

Evaluation of The Effect of Addition of Magnesium Sulfate to Local Anesthetics For Peribulbar Block: a Meta-Analysis for Randomized Trials

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ABSTRACT

Background: Magnesium sulphate has been used along with local anesthetics in different regional blocks and found to be have a great effect in decreasing the time of onset of the block , IOP and increasing the duration of the block. To evaluate the effect of addition of magnesium sulfate to local anesthetics mixture on the time for onset of the globe and lid akinesia ,IOP and duration of peribulbar block in different ophthalmic surgeries . A systematic literature search that performed to identify randomized controlled trials that compared addition of magnesium sulphate to local anaesthetics in peribulbar block against standard local anaesthetic in different eye surgeries . Using the random effects model, risk ratio (for binary variables), weighted mean difference (for continuous variables) and 95% confidence intervals were calculated. We applied trial sequential analysis to assess the risks of type I and II error, meta-regression for the study of the dose responsive relationship, and the Grading of Recommendations Assessment, Development, and Evaluation system. We identified 13 randomized controlled trials .When using conventional meta_analysis of nine low risk of bias trials, we found a statistically significantly longer duration of analgesia,.

1.Introduction:

Regional anesthesia is a preferred technique for ophthalmic surgery. It is safe, inexpensive and provides efficient ocular anesthesia for ophthalmic surgery. Among regional blocks, it has shown high success rate and safety in different ocular procedures including difficult and extended time surgeries. [1]

Peribulbar block is safer in comparison to retrobulbar block due to a lesser incidence of serious complications such as brainstem anesthesia, globe perforation, and retrobulbar hemorrhage.[2] However, the development of ocular akinesia with peribulbar block takes longer time in comparison to retrobulbar block, and the occurrence of inadequate analgesia is also more frequent in peribulbar block.[3]

The peribulbar block is a needle-based technique that varies from the retrobulbar block in terms of the depth and angulation of needle placement within the orbit [2]. The rate

of major complications under peribulbar anesthesia was reported to be 0.006%. However, its main disadvantage is the need for a larger volume of local anesthetic agent resulting increase in IOP .[4]

Magnesium has been used with a local anesthetic solution in different regional anesthesia techniques to decrease the onset time of block and to increase the quality and duration of anesthesia.[5]

Magnesium is a physiological calcium channel blocker and noncompetitive antagonist of N-methyl-D-aspartate (NMDA) receptors. [6]

Magnesium has been used with a local anesthetic solution in different regional anesthesia technique to decrease the onset time of block and to increase the quality and duration of anesthesia.[6]

2.Literature search:

2.1.Study design:

Meta-analysis study.

2.2.Review of literature:

We performed a systematic electronic literature search in the databases MEDLINE, Epub,NCBI ,Cochrane Central, Web of Science, and Google Scholar on August 4, 2019 in order to identify trials that used magnesium sulphate as adjuvant to local anaesthetics in peribulbar block in different eye surgeries.

Search was limited to randomized trials published in English language, conducted on humans over the last 13 years. All protocols

were approved by the local ethics committee or institutional review board of their respective institution.

2.3.Screening and evaluation of articles:

The following screening was used to screen the articles yielded by review of literature after ranking the articles according to authors and journal of publication. Only articles fulfilling the inclusion criteria was included for further steps of data collection, analysis and reporting.

3.Methods:

3.1.Inclusion criteria:

Age more than 16 years old.

Patients with previous complications and those refusing general anesthesia.
normal axial length (18-25mm.)
Randomized controlled trials over the last 10 years .

3.2.Exclusion criteria:

Age less than 16 years old.
Uncooperative patients.
Allergy to local anesthesia.
Patient refusal of local anesthesia.

3.3.Statistical Methods for Meta-Analysis:

Since there is a variety of procedures and population characteristics diversity, random effect modelling, the more logical approach will be used to pool results and analyze dichotomous and continuous outcomes through meta-analytic techniques.

The meta-analysis was performed using the Review Manager 5.3 (Cochrane Collaboration, Oxford, UK). Mean differences (MD) was calculated to compare continuous and dichotomous variables, respectively. All results were reported with 95% confidence intervals (CIs). Differences were considered statistically significant when the 95% CI did not include 1 for OR and 0 for the standardized mean difference. Continuous variables that presented as median and range values, mean and standard deviations were calculated. Heterogeneity was quantified using the I² statistic. When I² was 50% or lower, a low heterogeneity was rated, otherwise a high heterogeneity was rated.

Meta-analysis was performed using a random effects model. Statistical significance was set at a p-value ≤ 0.05 .

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed.

