CLINICAL TRIAL STUDY

Dexmedetomidine was Better at Lowering Intraocular Pressure than Magnesium when Combined with Local Anesthetics in Peribulbar Blocks for Posterior Segment Eye Surgery

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Abstract:

Background and Aim:

Many medications are combined with local anesthetics for peribulbar blocks to improve the quality of the block, however, few studies have compared the effect of dexmedetomidine and magnesium on intraocular pressure when combined with local anesthetics which was the primary endpoint of this double blinded study.

Materials and Methods:

A randomized controlled clinical trial was conducted on 60 ASA Physical Status (ASA PS) I-II patients scheduled for elective posterior segment eye surgeries under peribulbar anesthesia. Patients were randomly allocated to one of three groups of 20 each according to the medications they received. Local anesthetic solution was prepared using 8 ml of bupivacaine 0.5% and lidocaine 2% in a 1:1 ratio plus 1ml of hyaluronidase (150 units) making a total volume of 9 ml: **Group D** received: local anesthetic + 20 μg dexmedetomidine diluted with 1 mL of normal saline. **Group M** received: local anesthetic + magnesium sulphate 50 mg in 1 ml normal saline. **Group C** received local anesthetic + 1 ml normal saline. Intraocular pressure was measured with the Perkins applanation tonometer immediately before injection and at 1, 5, 10, 15 minutes (min) after injection and then at the end of the procedure, the onset and duration of lid and globe akinesia were assessed. Postoperative analgesia and the first dose of analgesic medication were also assessed.

Results:

Intraocular pressure measurements were statistically lower in group D than the other two groups at 10 and 15mins. The onset of globe and lid akinesia was the most rapid in Group D compared to the other two groups. The duration of globe and lid akinesia was the longest in group D. Time to first analgesic dose request was significantly longer in group D followed by group M then group C. Visual analogue score for pain was significantly less between group D and other two groups. There were no episodes of hypotension or bradycardia in the three groups. No side effects or complications as hemorrhage, globe perforation, brain stem anesthesia sedation were observed.

Conclusion:

In our study addition of dexmedetomidine to a peribulbar block was statistically better at reducing IOP, increasing the duration of optic anesthesia and delaying the need for postoperative analgesic dose request than magnesium.

Keywords: Peribulbar block, Dexmedetomidine, Magnesium sulphate, Intraocular pressure, Measurements, Local anesthetics, Postoperative analgesic dose.

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1. INTRODUCTION

Davis and Mandel [1] in 1986 described the peribulbar block, which has delayed onset and needs a higher volume of Local Anesthetic (LA) than a retrobulbar block but believed it was safer with a lower incidences of complications [2, 3]. However, peribulbar block can cause a transient increase in Intraocular Pressure (IOP), due to the increase in the orbital pressure caused by the injection of LA [4]. Many medications have been added to local anesthetics, such as clonidine, hyaluronidase, sodium bicarbonate, muscle relaxants, and opioids for ocular blocks to hasten the onset of the block and increase anesthetic duration [5 - 8].

Dexmedetomidine is a selective alpha two adrenoreceptor agonist. It provides dose-dependent sedation, analgesia, sympatholysis, and anxiolysis without relevant respiratory depression [9]. Recently, dexmedetomidine has been combined with local anesthetics in peripheral nerve block, brachial plexus block and intrathecal anesthesia and has been shown to improve the quality of both neuraxial and peripheral nerve blocks [10]. In addition, dexmedetomidine, as well as other alpha 2 agonist compounds have been shown to lower IOP in animals and humans since 1966 [11], hence making using dexmedetomidine use in posterior eye surgeries possibly beneficial.

Magnesium is a physiological calcium channel blocker and non-competitive antagonist of N-Methyl-D-Aspartate (NMDA) receptors [12]. It was used successfully with a local anesthetic solution in variable regional anesthesia techniques to reduce the onset time of block and to enhance the quality and duration of anesthesia [13 - 15].

This study was done to evaluate the efficacy of adding magnesium sulfate versus adding dexmedetomidine to local anesthetic mixture on the onset, duration of globe and lid akinesia, effect on intraocular pressure, and first analgesic request with peribulbar block in posterior segment eye surgeries.

