Original Article

Comparison of Preoperative Infusion of Magnesium Sulfate and Mannitol on Intraocular Pressure Changes in Patients Undergoing Phacoemulsification Surgery

Kamran Montazeri, Hasanali Soltani[1], Mojtaba Rahimi Varposhti, Leila Mohajeri[1]

Department of Anesthesiology, Anesthesiology and Critical Care Research Center, Isfahan University of Medical Sciences, [1]Department of Anesthesiology, Medical School of Isfahan University of Medical Sciences, Isfahan, Iran

Abstract

Background: The present study has been designed to compare the effect of magnesium sulfate with mannitol on reducing intraocular pressure (IOP). **Materials and Methods:** During the phacoemulsification surgery, 105 patients randomly divided into three groups receiving 20% mannitol at a dose of 0.3 g/kg, 50% magnesium sulfate at a dose of 20 mg/kg, and placebo (normal saline), with the same volume (100 ml) and infusion time (10 min), were used for the first, second, and third groups, respectively. The IOP was measured before and immediately after the injection and 5 min after the end of the surgery and compared between the groups. **Results:** The mean IOP immediately after the injection had a significant difference in three groups (mannitol: 15.2 ± 2.5, magnesium sulfate: 14.7 ± 1.9, and normal saline: 13.8 ± 2.8; $P = 0.044$), and the IOP had a significant difference between normal saline and mannitol groups (0.027) while there was no significant difference between mannitol and magnesium sulfate groups ($P = 0.34$) and also between magnesium sulfate and normal saline groups ($P = 0.2$). **Conclusion:** Using magnesium sulfate had no effect on changes in the IOP and hemodynamic of patients during the surgery. Using mannitol may be effective in reducing IOP while no effect of magnesium sulfate on IOP was found.

Keywords: *Intraocular pressure, magnesium sulfate, mannitol*

Introduction

Cataract is one of the most common causes of vision loss worldwide. The treatment of visual impairment due to cataract is based on surgical and pharmacological methods.

Surgical procedures include the manual removal of lens either through extracapsular or through phacoemulsification and replacing it with an intraocular lens. Phacoemulsification is a technique with a lot of advantages. In this technique, the lens is mechanically converted into 4–8 pieces. The required force is created by part of the device called a chopper. This technique is suitable for mature and nigra cataracts with weak zonules. An important issue of the technique is that it can only be used by experienced surgeons.

Intraocular pressure (IOP) is one of the most important factors that must be controlled within the surgery. Many factors including age, gender, type of anesthesia influence the IOP.[1]

The regulation of IOP is influenced by the production of aqueous humor, resistance to outflow of aqueous humor, and venous pressure of the scleral surface. By the same speed of outflow and inflow of the aqueous humor, the IOP remains constant; however, there is no appropriate and equal value for all patients. After the pressure treatment, the proper aim is the minimal visual impairment without any damage to the visual field; however, the normal IOP is 10–15 mm Hg.

An increase in IOP can even transiently cause choroidal hemorrhage and permanent vision loss.[2]

With regard to the results obtained from different studies, there is a controversy about the effect of ketamine on IOP. The effect of the drugs of other groups such as timolol and other beta-blockers, prostaglandins including latanoprost, adrenergic agonists such as clonidine, carbonic anhydrase inhibitors including acetazolamide and mannitol in decreasing IOP are remarkable.[3]

Most anesthetics reduce the IOP by mechanisms such as relaxing the skeletal

Address for correspondence:
Dr. Leila Mohajeri, Department of Anesthesiology, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: Leila.mohajeri@yahoo.com

