Original Article

Magnesium versus dexmedetomidine as adjuvant to local anaesthetic in peribulbar block for vitreoretinal surgery.

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ABSTRACT

Background: Peribulbar anaesthesia (PBA) is widely used in ophthalmic anaesthesia and is a suitable technique for vitreoretinal (VR) surgery. VR surgery requires dense analgesia and good akinesia. Longer acting local anaesthetic agents and adjuvants have been used to prolong the duration of anaesthesia, hasten onset of akinesia, reduce LA toxicity and offer greater patient satisfaction. The aim of our study was to find out the efficacy of adding magnesium or dexmedetomidine to 0.5% ropivacaine or 0.5% levobupivacaine in PBA for VR surgery.

Material and methods: One hundred and twenty adult patients undergoing VR surgery were randomized into the four groups. The composition of the drug used for peribulbar anaesthesia in the 4 groups were Group RM (8 ml of 0.5% Ropivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg), Group RD (8 ml of 0.5% Ropivacaine+ Hyaluronidase 150 IU+ 25µg Dexmedetomidine), Group LM (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg) and Group LD (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ 25 µg dexmedetomidine).

Results: The groups were comparable in terms of patient demographics, duration of surgery, onset of surgical anaesthesia and need for supplementation of block. Patients in Group RD (478±298 min) had prolonged post-operative pain relief when compared to RM (280±135 min). The time to first request for analgesia was 449±289 min in group LD and 405±285 min in group LM.

Conclusion: Addition of dexmedetomidine to 0.5% ropivacaine significantly improved the post-operative analgesia in VR surgery. 0.5% ropivacaine with dexmedetomidine is a good combination for peribulbar block in VR surgery. No hemodynamic disturbance occurred with dexmedetomidine 25µg or Magnesium 0.5 mg in peribulbar block.

Key Words: Peribulbar anaesthesia, dexmedetomidine, magnesium, ropivacaine, levobupivacaine, vitreoretinal

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Article History
Received: 18th October 2020
Revision: 28th October 2020
Accepted: 24th December 2020
Published: 14th January 2021

How to cite this article: Shalini Subramanian, Medha Bapat, Thirumalesh MB, Sherine Braganz. Magnesium versus dexmedetomidine as adjuvant to local anaesthetic in peribulbar block for vitreoretinal surgery. Indian J Ophthal Anaesth 2021;1(1):3-12

Introduction

Regional anaesthesia with a peribulbar technique is the preferred anaesthetic modality in patients undergoing vitreoretinal (VR) surgery. This is attributed to the better analgesia, early rehabilitation and increased safety in the presence of systemic comorbid illnesses that co-exist in 47.5% to 70% of patients undergoing VR surgery.[1,2]

The left isomers of bupivacaine, namely ropivacaine and levobupivacaine are preferred due to their long duration of action and reduced systemic toxicity in the event of overdose or accidental intravascular injection.[3]

Multimodal perineural anaesthesia using local anaesthetic (LA) with a synergistic adjuvant has been practised to reduce the cumulative dose of LA, augment block success and provide superior post-operative pain relief. These have also helped to reduce turnover time in a busy ophthalmic operating room. An assortment of opioid and nonopioid adjuncts are available, of which the $\alpha 2$ agonists- clonidine and dexmedetomidine, are a popular class. In one meta-analysis, dexmedetomidine as part of intrathecal or brachial plexus block prolonged duration of action without causing any significant hemodynamic instability.[4] Dexmedetomidine has been used in peribulbar anaesthesia (PBA) to hasten onset of akinesia and prolong duration of analgesia in cataract surgery. It also reduces intra-ocular pressure.[5]

Dexmedetomidine has been postulated to have a central and peripheral site of action.

Magnesium (Mg) is a physiological calcium channel blocker and non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors. Its site of action is presumed to be on the peripheral nerve where it inhibits calcium influx and blocks the release of excitatory neurotransmitter. Mg has been shown to potentiate LA action and have an opioid sparing effect.[6]

In this study, we aimed to study the efficacy of adding dexmedetomidine or Mg to 0.5% ropivacaine or 0.5% levobupivacaine in PBA for VR surgery. The primary outcome of the study was the time to onset of globe akinesia. The secondary outcome was the requirement of supplementation of peribulbar block prior to or during the surgery and post-operative analgesic requirement.