2. PATIENTS AND METHODS

After obtaining institutional ethical committee approval and written informed consent, between April 2015 till December 2016, 60 ASA PS I and II patients, undergoing posterior segment surgeries aged 18 to 60 years with axial eye length ranged from 22 to 28 mm were enrolled in this prospective randomized double blinded study. Patient refusal to participate, reduced mental capacity, history of bleeding disorder, allergy to drugs used and severe cardiac/respiratory disease were excluded from the study. Non-invasive blood pressure, heart rate and oxygen saturation (SpO2) were monitored throughout the operation and for the first two postoperative hours. After obtaining intravenous access, a combination of midazolam (1 mg) and fentanyl (30 μg) were given for sedation and (possible) intra-procedural amnesia for the placement of the blocks. Supplemental oxygen was given through nasal cannula at 4 L/minute (min). Topical anesthesia to the conjunctiva was done by applying 0.4% oxybuprocaine drops directly before performing the block.

The local anesthetic solution was a combination of 8 ml of bupivacaine 0.5% and lidocaine 2% in a 1: 1 ratio plus 1ml of hyaluronidase (150 units) was added to speed tissue penetration making a total volume of 9 ml. The patients were then divided randomly using a computer generated randomization table and opaque sealed envelopes into three groups (20 patients in each group). All patients had peribulbar anesthetic block according to the medications they received: **Group D** (Dexmedetomidine group) received: local anesthetic 9 ml + 20 μg dexmedetomidine (Precedex, 200 μg per 2 mL; Hospira, Lake Forest, IL) diluted with 1 mL of normal saline. **Group M** received: local anesthetic + magnesium sulphate 50 mg in 1 ml normal saline. **Group C** received local anesthetic + 1ml of normal saline. The study solution for peribulbar block was prepared by the anesthesiologist who was not involved in the study. All the blocks were performed by anesthesiologist who did not participate in the remainder of the study and were blinded to the drugs given in the block.

Light orbital compression was applied for 1 min then evaluation of the onset and duration of lid and globe akinesia were assessed at 1min., 3min., 5min., 10min., 15 min. until maximum blockade and then every 15 min after surgery until complete recovery of the block. Motor block evaluation includes lid akinesia (lid closure by orbicularis and lid opening by the levator muscles). For assessment of lid akinesia, the patients were asked to open their eyelids and then squeeze them together maximally. Globe akinesia was assessed using 3-point scale for each muscle. These were scored using the movements of the extra ocular muscles in all 4 main directions on a scale of 0 to 2 [16] as shown in Table **1**. The block was considered satisfactory with loss of at least two movements of the 4 cardinal directions. If the patient complained of pain during the surgery, subtenon's block was administered, and the patient was excluded from the study and replaced by another one. IOP was measured with the Perkins applanation tonometer, immediately before injection (0 min), and at 1, 5, 10, 15 min after injection and then at the end of the procedure.

Table 1. Scoring system of global akinesia [16].

Akinesia of Extra Ocular Muscles Including Levator Muscle
0: 0-1 mm movement in 1 or 2 main directions or 0-4 mm movement in levator muscle
1: 1 mm movement in > 2 main directions, 2 mm movement in any main direction, or > 4 mm movement in levator muscle
2: > = 2 mm movement in any main direction or 2 mm movement in 2 or more main directions

Significant changes in heart rate and blood pressure were defined as a 20% reduction in blood pressure and heart rate respectively in relation to pre-block values. Postoperative analgesia was assessed by using the first analgesic dose request together with Visual Analogue Score (VAS) every hour for 6 hours postoperatively as 0 (no pain) to 10 cm (maximum pain imaginable). If the VAS was > 3, diclofenac 75mg was injected intramuscular. Any side effect or complication (globe perforation, hemorrhage, brain stem anesthesia or sedation) of the block were recorded, and appropriate management was done according to standard protocol.

2.1. Statistical Analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0.Quantitative data were expressed as mean ± Standard Deviation (SD) or median and Interquartile Range (IQR) as appropriate. Qualitative data were expressed as frequency and percentage. Data were tested for normality.

