Dexmedetomidine versus magnesium sulphate as an adjuvant to local anesthesia in single-injection percutaneous peribulbar anesthesia for cataract extraction

Aya Abuelyossr M.*, N. A. Mohammad, Khaled M. Maghawry, Maha Sadek Elderh and Mai Mohsen AbdulAziz

Abstract

Background: The aim of the study was to evaluate the impact of addition of dexmedetomidine or magnesium sulphate to the standard local anesthetics mixture as a primary objective and to compare between both as a secondary objective utilizing the single-injection percutaneous technique for peribulbar block. In this prospective randomized double-blinded clinical trial (RCT), sixty patients, both sexes, aged 45 to 75, with an ASA of I to III, were scheduled for cataract extraction operation. They were divided into three equal groups; each received a single injection peribulbar block of a mixture of 0.5% bupivacaine (3 ml) + 2 percent lidocaine (3 ml) + 120 IU hyaluronidase + (control group (C): 0.5 ml of normal saline; group D: 50 μg of dexmedetomidine; group M: 50 mg of magnesium sulphate in 0.5 ml) with a total injected volume of 7 ml each. The duration of sensory, motor block, need for supplementary doses, hemodynamics, and satisfaction of patients and surgeons were assessed.

Results: For the primary outcome, both the dexmedetomidine and magnesium groups revealed statistically significant differences from the control group with shorter onsets of sensory block and lid akinesia (p value< 0.001 for both), shorter onset of globe akinesia for dexmedetomidine (p value<0.001) and for magnesium sulphate (p value=0.022), prolonged duration of lid and globe akinesia and sensory block (p value<0.001), better patient satisfaction (p value=0.044) but insignificant difference regarding surgeons’ satisfaction (p value= 0.117) and a less frequent, but statistically insignificant need for supplementary injection (p value=0.075). The demographic and clinical hemodynamics and oxygen saturation parameters were comparable between the three groups. For the secondary outcome, dexmedetomidine was superior to magnesium sulphate regarding onset of globe and lid akinesia (p value= 0.047 and 0.003, respectively), and durations of globe akinesia and sensory block (p value= 0.02 and 0.016, respectively). No complications related to the drugs or procedure were recorded.

Conclusions: When compared to 50 mg magnesium sulphate, dexmedetomidine at a dose of 50 μg is a superior adjunct to local anesthetic combination in peribulbar block for cataract procedures in terms of start and duration of peribulbar block.

Keywords: Magnesium sulphate, Dexmedetomidine, Peribulbar block, Cataract extraction

* Correspondence: ayaabuelyossr@med.asu.edu.eg

Department of Anesthesiology, Intensive care and Pain Management, Faculty of Medicine, Ain-Shams University, Cairo, Egypt

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Background
Because it is more secure, regional anesthesia is the primary method of anesthesia, especially in older individuals who are candidates for ocular surgeries (Mohamed & Genidy, 2017). Peribulbar block is a prevalent choice for patients undergoing phacoemulsification (Ripart et al., 2005). The single-injection method for percutaneous peribulbar anesthesia when compared to the traditional peribulbar block (at the junction of the lateral 1/3 and medial 2/3 of the lower orbital rim, using a longer needle of 25mm length), using a short neonatal needle (a short-bevel needle, 25 G, 16 mm), has been demonstrated to be a quick and simple technique that causes less discomfort, is safer, and uses less local anesthetic. It only takes one puncture instead of multiple punctures to achieve acceptable analgesia and akinesia (Ghali et al., 2011).

Dexmedetomidine is a sedative that works by acting as a centrally acting, highly selective α2-agonist. It has also been used as a supplement to local anesthetics in peripheral nerve block, brachial plexus block, subarachnoid anesthesia, and late peribulbar block, with proven efficacy and safety (Gandhi et al., 2012). Magnesium is a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist that reduces excitatory post-synaptic currents and represses voltage-gated calcium channels. It has been used as an adjunct to local anesthetic mixtures in a variety of regional anesthesia modalities to enhance anesthesia quality and duration (Elyazed & Mostafa, 2017).

Both medications have been used as adjuvants to peribulbar anesthesia previously, at various concentrations and in various surgeries, with varying findings in terms of the quality of the block (Mohamed & Genidy, 2017; Shoukry & Abd el Kawy, 2018). This study examined the effects of adding dexmedetomidine versus magnesium sulphate to typical local anesthetics combinations on the time of onset and duration of globe anesthesia and akinesia to suit phacoemulsification creating excellent operating conditions.