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muscle tone of eyes, depressing the central nervous system, increasing the outflow of aqueous humor, and reducing venous and arterial blood pressure. Sedative drugs decrease the IOP generally through eliminating the control effects of diencephalon on it. Propofol, thiopental, midazolam, fentanyl, droperidol, nondepolarizing relaxants, and lidocaine reduce the IOP, whereas ketamine and succinylcholine increase it.[4] Because reduction of neuroendocrine responses to surgical trauma during anesthesia is always considered by specialists, and previous studies suggest that magnesium sulfate adjusts hemodynamic responses in the response to intubation such as increasing IOP, systemic blood pressure, and heart rate,[5] the present study has been designed to compare the effect of this drug with mannitol which has known effects on reducing IOP but with many complications including seizure, pulmonary edema, and exacerbation of heart failure.[6] Therefore, it is not a suitable drug for all patients. Given the lack of previous studies on the effect of magnesium sulfate on patients undergoing venous sedation by phacoemulsification surgery and high prevalence of cataract and high frequency of doing phacoemulsification surgery in Isfahan, the study group was selected from them.

Materials and Methods

The study is a randomized, double-blind, controlled clinical trial which was conducted in the period of 2014 in Isfahan. The population included patients undergoing phacoemulsification.

Inclusion criteria were age range of 40–90 years, patients with American Society of Anesthesiologists (ASA) (1–2)/body mass index (BMI) (18–30), lack of renal failure (based on laboratory results and clinical signs), lack of heart block (based on ECG), lack of advanced heart failure (based on clinical signs), lack of hypocalcemia (based on clinical signs), lack of hyponatremia (based on laboratory results), lack of chronic eye disease, lack of eye surgery for healthy eye, not taking diazoxide, pentoxifylline, rituximab, monoamine oxidase inhibitors, and calcium blockers, no history of drug allergy, and patients agreement. In the case of revising the type of surgery (expected for phacoemulsification) and anesthesia (requiring intubation, general anesthesia, etc.) and an increase in IOP using magnesium sulfate and therapy with mannitol, the patient was excluded from the study.

Considering the confidence level of 95%, test power of 80%, standard deviation of IOP equivalent to 1.2, and the least significant difference between groups equal to 0.8, using sample size estimation formula, the sample size required for the study was estimated as 35 patients in each group to compare the means [Figure 1].

The methodology of the study is that after the adoption of the proposal and obtaining the authorization of the Medical Ethics Committee, 105 patients with inclusion criteria were selected and divided into three groups of 35 patients. During the phacoemulsification surgery, 20% mannitol at a dose of 0.3 g/kg, 50% magnesium sulfate at a dose of 20 mg/kg, and placebo (normal saline), with the same volume (100 ml) and infusion time (10 min), were used for the first, second, and third groups, respectively. The randomization was performed using random allocation software.

To maintain the double-blindness of the study, magnesium sulfate with suitable concentration in 20cc of 50% magnesium sulfate diluted in 500cc normal saline, each cc equivalent to 20 mg and an equal amount of three solutions was used. Three solutions were purred in three similar boxes with the volume of 500cc with tags of 1-2-3.

To randomize the study, the first, second, and third patients were put in one of the three groups in a lucky draw and other patients were consecutively distributed into three groups so that the sample size reached the required number.

In this study, patients underwent intravenous sedation with the maintenance of spontaneous breathing. The measured variables included body mass index, heart rate, blood pressure, and IOP. The patients' height and weight were measured by the same means before entering the operating room. Heart rate, blood pressure, and respiratory rate were monitored before and during the surgery (at the times of 5, 10, 15, 20, 25, and 30 min) and in recovery (at the time of entry and 15 min after it and at the time of exit from the recovery). Meanwhile, the pulse oximeter was used to assess the patient's breathing. The toxic level of mannitol was monitored based on the clinical signs and complications. The toxic level of magnesium sulfate was evaluated through investigating patellar reflex before entering the operating room and again in the recovery room, and loss of patellar reflexes to the basic level was considered as a toxic level and the patient was followed up until complete recovery. Despite the presence of various devices such as air pulse tonometer, Tono-pen, and Goldmann, the IOP of intact eye was measured by Schiotz tonometer by a surgeon. The IOP was measured before and immediately after the injection and 5 min after the end of the surgery, and if the IOP increased, patients were excluded from the study, received mannitol with the dose of 0.3 g/kg, and recorded in the collected data.