All of the 13 studies was published from 2011 to 2019 and designed as randomized trials. The dose of magnesium sulphate was given in the supine position in 4.5 ml

of 0.5% bupivacaine and 4.5 ml of 2% lidocaine mixed with hyaluronidase (150 U) with total volume 10 ml . All trials were designed with normal saline control group except (Manal and rehab 2019) 60 patients divided into 2 groups each contains 30 patients group D for dexmetomedine and group M for magnesium sulphate and total volume injected is 7 ml (3 ml bupivacaine 0.5 %,3 ml lidocaine 2% and 50 mcg dexmetomedine in 1 ml saline for dexmetomedine group and 50 mg magnesium sulphate in 1 ml saline in magnesium sulphate group .

3.4.Data Extraction:

We report the primary outcome of each study included into our meta-analysis. The primary outcome was the outcome explicitly mentioned as primary in the text or the variable for which a sample size calculation was done or the variable that was first reported in the results section of the study.

Data were extracted by authors from the reports that were considered eligible.

If two or more groups using magnesium sulphate with local anaesthetics in peribulbar block were studied, these data were combined for meta-analysis. Combining dichotomous data was by simple addition; for the combination of continuous data we used the formula published in the Cochrane handbook.

Assessment of risks of bias We used the Cochrane Risk of Bias tool to analyse the methodological quality of the studies.

This tool allows for an assessment of the risks of selection bias (random sequence generation, allocation concealment) ,performance bias (blinding of participant and personnel), detection bias (blinding of assessor), and attrition bias.

We considered a trial to be at low risk of bias when there was adequate random sequence generation, adequate allocation concealment and outcome assessment was adequately blinded.

Table (1) Criteria of the included studies :

Name of the study	Methods	participants	Interventions (adjuvants to local anaesthetics)	Outcomes
1-Sinha R ,et al 2016	A prospective randomized double-blind study	60 Patients (30 patients in each group)	Group NS received normal saline Group MS , received 50 mgmagnesium sulfate	Onset and duration of lid and globe akinesia
2-A.Z.E mohamed and M.M Genidy 2017	prospective, randomized, double blinded study.	66 patients scheduled for phaco-emulsification of cataract and intraocular lens implantation.	Group I (control group): Group II (magnesium sulphate group): Group III (dexmedetomidine group)	-Onset and duration of globe akinesia (min) -Time to 1st analgesic request (min)
3-Abd El hamid A.M 2011	not clear	60 patients for eye surgeries (20 for each group)	- group o received 1 ml normal saline . - group m received 50 mg magnesium, - group c received 30 mcg clonidine	
4-Aktham and Amr 2018	prospective randomized, double-blind, and controlled study	90 patients scheduled for vitreoretinal surgery (30 for each group)	- group C received 0.5 ml normal saline - groupM received 50 mg magnesium - group D received 50 mcg dexmetomedine	-onset of globe anesthesia and akinesia. -The duration of globe analgesia. -IOP
5-Dalia and Dina 2018	prospective randomized double blinded study	60 patients scheduled for posterior segment eye surgeries (20 for each group)	- group C received 1 ml normal saline. - group M received 50 mg magnesium . - group D received 50 mcg dexmetomedine.	-Onset and duration of lid and globe akinesia . -effect on IOP.
6-Hamawy and bestarous 2013	prospective double-blind randomized controlled study	75 patients scheduled for cataract surgery.(25 for each group)	- Group O received 1ml of normal saline. - Group M received 50 mg magnesium . - Group R received 0.06 mg /kg rocuronium .	-Lid and globe akinesia -Hemodynamics.
7-Abu el yazed and Mostafa 2017	prospective, randomized, double-blind trial	90 patients scheduled for cataract surgery (30 for each group)	- Group I received saline - Group II received 25 mcg fentanyl - Group III received 50 mg magnesium	
8-Manal and Rehab 2019	prospective randomized, comparative non controlled clinical study	60 patients scheduled for elective cataract surgery (30 for each group)	- group M received 50 mg magnesium - group D received 50 mcg Dexmetomedine	-Onset of globe akinesia ,corneal anaesthesia -1st analgesic request -IOP
9-Osama et al 2018	Not clear	75 patients scheduled for cataract surgery (25 for eacgh group)	- Group O received 1 ml saline - Group M received 50 mg magnesium . - Group D received 25 mcg dexmetomedine.	-Onset and duration of lid and globe akinesia . - time to 1st analgesic request.
10-Sherif ,et al 2019	prospective cohort study	54 patients scheduled for strabismus surgery (27 for each group)	- Group I received 50 mg magnesium - Group II received 1 ml normal saline	-Ocular anesthesia, akinesia (onset & duration) Hemodynamic parameters
11-Mogahed ,et al 2017	prospective, double-blind, randomized, and controlled trial.	105 patients scheduled for cataract surgery (35 patients in each group)	- GroupI received 1 ml normal saline - Group II received 50 mg magnesium - Group III received 100 mg magnesium	- duration sensory and motor block. -IOP
12-Sayed ,et al 2018	Not clear	100 patients scheduled for anterior and posterior eye surgeries (25 for each group)	- Group O received 1 ml saline - Group M received 50 mg magnesium - Group R received 0.06 mg/kg rocuronium - Group D received 1 mcg /kg dexmetomedine	-Globe akinesia at 2.5 ,5 ,7,10 min -Corneal anaesthesia at 2.5 ,5 ,7 ,10 min
13-Raof ,et al 2016	Not clear	40 patients scheduled for posterior segment eye surgery (20 for each group)	- Group M received 50 mg magnesium in ldcac anaesthetic. - Group C only locacal anaesthetic	Onset and duration of globe akinesia IOP