Methods
This prospective, randomized, double-blinded clinical trial was approved by the Research Ethics Committee at the Faculty of Medicine and registered in the Pan African Clinical Trials Registry (https://pactr.samrc.ac.za/) with the following ID (PACTR202103648671596). The study was carried out in the ophthalmic surgery unit at university hospitals in the period between March 2018 to February 2020. After we conducted a point-by-point clarification of the studied technique and adjuvants used and its conceivable results and adverse effects were clarified to each patient, informed written consents were obtained from sixty patients, from 45 to 75 years old, ASA physical status I–III of both sexes, having an axial length ranged between 22 and 30 mm who were going to have peribulbar anesthesia for cataract phacoemulsification and intraocular lens implantation.

Exclusion criteria included patients with ASA physical status IV and V, axial length (AXL) of the globe >30 mm; patients with contraindications to the block (with coagulopathies or on anticoagulant drugs); patients with contamination at the location of infusion or hypersensitivities to the test medications; patients with involuntary movements or agitated; patients who could not lie supine for long periods of time; patients with single-seeing eye; patients declined participating in the study; patients with communication challenges, such as mental retardation, hearing impairment, or a disturbed conscious state; and patients with prolonged or complicated surgeries lasting more than 3 h.

Patients were divided into three equal groups at random. Each one had twenty patients, the randomization approach was computer-generated randomized numbers, and the allocation was hidden behind fixed dark envelopes.

The three groups were:

- **Control group (group I):** received 3 ml of lidocaine 2% + 3 ml bupivacaine 0.5% + 120 international unit (IU) of hyaluronidase + 0.5 ml of 0.9% normal saline with a total volume of 7 ml.

- **Dexmedetomidine group (group D):** received 3 ml of lidocaine 2% + 3 ml bupivacaine 0.5% + 120 international unit (IU) of hyaluronidase + 50 mcg dexmedetomidine with a total volume of 7 ml.

- **Magnesium group (group M):** received 3 ml of lidocaine 2% + 3 ml bupivacaine 0.5% + 120 international unit (IU) of hyaluronidase 50 mg magnesium sulphate with a total volume of 7 ml.

An anesthetist involved in the study prepared the local anesthetic blend, and a single-injection percutaneous peribulbar block was given to the selected patients by an experienced anesthetist that was not involved in the study, so the anesthetist, the ophthalmologist, and the patient were all unaware of the type of anesthetic mixture. All the patients fasted for 6 h before the procedure and were given 20 mg oral pantoprazole the morning of the procedure.

A 22-G cannula was put on the dorsum of the non-dominant hand when the patient arrived in the pre-anesthesia room. All patients were premedicated by 0.25–0.5 mcg/kg fentanyl, unless contraindicated. Then, standard monitoring was applied (pulse oximetry, non-invasive blood pressure, and 5-lead electrocardiogram) with recording the baseline vital data. Patients were positioned in a supine position, with a nasal cannula giving supplemental oxygen at a flow rate of 2–3 l/min.
After proper sterilization, an experienced anesthesiologist administered a single-injection percutaneous peribulbar block to all patients. A 25-G beveled 16-mm needle (neonatal needle) was inserted 5 mm below the inferior lacrimal punctum along the lower orbital margin, then advanced vertically till half its length then obliquely towards the optic foramen. Seven milliliters of the local anesthetic mixture was administered gently and evenly after gentle negative aspiration. After that, the needle was gradually removed, and light digital pressure was applied intermittently to help the local anesthetic diffuse.

The parameters that were recorded were as follows:

- Vital signs such as heart rate (beats per minute), non-invasive systolic and diastolic blood pressure (mmHg), and oxygen saturation were measured before and after the peribulbar injection (baseline) (5, 10, 15, 30, 45, 60, 90 till 120 min).
- Sensory onset in minutes, measured from the moment of entire infusion to complete loss of corneal sensation, measured using a cotton swab.
- Sensory duration was measured and recorded from the moment of total anesthetic mixture injection until the onset of pain (time to first analgesic enquiry). The existence of pain in the patients was examined at the completion of the surgery and hourly until 4 h afterward. Patients who suffered intolerable postoperative pain were given 1 g paracetamol intravenously once.
- The onset and duration of global akinesia were assessed using a three-point scale ranging from 0 to 2 in each of the four directions to calculate the akinesia score (the sum of the scores within the four directions starting from 0 to eight). The start of globe akinesia was recorded from the time of finishing injection of the anesthetic mix till attaining akinesia score of eight, and the length was determined from the injection time to the time of reaching akinesia score zero.
- The onset and length of upper eyelid akinesia were determined by examining the patient’s ability to open and close the eye and recording a score of 0 = entire akinesia, 1 = midway movement in either or both eyelid edges, and 2 = usual movement. The onset was measured from the time of entire infusion of the local anesthetic mixture to total lid akinesia of score 0. The length of the lid akinesia was assessed from the time of total infusion of the local anesthetic combination till regaining normal lid movement.
- If the block was insufficient after 10 min from the main injection, as evidenced by ineffective akinesia (akinesia score of 2) and the patient’s inability to tolerate the initial stages in cataract surgery, a supplementary injection of (3 ml) of the local anesthetic combination may be required. Injection aimed posteriorly at the medial canthus, between the medial canthus and the caruncle. In each group, the number of patients who required a second injection was reported. These supplementary injections were extracted from extra syringes that had already been prepared with the identical medication mixture and concentration for each group.