The following tests were done

- A one-way Analysis of Variance (ANOVA) when comparing between more than two means of parametric data.
- Kruskall Wallis test: for multiple-group comparisons in non-parametric data.
- If a significant difference was found, post Hoc test: Least Significant Difference (LSD) was used for multiple comparisons between different variables.
- Chi-square (X^2) test or Fisher's exact test was used in order to compare proportions between qualitative parameters.
- Probability (*P-value*)
- *P-value* < 0.05 was considered significant.
- *P-value* > 0.05 was considered insignificant.

3. RESULTS

There were no statistically significant differences between the three groups regarding demographic data and duration of surgery (Table **2**).

Table 2. Comparison among the three groups as regard the patients' characteristics and duration of surgery.

Variables	Group C (n=20)	Group M (n=20)	Group D (n=20)	*P-Value*
Age (years)	48.2 ± 17.3	50.5 ± 16.4	49.9 ± 16.8	> 0.05
Weight (kg)	64.3 ± 10.4	65.7 ± 9.5	66.2 ± 10.2	> 0.05
Sex (M/F)	9/11	8/12	10/10	> 0.05
ASA PS (I/II)	8/12	9/11	11/9	> 0.05
Duration of surgery (min)	95.1 ± 12.5	94.9 ± 13	96.5 ± 12.9	> 0.05

Data are presented as number and mean ± SD.

Table **3** shows that IOP measurements were comparable between the three groups at 0, 1, 5 min and at the end of operation, whereas IOP measurements were statistically lower in group D than the other two groups (M and C) at 10 and 15 mins.

Table 3. Comparison between IOP (mmHg) among the 3 groups at different times.

IOP	Group C (n=20)	Group M (n=20)	Group D (n=20)	ANOVA	*P-Value*
0min.	17.5 ± 8.3	16.9 ± 9.1	17.1 ± 8.2	0.218	> 0.05
1min.	28.2 ± 9.9	27.8 ± 8.8	26.7 ± 10.3	0.477	> 0.05
5min.	18.3 ± 5.1	17.5 ± 4.9	16.9 ± 6.1	0.787	> 0.05
10min.	17.8 ± 4.9	17.1 ± 4.5	13.3 ± 5.1	2.845	**< 0.05***
15min.	17.7 ± 5.3	16.9 ± 4.9	11.1 ± 6.1	3.653	**< 0.05***

(Table 3) contd.....

IOP	Group C (n=20)	Group M (n=20)	Group D (n=20)	ANOVA	*P-Value*
At the end of operation	16.9 ± 5.11	16.5 ± 4.9	16.9 ± 6.1	0.482	> 0.05

Data are expressed as mean± SD. * P-value <0.05 significant difference between Group D and the other two groups.

The onset of lid akinesia at 1 min was statistically the fastest in D group (12 patients) compared to C and M groups (2 and 4 patients respectively) and was statistically comparable between group C and group M at 1 min. Onset of lid akinesia was comparable between group D and M at 3 min and they were both faster than group C. Onset of lid akinesia was comparable between the three groups at 5, 10 and 15 min. The duration of lid akinesia was significantly shorter in group C compared to group M and D, whereas it was significantly longer in group D compared to group M (Table **4**).

Table 4. Comparison between groups regarding onset and duration of lid akinesia.

Lid Akinesia	Group C (n=20)	Group M (n=20)	Group D (n=20)	*P-Value*
1min.	2 (10%)	4 (20%)	12(60%)	**< 0.05***
3min.	16 (80%)	19(95%)	20 (100%)	**< 0.05***
5min.	18 (90%)	20 (100%)	20 (100%)	> 0.05
10min.	20 (100%)	20 (100%)	20 (100%)	1
15min.	20 (100%)	20 (100%)	20 (100%)	1
Duration of Lid akinesia (min)	135 ± 6.6[a]	161 ± 7.4[b]	182 ± 5.5[c]	**< 0.05***

* P value <0.05 significant difference. Data are presented as number, percent and mean ± SD (**a**) Significant between Group C and Group M. (**b**) Significant between Group M and Group D. (**c**) Significant between Group C and Group D.