Materials and methods

This prospective double blinded randomized controlled study was conducted after approval of the institutional ethics committee. One hundred and twenty ASA I-III adult patients aged greater than 18 years, undergoing VR surgery under peribulbar block were included in the study after obtaining a written informed consent. Patients with a history of hypersensitivity to the study drugs, significant cardiovascular disease, impaired mental status, refusal to use local anaesthestic technique and pregnant women were excluded from the study.

All patients underwent routine pre-operative evaluation for VR surgery. Details of the anaesthetic technique and study protocol were explained to the patients at the preoperative visit. No topical anaesthetic or sedative medications were used before or during the block. Details regarding the side, surgery and whether it was a redo procedure were noted.

In the operating room, an intravenous cannula was secured and standard monitors including ECG, pulse oximeter and non-invasive blood pressure were applied. The patients were randomized using a computer generated random number table into one of the four groups. The composition of the study drug used for peribulbar anaesthesia in each of the 4 groups was Group RM (8 ml of 0.5% Ropivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg), Group RD (8 ml of 0.5% Ropivacaine+ Hyaluronidase 150 IU+ 25µg Dexmedetomidine), Group LM (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ Magnesium sulphate 0.5 mg) and Group LD (8 ml of 0.5% levobupivacaine + Hyaluronidase 150 IU+ 25 µg dexmedetomidine). The total volume was 8.5 ml in all groups.

The peribulbar block was administered by an anaesthesiologist with adequate experience in ophthalmic regional anaesthesia. All healthcare personnel including the anaesthesiologist and surgeon involved in direct patient care were blinded to the study drug.

Peribulbar block was administered using a 24G, 25mm needle using a transcutaneous two injections technique. The first injection was in the inferotemporal quadrant, as far lateral as possible where 4.5ml of the drug administered after negative aspiration. Gentle compression was applied on the eyeball using the middle three fingers. The second injection was given 2mm medial and inferior to the supraorbital notch where the remaining 4 ml of drug was deposited. If the eyeball was firm or tense after the first injection, gentle pressure was applied until the eyeball was soft before the second injection. After the second injection the eye was examined every 30 second for onset of corneal anaesthesia and akinesia. Corneal anaesthesia was assessed by checking the corneal reflex in response to instillation of physiological solution of saline. Onset of motor block was assessed by grading the movement of the eyeball in the four directions- superior, inferior, lateral and medial using a score of 0, 1 or 2. [0= no movement, 1= mild movement, 2= full movement]. A total score ≤1 was considered adequate for surgery. Onset of lid akinesia was assessed by testing the ability of the patient to open, and close the eye and graded as 0 = Complete akinesia, 1 = Partial movement in either or both eyelid margins, 2 = Normal movement in either or both eyelid margins. A lid akinesia score of zero was considered acceptable. The time to onset of sensory and motor block and lid akinesia was noted.

A supplementary block was given in the inferotemporal quadrant with 3 ml of 2% xylocaine if satisfactory anaesthesia or akinesia was not achieved by ten minutes. The supplementation was repeated if the anaesthesia was incomplete after another 5 minutes.

Intra-operative details including the hemodynamic variables (heart rate, blood pressure, SpO2), Richmond agitation sedation scale (RASS) were noted every 15 min for one hour and every 30 minutes thereafter till completion of the surgery. The duration of surgery was noted. Any need for intra-operative analgesia or akinesia was achieved by administering a Sub Tenon's block with 3 ml of 2% xylocaine. The patient was excluded from the study if more than two supplementary injections were needed after the initial peribulbar block. The patient was encouraged to communicate verbally for pain during the surgery. At the end of surgery, the surgeon's satisfaction score was obtained using a grading for the efficacy of anaesthesia. 1 = poor (inadequate for surgery) 2 = acceptable (block is incomplete but the surgeon could proceed) 3 = perfect (effective block). The patient satisfaction is recorded as 1 = Complete dissatisfaction, 2 = some dissatisfaction, 3 = Complete satisfaction. The requirement of intra-operative sedation is also noted. All patients were given an eye patch that was opened only the next morning. The pain relief was scored using a verbal numerical rating scale (NRS) of 0-10 with 0 representing "no pain" and 10 representing "worst pain".