Patients received midazolam (with the dose of 0.03 mg/kg), fentanyl (2 mg/kg), ketamine 10 mg, and thiopental (based on the target level of patient response to drug sedation with score (2 and 3) for intravenous sedation and tetracaine of 0.5% for topical anesthetic.

The duration of stay in the recovery room was based on modified Aldrete score. In this scoring system, patients receive 0–2 scores for every 5 items of physical activity, level of consciousness, hemodynamic stability, respiratory stability, and oxygen saturation status, and patients

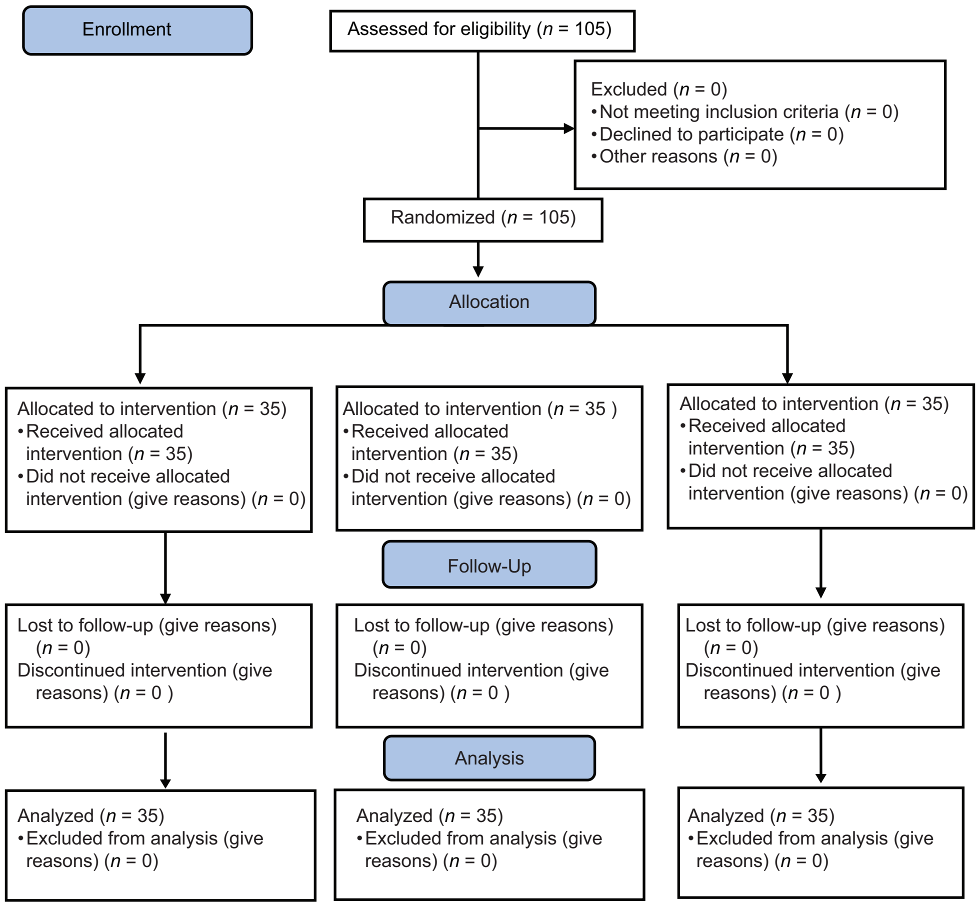

Figure 1: Consort study flowchart

with scores 9–10 can be safely discharged from the recovery room. Nitroglycerin (50 mcg) was used to treat hypertension (blood pressure [BP] >20% of primary BP), ephedrine (5 mg) and atropine (0.5 mg) were used to treat hypotension and bradycardia, and metoclopramide (10 mg) was used to treat vomiting caused by drugs. All information obtained for each patient was recorded in a special questionnaire developed for this purpose.