The onset of globe akinesia was comparable in the three groups at 1 min. At 3 and 5 min, the onset of globe akinesia was the most rapid in Group D with significantly higher number of patients (16 patients at 3 min, 20 patients at 5 min) compared to group C (4 patients at 3 min, 16 patients at 5 min) and group M (5 patients at 3 min, 16 patients at 5 min). Onset of globe akinesia was comparable between group M and group C at 3 and 5 min. Onset of group akinesia was comparable between the three groups at 10 and 15 min. The duration of globe akinesia was significantly longer in group D compared to the other two groups and it was shorter in group C when compared to group M (Table **5**). None of the cases required performance of subtenon's block.

Table 5. Comparison between groups according to onset and duration of globe akinesia.

Globe Akinesia	Group C (n=20)	Group M (n=20)	Group D (n=20)	*P-Value*
1min.	0 (0%)	0(0%)	3 (15%)	> 0.05
3min.	4 (20%)	5(25%)	16 (80%)	**< 0.05***
5min.	16 (80%)	16(80%)	20 (100%)	**< 0.05***
10min.	20 (100%)	20 (100%)	20 (100%)	1
15min.	20 (100%)	20 (100%)	20 (100%)	1
Duration of globe akinesia (min)	152 ± 8.3[a]	190 ± 7.5[b]	221 ± 6.2[c]	**< 0.05***

* P value <0.05 significant difference. Data are presented as number, percent and mean ± SD. (**a**) Significant between Group C and Group M. (**b**) Significant between Group M and Group D. (**c**) Significant between Group C and Group D.

Time to first analgesic dose request was significantly longer in group D compared to group M and C while it was significantly longer in group M compared to group C (Table **6**).

Table 6. Comparison among the three groups as regard the time to first analgesic dose request.

Variable	Group C (n=20)	Group M (n=20)	Group D (n=20)	*ANOVA test*	p-value
First analgesic request (hours)	1.9 ± 1.02a	2.7 ± 0.86b	3.1 ± 0.76c	3.211	**< 0.05***

* p value < 0.05 significant difference. Data are presented as mean± SD. (**a**) Significant between Group C and Group M. (**b**) Significant between Group M and Group D. (**c**) Significant between Group C and Group D.

VAS of pain was significantly less in group D compared with the other two groups at 1 and 2 hour with no significant difference between group M and C at 1 hour, while VAS at 2 hour was significantly lower in group M compared to group C. VAS was insignificantly different between the three groups at time 3, 4, 5 and 6 hours (Table **7**).

There were no episodes of hypotension and bradycardia in the three groups. No side effects or complications such as (hemorrhage, globe perforation, brain stem anesthesia, sedation) were recorded.

Table 7. Comparison among the three groups as regard the VAS of pain.

VAS	Group C Median (IQR) (n=20)	Group M Median (IQR) (n=20)	Group D Median (IQR) (n=20)	Kruskal-Wallis	p-value
1 hr	3 (3-4)	2(1-2)	0 (0-0)[a]	2.338	**< 0.05***
2 hr	3 (3-5)	2 (2-3)[b]	0 (0-0)[a]	2.138	**< 0.05***
3 hr	4 (3-5)	3 (2-5)	3 (2-5)	0.930	> 0.05
4 hr	4 (4-5)	3 (3-5)	3 (3-4)	0.913	> 0.05
5 hr	4 (3-5)	4 (2-5)	4 (3-5)	0.869	> 0.05
6 hrs	4(3-5)	4(2-5)	4(3-5)	0.869	> 0.05

*P value <0.05 Significant difference. Data are presented as median and IQR. (**a**) Significant between Group D and other two groups. (**b**) Significant between Group C and Group M.

4. DISCUSSION

This study demonstrated that the addition of dexmedetomidine to local anesthetics in posterior segment eye surgeries decreases the IOP when compared with both magnesium and control groups. The onset of lid and globe akinesia was the most rapid in dexmedetomidine group compared to the other two groups. The duration of lid and globe akinesia was the longest in the dexmedetomidine group. The first analgesic dose request was delayed and VAS was less for 2 hours postoperatively in the dexmedetomidine group compared to the other two groups.