The pain score was recorded at 1h, 2h, 6h and 24 h post op. A pain score ≥4 was treated with tablet paracetamol 650mg. This tablet was repeated not earlier than 6 hours and not more than three tablets in 24h. Pain not responding to paracetamol was treated with intravenous injection of tramadol 50mg. The time to first request for analgesia and total analgesic requirement in 24 hours was noted. The end point of the study was at 24 hours.

Statistics

The sample size was calculated assuming a type I error of 0.05. It was estimated that a sample size of 20 patients in each study group would be required to achieve a power of 80% to detect an effect size (d) of 0.4 in the primary outcome of interest. The statistical software R version 4.0.2 (R core team, 2020) was used for the analysis of the data and the graphs were drawn on Microsoft Excel. Results on continuous measurements are presented as mean ± SD, if parametric and in median (interquartile range), if the distribution is non-Gaussian. Results on categorical measurements are presented in number (%). Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale, non-parametric setting and for qualitative data analysis. Analysis of variance (ANOVA) was used to find the significance of normally distributed continuous data between the three groups. Continuous data with non-parametric distribution was analysed using Kruskal Wallis test. A p value <0.05 was considered significant.

Results

Thirty patients were enrolled in each group. All 120 patients were included in the analysis. There was no statistical difference between the 4 groups with regards to the patient demographics or surgical details. (Table 1)

Table 1: Patient demographic and surgical details

		LD (n=30)	LM(n=30)	RD(n=30)	RM(n=30)	P value
Age (years) (Mean±SD)		**58.1±13.3**	**57.8±9.79**	**58±12.9**	**59.2±7.36**	**0.93**
Gender (M/F)		15/15	25/5	19/11	23/7	0.03*
Weight (kg) (Mean±SD)		62.2±12.8	67.9±9.6	64.6±9.78	65.7±13.4	0.29
ASA grade (I/II/III)		4/21/5	1/24/5	5/17/8	1/27/2	0.13
Resurgery (Y/N)		1/29	4/26	1/29	3/27	0.6
Right eye/Left eye		15/15	13/17	10/20	17/13	0.25
Surgery	**Vitrectomy + oil / gas insertion**	12	13	10	15	0.72
	Cataract+ vitrectomy	16	14	16	14	
	Buckling procedures (including sclera buckle ±vitrectomy ± cataract)	2	3	4	1	
Duration of surgery (min) (Mean±SD)		91.5±35.3	78.5±38.2	84.3±27.5	73.5±30.2	0.19

***- p<0.05, significant LM vs LD**

The characteristics of the peribulbar block in terms of time to onset of anaesthesia and post-operative analgesia are given in Table 2.

Table 2: Onset of anaesthesia and time to first request for analgesia

	LD (n=30)	LM(n=30)	RD(n=30)	RM(n=30)	p value
Onset of corneal anaesthesia (sec)	58±106.6	54.5±117.3	31±28.9	65±154.6	0.29
Onset of globe akinesia (sec)	376±312.4	276.2±298.4	234±248.4	225±291.3	0.21
Onset of lid akinesia (sec)	219.5±280.6	178.9±228.1	144.3±191.1	180±236.7	0.68
Time to first request for analgesia (min)	449±289	405±285	478±298*	280±135*	0.04*

*** : p<0.05, significant RM vs RD, values are in Mean±SD**

There was no difference between the four groups with regards to onset of corneal anaesthesia (p=0.29), globe akinesia (p=0.20) and lid akinesia (p=0.68). No statistical difference existed in the proportion of patients not requesting for any pain relief in the first 24 hours after surgery (p=0.18). Among those requesting for analgesia, the time to first request for analgesia was shortest in RM (280±135 min) and longest in RD (478±298 min) group (p=0.04). The groups were comparable in the need for block supplementation (pre-operative or intra-operative) with 40%, 43.3%, 16.7% and 23.3% of patients in group LD, LM, RD and RM respectively, needing an additional LA injection (p=0.07) (Fig 1). The proportion of patients in these four groups requesting for post-operative analgesia was 63.3%, 53.3%, 80% and 66.7% respectively (p=0.18) (Fig 2).