- Surgeon’s satisfaction at the end of the surgery was assessed by providing a general satisfaction level on a scale of 1–5 with 1 being least satisfied and 5 being most satisfactory.
- Patients were asked to provide a general satisfaction level with the whole process on a scale of 1–5 with 1 being least satisfied and 5 being most satisfactory.
- Adverse effects of the peribulbar block such as retrobulbar bleeding, globe injury, or spread to the brainstem and also adverse reactions that might be caused by the tested drugs as profound decrease in heart rate or blood pressure, nausea, vomiting, disorientation, or somnolence were recorded to be managed if found.

Postoperatively, patients were delivered to the postanesthesia care unit (PACU) for monitoring of vital data before discharging to the ward.

Drugs used in the study:

- Lidocaine 2% vial (Alex pharmaceutical, Egypt)
- Bupivacaine 0.5% vial (Sunny pharmaceutical, Egypt)
- Magnesium sulphate (10%) 100 mg/mL ampule (Egyptian Int. Pharmaceutical Industries CO. (E.I.P.I.CO.), Egypt)
- Dexmedetomidine 200ug/ 2mL (Hospira, USA)
- Hyaluronidase injection IP 1500 IU (Shreya Life Sciences Pvt Ltd, ABBOT, India)

Statistical analysis

Sample size was calculated using PASS program 11.0 sample calculation program based on a study carried out by Mohamed and Genidy (2017) that showed that the duration of globe akinesia for control, dexmedetomidine, and magnesium sulphate groups were 115.7±24.6, 187.4±26.8, and 174.6±25.1 respectively. Based on this information, it was determined that a sample size of at least 20 patients in each group was required to detect a difference at the 5% significance level and give the trial 90 percent power.

Using SPSS 23.0 for Windows, we analyzed our data (SPSS, Chicago, IL, USA). For quantitative parametric data, an analysis of variance was used with post hoc tests.
to compare the three groups. If there was a significant difference between the groups, Tukey’s analysis was applied. For the comparison of subjective data, the chi-square test was used. Continuous parametric data was presented as mean SD, and categorical data as number of patients. Significant P-values were set at 0.05.

Results

Seventy-five patients were screened to see if they were eligible for the trial. Nine patients declined to participate in the study, six patients did not match all the inclusion criteria, and the remaining sixty patients were followed up on. Each of the three groups had twenty patients (Fig. 1).

Patients in the three groups showed no statistically significant difference as regards the demographic data (age, sex, and weight) (Table 1).

Regarding the effects on the single injection peribulbar block properties, the following results were concluded (Table 2):

- Regarding the primary outcome, both dexmedetomidine (group D) and magnesium sulphate (group M) showed significant shortening of the onsets and prolongation of the durations of sensory block, globe akinesia, and upper lid akinesia compared to the control group (group C).
- Regarding the secondary outcome, dexmedetomidine group (group D) had statistically significant shorter onsets of globe and upper lid akinesia with significantly longer durations of globe akinesia and sensory block when compared to magnesium sulphate group (group M) without significant distinction in their sensory onsets nor recovery from upper lid akinesia.

With the following results:

- Regarding the onset of sensory block, globe akinesia, and upper lid akinesia:
  - They were significantly shorter in dexmedetomidine group (group D) with the

| Table 1 Comparison between the three study groups regarding demographic data |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|                             | Group C (n=20)              | Group D (n=20)              | Group M (n=20)              | p-value                     |
| Age (years)                | 59.7±6.55                  | 62.1±6.82                  | 60.6±5.89                  | 0.519                       |
| Sex (M/F)                  | 9/11                       | 9/11                       | 9/11                       | 1                           |
| Weight (kg)                | 84.5±8.26                  | 86.5±6.3                   | 84.5±6.26                  | 0.584                       |

Data are presented as mean ±SD

P >0.05 was considered statistically non-significant between the 3 groups.
following averages: 1.09 min, 3.3 min, and 2.93 min respectively.
- Also, they were significantly accelerated in magnesium sulphate group (group M) with the following averages: 1.04 min, 3.3 min, and 2.93 min respectively.
- While in comparison to the control group (group C) their averages were 1.55 min, 3.99 min, and 3.94 min respectively.