3.5.Monitoring:

All patients undergoing any eye surgery under local anesthesia were monitored with pulse oximetry, ECG, non-invasive blood pressure measurement. Patients received an oxygen-enriched breathing atmosphere to prevent hypoxia and at a flow rate enough to prevent

re-breathing and the ensuing hypercarbia once draped. ECG and pulse oximetry were continued and recorded every 15 min during the entire procedure and every 30 minute during the first two postoperative hours

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Sinha R, Sharma A, et al 2016	+	?	+	+	?	+	+
A.Z.E. Mohamed, M.M. Genidy 2017	+	+	+	?	?	+	+
Abd El-Hamid AM 2011	+	?	?	+	?	+	+
aktham and amr 2018	+	?	+	?	?	+	+
Dalia Ahmed Ibrahim, Dina Salah Hamawy and Bestarous 2013	+	?	+	+	?	+	+
M.M. Abu Elyazed, S.F. Mostafa 2017	+	?	?	?	?	+	+
manal and rehab 2019	+	?	?	?	?	+	+
Mogahed MM, Anwar AG, Abo-elazm WN (2017)	+	?	?	?	?	+	+
Mohamed Abd El-Raouf, et al 2016	+	+	+	?	?	+	+
Osama A.H. et al. 2018	+	?	+	?	?	+	+
Sayed ahmed ,et al 2018	+	?	?	?	?	+	+
Sherif et al 2019	+	?	?	?	?	+	+

Fig 1 Risk of bias summary: review authors' judgements about each risk of bias item for each included study..

3.6.Selection criteria:

We included randomized controlled clinical trials which used magnesium sulphate in peribulbar block .

3.7.Inclusion and exclusion criteria:

We defined inclusion and exclusion criteria a priori. For inclusion, studies had to have the following characteristics (specified according to the PICO acronym)

4.Patients adults undergoing surgery under regional anaesthesia alone or combined with mild sedation with midazolam.

4.1.Intervention addition of Magnesium sulphate to local anaesthetic in peribulbar block .

4.2.Comparator: with control group usually normal saline or with dexametomedine or clonidine or rocuronium.

4.3.Outcomes:

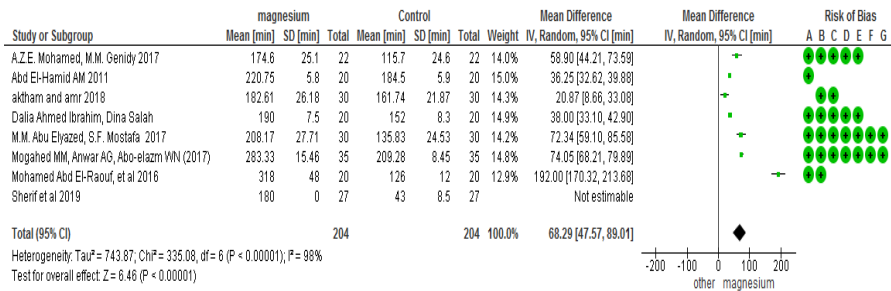
Primary outcome - duration of global akinesia ,onset of block

Secondary outcomes – effect on IOP , 1st analgesic request, Incidence of Oculo-Cardiac Reflex (OCR)

5.Results:

Study characteristics

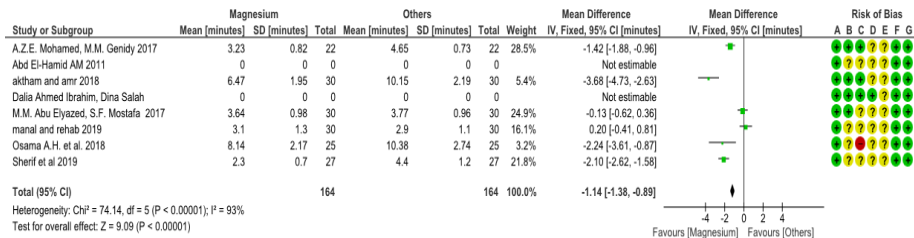
In all studies, long-acting local anesthetics were used and provides exact definitions of the outcomes analysed in the included studies.