To observe the moral conditions, possible complications were explained to patients, and in so doing, a consent form was signed by the patients before the surgery, and if possible complications occurred, the treatment was done completely.

The study data were entered into a computer and analyzed using SPSS software version 22 (SPSS INC, Chicago, IL, USA) and Chi-square, one-way ANOVA tests with repeated observations.

Results

In this study, 105 patients undergoing cataract surgery with specifications listed in Table 1 were studied. According to one-way ANOVA, the mean age, weight, height, and BMI of patients in the three groups were not significantly different. Furthermore, according to the Chi-square test, the frequency distribution of ASA in three groups was not different while the gender distribution had a statistical significance in the three groups ($P = 0.031$).

In Figures 2-5, the mean systolic and diastolic pressure, heart rate, and respiratory rate are given per minute. In terms of ANOVA with repeated observations, the mean changes in systolic and diastolic blood pressure and respiratory rate of the patient had no significant differences with the onset of surgery until the time of existing from the recovery room whereas changes in heart rate were significantly different among three groups during the mentioned period ($P = 0.023$), and patients in the normal saline group had lower mean heart rate during the study period.

In the three groups, the mean of IOP before injection, immediately after injection, and 5 min after the operation are shown in Table 2. Based on one-way ANOVA, the mean IOP immediately after the injection had a significant difference in three groups ($P = 0.044$) and the IOP had a significant difference between normal saline group and mannitol group (0.027) whereas there were no significant difference between mannitol and magnesium sulfate groups ($P = 0.34$) and also between magnesium sulfate and normal saline groups ($P = 0.2$). On the other hand, according to repeated measures ANOVA,

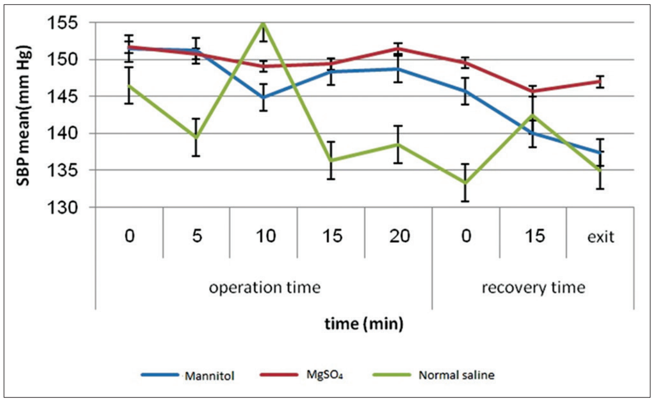

Figure 2: Mean systolic blood pressure since the start of operation until out of recovery room (P = 0.76)

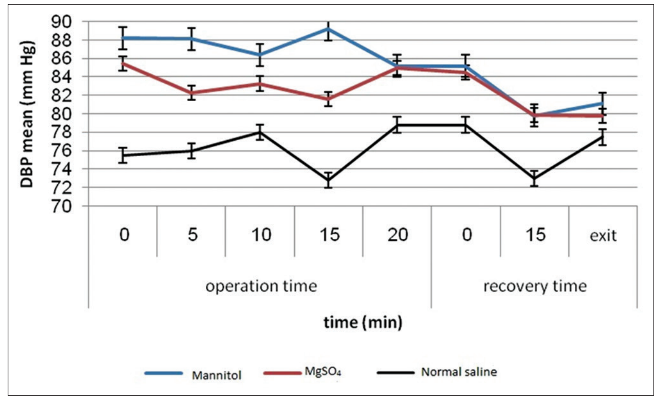

Figure 3: Mean diastolic blood pressure since the start of operation until out of recovery room (*P* = 0.22)