Due to the importance of regional anesthesia in ophthalmic surgery when compared to general anesthesia, multiple studies have attempted to optimize and improve the quality of local anesthesia to offer more patient comfort and hemodynamic stability. However, these studies gave little attention to the acute increase in the IOP after local anesthesia injection in peribulber block as it may reach up to 25 mmHg in some patients with glaucoma [8]. This is due to the fact that the orbit is a rigid non-compliant cavity with a volume of about 30 ml whereas the injection volume is about 10 ml so a definite rise in IOP occurs and it differs from one patient due to variation in eye size (volume) in relation to the size of the orbit and especially with glaucoma. This acute rise in IOP should be lowered even less than the baseline measures for more comfortable operative field for both the patient and the surgeon satisfaction.

Throughout our literature research, no study was found that compared dexmedetomidine with magnesium as adjuvants to local anesthesia in ophthalmic blocks.

Orbital compression was used to solve the problem of increased IOP after local anesthetic injection in ophthalmic blocks in several studies [17, 18]. In the current study, the addition of dexmedetomidine to local anesthetic in peribulbar block for posterior segment surgery attenuated the rise in IOP significantly when compared to M group and control group as dexmedetomidine, an α_2 agonist lowers the production of aqueous humor by direct vasoconstriction of afferent vessels in the ciliary body and facilitating the drainage of aqueous humor by decreasing the sympathetically mediated vasomotor tone in the ocular drainage system [19, 20]. This finding was consistent with Jaakola *et al.* [21] who found that using IV and topical dexmedetomidine reduced both normal and high IOP.

This effect on IOP, however, was not observed in both the control and M groups. Magnesium sulphate which is a competitive NMDA antagonist has no effect on IOP reduction because it does not cross the blood brain barrier. Bianco *et al.* [22] found that magnesium sulphate failed to decrease IOP after succinylcholine injection.

In the present study, it was found that using dexmedetomidine locally shortened the onset of the block, prolonged its duration, and delayed the first post-operative analgesic dose. This is supported by Channabasappa *et al.* [23] as they reported that the addition of dexmedetomidine to local anesthetic mixture in peribulber block shortened the onset of the block, prolonged the duration and helped significantly in decreasing IOP. Many studies have identical results that the dexmedetomidine delays the first post-operative analgesic dose request as Ge *et al.* [24] and Olutoye *et al.* [25].

Comparing dexmedetomidine to magnesium sulphate in the current study showed that dexmedetomidine use decreases the onset time of the block, prolongs its duration and delays the first analgesic dose request more than magnesium sulphate. This is consistent with other studies comparing these two drugs as adjuvants in intrathecal and epidural blocks as Shukla *et al.* [26] and Shahi *et al.* [27]. In the present study, magnesium sulphate use shortened the onset time of the block and increased its duration more than the control group which is in accordance with other studies as El-Hamid [28] and Gunduz *et al.* [29].

No side effects were observed in this study which is consistent with other studies that did not report any complications [23, 28]. Further studies are needed to investigate the effect of dexmedetomidine on IOP in glocumatous eye.

CONCLUSION

In conclusion, although dexmedetomidine and magnesium sulphate are both useful adjuvants to local anesthetics used in peribulbar blocks, the advantage of dexmedetomidine effect in decreasing the IOP makes it more attractive and suitable alternative in posterior segment eye surgeries.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was done after obtaining institutional ethical committee approval from Ain Shams Ethics Committee and written informed consent was taken from all the patients.