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

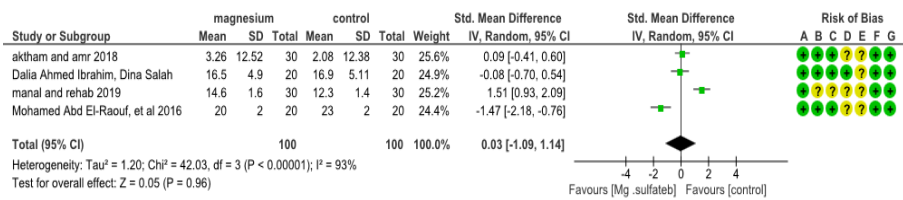
Fig 2 Forest Plot comparison of duration of globe akinesia



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Fig 3 Forest plot of comparison: Onset of globe akinesia.



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Fig 4 Forest plot of comparison outcome: IOP

5.Discussion:

The effect of administration of magnesium when compared with administration of 50 dexmedetomidine in peribulbar anesthesia, it found that administration of mg magnesium sulphate 10% or 25 mg dexmedetomidine to mixture of lidocaine 2% and bupivacaine 0.5% in peribulbar anesthesia for phacoemulsification of cataract and intraocular lens

implantation accelerated the onset time of sensory block, globe akinesia, lid akinesia, and time for suitable conditions to start surgery and prolonged the duration of globe akinesia, lid akinesia, and time to 1st analgesic request .[7]

Addition of fentanyl (2 lg/ml) or magnesium sulphate (50 mg) to peribulbar block in patients undergoing cataract surgery equally

prolongs the duration of postoperative analgesia.[8]

Co-administration of 50 mg or 100 mg of magnesium sulfate to ropivacaine in peribulbar block in cataract surgery enhances the onset and prolong the duration of sensory and motor blockade without adverse effects with reduction of the postoperative analgesic requirements with a higher dose of magnesium sulphate. The results were more significant on using 100 mg magnesium sulfate.[9]

The addition of rocuronium to the local anesthetic mixture results in a better akinesia score and faster establishment of suitable conditions to start cataract surgery compared with those in the magnesium and placebo groups.[10]

Addition of 50 mg of magnesium 10% or 15 mic of dexmedetomidine to local anesthetic mixture for peribulbar anesthesia in the operations of phacoemulsification of cataract and intraocular lens implantation accelerated onset of globe anesthesia, akinesia of the globe and the lid, prolonged the duration of globe akinesia, lid akinesia, time to 1st analgesic request, and enhanced the satisfaction of the patients and quality of the operative conditions.[11]

Use of 50ug dexmedetomidine or 50mg magnesium sulphate 10% with mixture of lidocaine 2% plus bupivacaine 0.5% for peribulbar anesthesia in cataract surgery enhances the onset of globe anesthesia and akinesia . Dexmedetomidine causes more decrease in intraocular pressure magnesium sulphate .[12]

Co-administration of 100 mg magnesium sulphate with the local anesthetics was effective and safe. It achieved suitable conditions to start surgery rapidly. Further, it improved the quality of operative conditions and patient satisfaction[13]

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.[14]

The onset of globe anesthesia and akinesia was significantly shorter in M group in comparison with D and C Groups, with a significant increase in the duration of globe analgesia and akinesia in the D Group when compared to both M & C groups. Groups D and M showed a statistically significant

decrease in the IOP at 5 min and 10 min when compared to the baseline measurement of the same groups & to C Group, no complications or adverse effects related to the drug or technique were recorded.[15]

Co-administration of peribulbar magnesium local anesthetic produces predictable rapid onset of anesthesia without any side-effects, and also addition of clonidine to local anesthetic resulting in prolonged duration of block .[16]

The addition of magnesium sulfate to the local anesthetic mixture results in the earlier onset of akinesia and establishment of suitable conditions to start the ophthalmic surgeries. Magnesium sulfate does not cause any side-effect at given dose and saves time in a busy ophthalmic theatre.[17]

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