Regarding the durations of lid akinesia, globe akinesia, and sensory block:
- Significantly longer durations were recorded in dexmedetomidine group (group D) with the following averages: 173.8 min, 198.5 min, and 239.4 min respectively.
- Also, the magnesium group (group M) showed longer durations than the control group with the following averages: 167.6 min, 188.3 min, and 228.2 min respectively.
- While the control group (group C) had the following averages: 108.2 min, 129.2 min, and 168.1 min respectively.

- Compared to the dexmedetomidine and magnesium sulphate groups, the control group (group C) had a higher number of patients who needed a supplementary injection of the anesthetic mixture with inadequate block after 10 min from the main administration, with no statistical significance (Table 3).
- There was no statistical difference in surgeon satisfaction across the three groups, but patient satisfaction was considerably higher in the dexmedetomidine (group D) and magnesium (group M) groups compared to the control group (group C) (Table 4).
- Vital data (blood pressure, heart rate, and O2 saturation results) were all comparable in the three groups (Figs. 2, 3, and 4).
- There were no recorded adverse outcomes during the execution of this study.

### Discussion

The goal of this study was to examine the effects of adding dexmedetomidine or magnesium sulphate to the local anesthetic mixture using Rizzo and his colleagues’ single-injection approach of percutaneous peribulbar anesthesia from 2005 (Rizzo et al., 2005). The addition of dexmedetomidine and/or magnesium sulphate to the anesthetic combination in the peribulbar block has been studied in the past, albeit with different measurements or strategies than this study. In terms of the onset and duration of peribulbar block, our findings revealed that adding 50 mcg dexmedetomidine to the local anesthetic combination was preferable to adding 50 mg magnesium

### Table 2

Comparison between the three groups regarding the characteristics of the peribulbar block

|                         | Group C (n=20) | Group D (n=20) | Group M (n=20) | C vs D | C vs M | D vs M | p-value (ANOVA) | Post hoc Tukey’s test |
|-------------------------|----------------|----------------|----------------|--------|--------|--------|-----------------|----------------------|
| Onset of sensory block  | 1.55± 0.07     | 1.09 ± 0.21    | 1.04± 0.20     | < 0.001        | < 0.001        | 0.580   | <0.001         | A1                    |
| (min)                   |                |                |                |        |        |        |                 | 1                     |
| Onset of globe akinesia| 3.99± 0.602    | 3.3 ± 0.21     | 3.63± 0.34     | < 0.001        | 0.022        | 0.047    | <0.001*         | A2                    |
| (min)                   |                |                |                |        |        |        |                 | 2                     |
| Onset of lid akinesia  | 3.94± 0.33     | 2.93± 0.18     | 3.28± 0.42     | < 0.001        | < 0.001        | 0.003    | <0.001*         | A3                    |
| (min)                   |                |                |                |        |        |        |                 | 3                     |
| Duration of lid akinesia| 173.8± 8.96    | 167.6± 7.66    | 188.3±9.07     | < 0.001        | < 0.001        | 0.0535   | <0.001†         | A1                    |
| (min)                   |                |                |                |        |        |        |                 | 1                     |
| Duration of globe akinesia | 129.2± 7.9    | 198.56 ± 10.53 | 198.3±10.53    | < 0.001        | < 0.001        | 0.002    | <0.001*         | A2                    |
| (min)                   |                |                |                |        |        |        |                 | 2                     |
| Duration of sensory block (time to 1st analgesic inquiry) (min) | 168.1± 8.8    | 239.4±15.3     | 228.2±12      | < 0.001        | < 0.001        | 0.016    | <0.001*         | A3                    |

Data are presented as mean±SD

*P <0.05 was considered statistically significant between the 3 groups

†P <0.05 was considered statistically significant between group C and groups D and M

Using the post hoc Tukey’s test for pairwise comparison within the ANOVA data: A1 was considered significant between group C and group D. A2 was considered significant between group C and group M. A3 was considered significant between group D and group M

### Table 3

Comparison between the three groups regarding the need for supplementary injections of the anesthetic mixture

| Extra doses | Group C (n=20) | Group D (n=20) | Group M (n=20) | p-value |
|-------------|----------------|----------------|----------------|---------|
|             | 5              | 1              | 1              | 0.075   |

Data are presented as number of patients

p-value < 0.05 is considered statistically significant between groups D and M and group C
sulphate. Furthermore, when compared to the control group, both groups of dexmedetomidine (group D) and magnesium sulphate (group M) had a faster onset, longer duration of the peribulbar block, and less frequent need for supplementary injections during the surgery, resulting in better patient satisfaction and postoperative hemodynamics.