HUMAN AND ANIMAL RIGHTS

No Animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Written informed consent was taken from all the patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1]   Davis DB II, Mandel MR. Posterior peribulbar anesthesia: An alternative to retrobulbar anesthesia. J Cataract Refract Surg 1986; 12(2): 182-4.
[http://dx.doi.org/10.1016/S0886-3350(86)80040-2] [PMID: 3701637]

[2]   Davis DB II, Mandel MR. Efficacy and complication rate of 16,224 consecutive peribulbar blocks. A prospective multicenter study. J Cataract Refract Surg 1994; 20(3): 327-37.
[http://dx.doi.org/10.1016/S0886-3350(13)80586-X] [PMID: 8064611]

[3]   Riad W, Akbar F. Ophthalmic regional blockade complication rate: A single center audit of 33,363 ophthalmic operations. J Clin Anesth 2012; 24(3): 193-5.
[http://dx.doi.org/10.1016/j.jclinane.2011.07.012] [PMID: 22459339]

[4]   Johnson RW, Forrest FC. Anaesthesia of ophthalmic surgery.Oxford: Butterworth-Heinemann: International Practice of Anaesthesia 1996; 110: pp. 1-29.

[5]   Eldeen HM, Faheem MR, Sameer D, Shouman A. Use of clonidine in peribulbar block in patients undergoing cataract surgery. Aust J Basic Appl Sci 2011; 5: 247-50.

[6]   Sarvela PJ. Comparison of regional ophthalmic anesthesia produced by pH-adjusted 0.75% and 0.5% bupivacaine and 1% and 1.5% etidocaine, all with hyaluronidase. Anesth Analg 1993; 77(1): 131-4.
[http://dx.doi.org/10.1213/00000539-199307000-00026] [PMID: 8317720]

[7]   Zahl K, Jordan A, McGroarty J, Gotta AW, Gotta AW. pH-adjusted bupivacaine and hyaluronidase for peribulbar block. Anesthesiology 1990; 72(2): 230-2.
[http://dx.doi.org/10.1097/00000542-199002000-00003] [PMID: 2405735]

[8]   Abdellatif AA, El Shahawy MA, Ahmed AI, Almarakbi WA, Alhashemi JA. Effects of local low-dose rocuronium on the quality of peribulbar anesthesia for cataract surgery. Saudi J Anaesth 2011; 5(4): 360-4.
[http://dx.doi.org/10.4103/1658-354X.87263] [PMID: 22144920]

[9]   Paris A, Tonner PH. Dexmedetomidine in anaesthesia. Curr Opin Anaesthesiol 2005; 18(4): 412-8.
[http://dx.doi.org/10.1097/01.aco.0000174958.05383.d5] [PMID: 16534267]

[10]   Gandhi RR, Shah AA, Patel I. Use of dexmedetomidine along with bupivacaine for brachial plexus block. Natl J Med Res 2012; 2: 67-9.

[11]   Makabe R. Ophthalmologische Untersuchungen mit Dichlorophenyl aminoimidazolin. Dtsch Med Wochenschr 1966; 91: 1686.
[http://dx.doi.org/10.1055/s-0028-1111575] [PMID: 5917871]

[12]   Do SH. Magnesium: A versatile drug for anesthesiologists. Korean J Anesthesiol 2013; 65(1): 4-8.
[http://dx.doi.org/10.4097/kjae.2013.65.1.4] [PMID: 23904932]

[13]   Malleeswaran S, Panda N, Mathew P, Bagga R. A randomised study of magnesium sulphate as an adjuvant to intrathecal bupivacaine in patients with mild preeclampsia undergoing caesarean section. Int J Obstet Anesth 2010; 19(2): 161-6.
[http://dx.doi.org/10.1016/j.ijoa.2009.08.007] [PMID: 20171080]

[14]   Farouk S. Pre-incisional epidural magnesium provides pre-emptive and preventive analgesia in patients undergoing abdominal hysterectomy. Br J Anaesth 2008; 101(5): 694-9.
[http://dx.doi.org/10.1093/bja/aen274] [PMID: 18820247]

[15]   Gunduz A, Bilir A, Gulec S. Magnesium added to prilocaine prolongs the duration of axillary plexus block. Reg Anesth Pain Med 2006; 31(3): 233-6.
[http://dx.doi.org/10.1097/00115550-200605000-00010] [PMID: 16701189]

[16]   Sarvela PJ. Comparison of regional ophthalmic anesthesia produced by pH-adjusted 0.75% and 0.5% bupivacaine and 1% and 1.5% etidocaine, all with hyaluronidase. Anesth Analg 1993; 77(1): 131-4.
[http://dx.doi.org/10.1213/00000539-199307000-00026] [PMID: 8317720]

