-7. [PubMed] DOI: 10.1177/1120672103013009-1011
7. Dowd FJ, Johnson BS, Mariotti AJ, Haas DA, Quinn CL. Local Anesthetics. In: Pharmacology and Therapeutics for Dentistry; 2017. p. 206–220. DOI: 10.1016/B978-0-323-39307-2.00014-X
8. Gioia L, Prandi E, Codenotti M, Casati A, Fanelli G, Torri TM, et al. Peribulbar anesthesia with either 0.75% ropivacaine or a 2% lidocaine and 0.5% bupivacaine mixture for vitreoretinal surgery: a double-blinded study. Anesth Analg. 1999 Sep;89(3):739-42. [PubMed] DOI: 10.1097/00000539-199909000-00039
9. Lee K, Chung JM, Lee SD. The safety of a mixture of bupivacaine and lidocaine in children after urologic inguinal and scrotal surgery. Investig Clin Urol. 2018 Mar;59(2):141-147. [PubMed] DOI: 10.4111/icu.2018.59.2.141
10. Scarparo HC, Maia RN, Filho ED, Soares E, Costa F, Fonteles C, et al. Plasma mepivacaine concentrations in patients undergoing third molar surgery. Aust Dent J. 2016;61(4):446-454. [PubMed] DOI: 10.1111/adj.12410
11. Ngwu RA, Adekoya BJ, Adejumo OA, Ibidapo OO, Vera OA. Comparison of the akinetic properties of subtenon's anaesthesia versus peribulbar anaesthesia among cataract patients in Nigeria. Nigerian J Ophthalmol. 2017;25(2):95. DOI: 10.4103/njo.njo_8_17
12. Jafari S, Kalstein AI, Nasrullah HM, Hedayatnia M, Yarmush JM, SchianodiCola J. A randomized, prospective, double-blind trial comparing 3% chloroprocaine followed by 0.5% bupivacaine to 2% lidocaine followed by 0.5% bupivacaine for interscalene brachial plexus block. Anesth Analg. 2008 Nov 1;107(5):1746-50. [PubMed] DOI: 10.1213/ane.0b013e318185cd5e
13. Moore DC, Bridenbaugh LD, Bridenbaugh PO, Thompson GE, Tucker GT. Does compounding of local anesthetic agents increase their toxicity in humans?. Anesth Analg. 1972 Jul

1;51(4):579-85. [PubMed]

14. Urmey WF. Spinal anaesthesia for outpatient surgery. Best Pract Res Clin Anaesthesiol. 2003 Sep 1;17(3):335-46. [PubMed] DOI: 10.1016/s1521-6896(03)00015-6
15. Tagariello V, Bertini L. Unusually prolonged duration of spinal anesthesia following 2% mepivacaine. Reg Anesth Pain Med. 1998 Jul 1;23(4):424-6. [PubMed] DOI: 10.1016/s1098-7339(98)90018-9
16. Ripart J, Lefrant JY, L'Hermite J, Borzli F, Nouvellon E, Fabbro-Peray P, et al. Caruncle single injection episcleral (Sub-tenon) anesthesia for cataract surgery: mepivacaine versus a lidocaine-bupivacaine mixture. Anesth Analg. 2000;91(1):107-9. [PubMed] DOI: 10.1097/00000539-200007000-00020
17. Ding S, Zhu YQ, Wu YN, Cao D. [Efficacy and safety of 3% mepivacaine hydrochloride injection for oral local anesthesia]. Shanghai Kou Qiang Yi Xue. 2008;17(3):328-31. [PubMed]
18. Ripart J, Lefrant JY, de La Coussaye JE, Prat-Pradal D, Vivien B, Eledjam JJ. Peribulbar versus retrobulbar anesthesia for ophthalmic surgery: an anatomical comparison of extraconal and intraconal injections. Anesthesiology. 2001;94(1):56-62. [PubMed] DOI: 10.1097/00000542-200101000-00013
19. Fanelli G, Casati A, Beccaria P, Aldegheri G, Berti M, Tarantino F, et al. A double-blind comparison of ropivacaine, bupivacaine, and mepivacaine during sciatic and femoral nerve blockade. Anesth Analg. 1998;87(3):597-600. [PubMed] DOI: 10.1097/00000539-199809000-00019
20. Darwish A, Sami R, Aref R, Samir D. Single Injection Peribulbar Anesthesia in Patients With Axial Myopia for Cataract Surgery. Med Cairo Univ. 2013;81(1):445–448.
21. Loots JH, Koorts AS, Venter JA. Peribulbar anesthesia: A prospective statistical analysis of the efficacy and predictability of bupivacaine and a lignocaine/bupivacaine mixture. J Cataract Refract Surg. 1993 Jan 1;19(1):72-6. [PubMed] DOI: 10.1016/s0886-3350(13)80286-6
22. Gadsden J, Hadzic A, Gandhi K, Shariat A, Xu D, Maliakal T, et al. The effect of mixing 1.5% mepivacaine and 0.5% bupivacaine on duration of analgesia and latency of block onset in ultrasound-guided interscalene block. Anesth Analg. 2011;112(2):471-6. [PubMed] DOI: 10.1213/ANE.0b013e3182042f7f
23. Jaichandran VV, Raman R, Gella L, Sharma T. Local anesthetic agents for vitreoretinal surgery: no advantage to mixing solutions. Ophthalmology. 2015 May 1;122(5):1030-3. [PubMed] DOI: 10.1016/j.ophtha.2014.11.026
24. Lammers E, Nusstein J, Reader A, Drum M, Beck M, Fowler S. Does the combination of 3% mepivacaine plain plus 2% lidocaine with epinephrine improve anesthesia and reduce the pain of anesthetic injection for the inferior alveolar nerve block? A prospective, randomized, double-blind study. J Endod. 2014 Sep 1;40(9):1287-92. [PubMed] DOI: 10.1016/j.joen.2014.04.015
25. Mahan MC, Jildeh TR, Tenbrunsel TN, Davis JJ. Mepivacaine spinal anesthesia facilitates rapid recovery in total knee arthroplasty compared to bupivacaine. J Arthroplasty. 2018;33(6):1699-704. [PubMed] DOI: 10.1016/j.arth.2018.01.009
26. Borel M, Ousmane L, Lebuffe G, Robin E, Cantineau D, Vallet B, et al. Lidocaine vs. mepivacaine for peribulbar anaesthesia in cataract surgery: a randomized double-blind study. Eur J Anaesthesiol. 2006 Jun;23(6):532-4. [PubMed] DOI: 10.1017/S0265021506250750
27. Küçükyavuz Z, Arici MK. Effects of atracurium added to local anesthetics on akinesia in peribulbar block. Reg Anesth Pain Med. 2002;27(5):487-90. [PubMed]
28. Reah G, Bodenham AR, Braithwaite P, Esmond J, Menage MJ. Peribulbar anaesthesia using a mixture of local anaesthetic and vecuronium. Anaesthesia. 1998;53(6):551-4. [PubMed] DOI: 10.1046/j.1365-2044.1998.00433.x