Fig 1: Need for supplementation of peribulbar anaesthesia

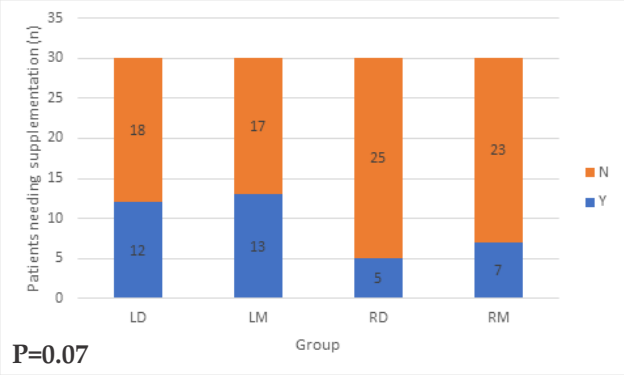
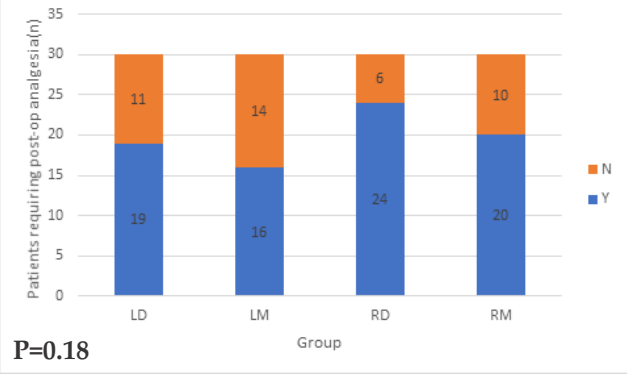


Fig 2: Requirement of post-operative analgesia



The requirement of intra-operative sedation(p=0.86), pain score at 1h, 2h, 6h and 24h was similar across the four groups. The patient as well as surgeon satisfaction scores were similar across the four groups (p=0.60 and p=0.11 respectively) (Table 3).

Table 3: Sedation requirement, pain and satisfaction scores

	LD(n=30)	LM(n=30)	RD(n=30)	RM(n=30)	P value
Need for intra-operative sedation n(%)	7(23.3)	10(33.3)	9(30)	9(30)	0.86
Median NRS at 1h/2h/6h/24h	0/1.5/3/2	0/1/3/2	0/1/4/2	0/2/3/1.5	>0.05
Surgeon satisfaction score(median) 1/2/3	0/3/27	2/5/23	0/7/23	0/2/28	0.11
Patient satisfaction score(median) 1/2/3	0/7/23	1/8/21	0/5/25	0/5/25	0.60

1=poor, 2=acceptable, 3=good: NRS= Numerical rating score

On analysing the hemodynamic parameters, patients in the RD group had significantly lower heart rate than LM at 15 and 60 minutes and mean arterial pressure at 30 and 45 minutes was significantly lower in the LD group compared to RM. No intervention was needed. There was no significant alteration in other parameters like SpO2, respiratory rate and RASS score.

Discussion

Several nonopioid additives have been used in PBA to hasten the onset of action, reduce the need for supplementation, enhance analgesic profile and improve surgeon satisfaction.[7] The uniqueness of this study is that it analyses four groups including various combinations of two long acting LA and two adjuvants in patients undergoing VR surgery.

In a meta- analysis, Li et al found no significant difference in onset time, duration of motor block and patient overall satisfaction between ropivacaine and levobupivacaine in peripheral nerve block though patients receiving levobupivacaine had significantly less request for post-operative rescue analgesia.[8] 0.75% Ropivacaine and 0.5% levobupivacaine compared by other authors in PBA who have shown that 0.5% levobupivacaine has better anaesthetic property than 0.75% ropivacaine in terms of block onset and offset times.[9,10]

In our study, no difference was found between the four groups in the onset time. Although the ropivacaine containing groups (RM, RD) required fewer supplementary injection and took lesser time to achieve globe akinesia but this was not statistically significant. Ghali et al observed that block failure and need for supplementation was greater with 0.5% ropivacaine (25%) than 0.5% levobupivacaine(8.3%) after single injection peribulbar block.[9] This is in contrast to our findings where 0.5% ropivacaine had lower failure rate.