– This study’s findings are consistent with those of Mohamed and Genidy (Mohamed & Genidy, 2017), who examined the effects of adding 50 mg of magnesium sulphate and 25 mcg of dexmedetomidine to a 10 mL anesthetic blend for cataract procedures using the conventional percutaneous inferolateral peribulbar block administered by a 25-G, 25-mm length needle. They discovered that, in comparison to the control group, both expedited the onset and lengthened the duration of the usual peribulbar block, with a higher rate of need for supplemental injections in the control group, as we discovered in our study. They discovered no significant differences between the dexmedetomidine (25 mcg) and magnesium sulphate (50 mg) groups.

– These results moreover concur with the results of a study done by Shoukry and Abd El Kawy (Shoukry & Abd el Kawy, 2018) on 90 patients examining the impacts of including 50 Mg magnesium sulphate and 50 mcg dexmedetomidine to LA blend for single-injection percutaneous peribulbar block for vitrectomy surgeries. In their study, they found out that both magnesium and dexmedetomidine accelerated the onset of the block and drawn out its duration compared to the control group as in this study. But in difference to our study, they found that magnesium had a measurably critical shorter onset of both sensory anesthesia and globe akinesia required to begin the surgery compared to dexmedetomidine.

– This is in line with the findings of Hafez and colleagues (Hafez et al., 2016), who compared the effects of three dosages of dexmedetomidine (15μg, 20μg, and 25μg) as adjuvants to lidocaine 2%, bupivacaine 0.5%, and 120 IU of hyaluronidase for traditional peribulbar block in posterior chamber procedures. They used 160 patients in their trial and discovered that dexmedetomidine has a faster start and longer duration of sensory and motor blockage, with the highest dose of 25 g being the most effective.

– In agreement with Channabasappa and colleagues (Channabasappa et al., 2013) who compared two doses of dexmedetomidine 25 mcg and 50 mcg added to 3 ml lidocaine 2% and 3 ml bupivacaine 0.5% in a conventional peribulbar block for cataract surgery on 90 patients and found that dexmedetomidine shortened the onset and lengthened the block.

– Also, Abu Elyazed and Mostafa (Elyazed & Mostafa, 2017) compared the effects of 50 mg magnesium sulphate and 20 g fentanyl added to (lidocaine 2 percent and bupivacaine 0.5% + 150 IU of

| Table 4 Comparison between the three groups regarding the satisfaction |
|---------------------------------|----------------|----------------|----------------|
| | Group C (n=20) | Group D (n=20) | Group M (n=20) | p-value (ANOVA) |
| Patient satisfaction | 5 (4–5) | 5 (5–5) | 5 (5–5) | 0.0444* A_2 |
| Surgeon satisfaction | 5 (5–5) | 5 (5–5) | 5 (5–5) | 0.117 |

Data are presented as median (IQR)

*p-value < 0.05 is considered statistically significant between the 3 groups

A_2 p is considered significant between group C and groups D and M

![Fig. 2 Linear chart of systolic blood pressure between the three groups](image)

![Fig. 3 Linear chart of heart rates between the three groups](image)
Authors’ contributions
MN designed the study, revised the literature, followed the patients, and critically reviewed the manuscript. KM designed the study, analyzed the data, and wrote and critically revised the manuscript. MM and MS revised the

Conclusions
When compared to adding 50 mg magnesium sulphate to the same mixture for cataract surgery, our study found that adding 50 mcg dexmedetomidine to a mixture of lidocaine 2% and bupivacaine 0.5%, ophthalmic surgeries using the traditional peribulbar block on 60 patients, concluding that magnesium sulphate significantly accelerated the onset of the block.

Limitations
The small number of patients in the trial; the single type of ophthalmic operation; cataract extraction, which is

Abbreviations
ASA: American Society of Anesthesia; AXL: Axial length; ECG: Electrocardiogram; IU: International unit; LA: Local anesthetic; NMDA: N-Methyl-D-aspartate; PACU: Postanesthesia care unit; SD: Standard deviation

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