[17]   Constable PH, Porter EJB. Extraocular compression prior to cataract surgery: Time course of reduction and subsequent recovery of intraocular pressure. Eye (Lond) 1993; 7(Pt 6): 731-4.
[http://dx.doi.org/10.1038/eye.1993.170] [PMID: 8119420]

[18]   Kallio H, Harju MP, Ihanamäki T, Vesti ET, Kivelä T. Reduction of intra-ocular pressure by ocular compression before combined peri- and retrobulbar block. Anaesthesia 2011; 66(4): 278-82.
[http://dx.doi.org/10.1111/j.1365-2044.2011.06627.x] [PMID: 21401541]

[19]   Macri FJ, Cevario SJ. Effects on aqueous humor formation and intraocular pressure. Arch Ophthalmol 1978; 96(11): 2111-3.
[http://dx.doi.org/10.1001/archopht.1978.03910060491022] [PMID: 718505]

[20]   Vartiainen J, MacDonald E, Urtti A, Rouhiainen H, Virtanen R. Dexmedetomidine-induced ocular hypotension in rabbits with normal or elevated intraocular pressures. Invest Ophthalmol Vis Sci 1992; 33(6): 2019-23.
[PMID: 1349879]

[21]   Jaakola ML, Ali-Melkkilä T, Kanto J, Kallio A, Scheinin H, Scheinin M. Dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in patients undergoing ophthalmic surgery. Br J Anaesth 1992; 68(6): 570-5.
[http://dx.doi.org/10.1093/bja/68.6.570] [PMID: 1351736]

[22]   Bianco F, Candela L, Laveneziana D, Riva A. Magnesium sulfate does not inhibit the increase in ocular tonus induced by succinylcholine. Minerva Anestesiol 1987; 53(6): 369-72.
[PMID: 3444542]

[23]   Channabasappa SM, Shetty VR, Dharmappa SK, Sarma J. Efficacy and safety of dexmedetomidine as an additive to local anesthetics in peribulbar block for cataract surgery. Anesth Essays Res 2013; 7(1): 39-43.
[http://dx.doi.org/10.4103/0259-1162.113987] [PMID: 25885718]

[24]   Ge DJ, Qi B, Tang G, Li JY. Intraoperative dexmedetomidine promotes postoperative analgesia and recovery in patients after abdominal hysterectomy: A double-blind, randomized clinical trial. Sci Rep 2016; 6: 21514.
[http://dx.doi.org/10.1038/srep21514] [PMID: 26903197]

[25]   Olutoye OA, Glover CD, Diefenderfer JW, *et al.* The effect of intraoperative dexmedetomidine on postoperative analgesia and sedation in pediatric patients undergoing tonsillectomy and adenoidectomy. Anesth Analg 2010; 111(2): 490-5.
[http://dx.doi.org/10.1213/ANE.0b013e3181e33429] [PMID: 20610555]

[26]   Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine. J Anaesthesiol Clin Pharmacol 2011; 27(4): 495-9.
[http://dx.doi.org/10.4103/0970-9185.86594] [PMID: 22096283]

[27]   Shahi V, Verma AK, Agarwal A, Singh CS. A comparative study of magnesium sulfate *vs* dexmedetomidine as an adjunct to epidural bupivacaine. J Anaesthesiol Clin Pharmacol 2014; 30(4): 538-42.
[http://dx.doi.org/10.4103/0970-9185.142852] [PMID: 25425781]

[28]   El-Hamid AM. Evaluation of the effect of magnesium sulphate *vs* clonidine as adjuvant to local anesthetic during peribulbar block. Ain Shams J Anesthesiol 2011; 4: 21-6.

[29]   Gunduz A, Bilir A, Gulec S. Magnesium added to prilocaine prolongs the duration of axillary plexus block. Reg Anesth Pain Med 2006; 31(3): 233-6.
[http://dx.doi.org/10.1097/00115550-200605000-00010] [PMID: 16701189]