A meta-analysis by Abdallah et al showed that dexmedetomidine in peripheral nerve blocks significantly prolonged motor block and time to first analgesic request but not onset time.[4] Hafez et al opined that 25µg is the most appropriate dose of dexmedetomidine for PBA.[11] The addition of dexmedetomidine has been associated with reduced need for additional LA injection but no such benefit was observed in our study. Similar to our study, Gujral et al found no added benefit in speeding block onset with dexmedetomidine but they observed greater surgeon satisfaction, probably due to co-operative sedation with 20µg dexmedetomidine in VR surgery.[12]

When added to a mixture of 0.5% bupivacaine and 2% lidocaine in PBA for phacoemulsification, Mg has been shown to accelerate onset of akinesia and delay first request for pain relief.[13] Sinha et al observed that adding Mg to PBA improved block onset time without any side effect.[14] Adding 100 mg Mg was not more useful than 50 mg.[15] It has been found to be inferior to fentanyl and rocuronium in establishing condition suitable for cataract surgery in terms of better akinesia and speed of onset.[16,17]

El-Hamid compared Mg with clonidine in PBA and observed that the use of Mg resulted in faster onset while clonidine provided longer pain relief post-operatively.[18]

In PBA, dexmedetomidine and Mg have been compared previously. Mohamed and Genidy found no difference between the groups receiving dexmedetomidine or Mg as an additive in peribulbar block though both enhanced the quality of anaesthesia in terms of speed of onset, patient satisfaction and need for second injection as compared to a mixture of 2% lignocaine and 0.5% bupivacaine.[19] Previous studies have compared dexmedetomidine and Mg with plain LA in PBA in cataract surgery and found significant difference between the control and study groups but did not publish post hoc tests to identify inter-group differences.[20,21] Shoukry et al found that Mg is superior to dexmedetomidine in establishing a block rapidly while dexmedetomidine provided longer post-operative analgesia in VR surgery. They concluded that Mg was a more economical additive with qualities comparable with dexmedetomidine.[22]

Ocular anaesthesia is achieved by blockade of saltatory conduction of the sensory and motor nerves traversing the intraconal area. Extraconal blocks have a longer latency period in view of the greater diffusion barrier for the LA before it reaches its site of action. Winder et al visualised LA in the muscle cone when B scan was done 10 minutes after administration of the peribulbar block.[23] The rapidity of perineural anaesthesia onset is a function of LA used including its lipophilicity, degree of ionisation and pKa.[24] Drugs like hyaluronidase and ocular compression serve to improve diffusion across the muscle cone.[25]

In our study, difference in the time to onset of globe akinesia was not statistically significant in all the groups. The onset time of PBA is a function of the type of LA. RD and RM group with 0.5% ropivacaine showed quicker onset but it didn't provide significant advantage in our study. Dexmedetomidine provided prolonged post-operative analgesia as compared to Mg. No hemodynamic disturbance occurred with dexmedetomidine 25µg or Mg 50 mg in PBA.

Limitation

This study lacks a true control group with only LA. A study including such a group would better explain the rightful effect of adjuvant on LA.

Conclusion

0.5% ropivacaine had a higher success rate for PBA with lesser rate of supplementation needed in comparison to 0.5% levobupivacaine. Addition of dexmedetomidine significantly improves the post-operative analgesia in VR surgery. 0.5% ropivacaine with dexmedetomidine is a good combination for peribulbar block in VR surgery.

Presentation:

Presented at the World Congress of Ophthalmic Anaesthesia, Jakarta, Indonesia in Feb 2020

Acknowledgement:

The author wish to acknowledge the operating room technicians and nurses in Narayana Nethralaya (NN-2) who have provided us support in managing these patients.

Financial Disclosure:

All authors have no financial interest to disclose

Conflict of Interest:

There are no conflict of interest.

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