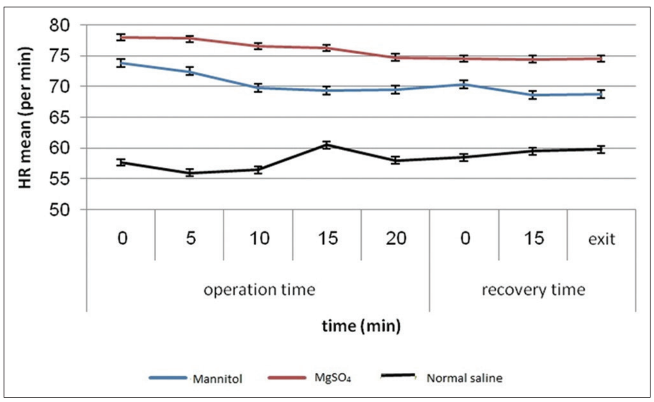

Figure 4: Mean heart rate since the start of operation until out of recovery room (*P* = 0.023)

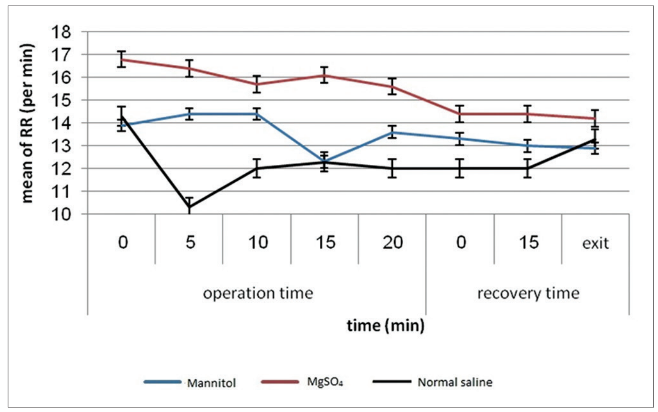

Figure 5: Mean respiratory rate since the start of operation until out of recovery room (*P* = 0.13)

Table 1: Demographic and general information of patients in three groups of Mannitol, Magnesium sulfate, Normal saline

Variable	Group			*P*
	Mannitol (0.3 g/kg)	Magnesium sulfate (20 mg/kg)	Normal saline (100 ml)	
Mean age (years)	68.9±11.9	64.1±13.8	67.4±10.6	0.25
Weight (kg)	70.8±9.5	69.3±19.8	67.9±10.4	0.69
Height (cm)	167.2±6.6	159.1±25.1	159.7±8.4	0.06
BMI (kg/m^2)	25.3±2.9	24.8±3.7	26.6±3.4	0.07
Sex, *n* (%)				
Male	23 (65.7)	13 (37.1)	4 (40)	0.031
Female	12 (34.3)	22 (62.9)	21 (60)	
ASA, *n* (%)				
I	7 (21.2)	15 (42.9)	9 (26.5)	0.13
II	26 (78.8)	20 (57.1)	25 (73.5)	

BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 2: Mean intraocular pressure before the injection until 5 min after the surgery in three groups

Group time	Mannitol (g/kg)	Magnesium sulfate (mg/kg)	Normalsaline (ml)	*P*
Before infusion	15.6±2.5	14.5±1.8	13.8±2.8	0.083
Immediately after infusion	15.2±2.5	14.7±1.9	13.8±2.8	0.044
5 min after operation	13.5±2.7	14.7±2	13.9±3.5	0.15
P		0.28		

changes in IOP had no significant difference in the three mentioned groups ($P = 0.28$). It is noteworthy that before the injection of drug, 10, 9, and 8 patients from the groups with mannitol, magnesium sulfate, and normal saline, respectively, had IOP higher than 15 mm Hg (28.6%, 25.7%, and 22.9%, respectively) and there was no significant difference among the three groups according to Chi-square test ($P = 0.96$). After the injection, IOP was higher than 15 mm Hg for 12, 10, and 9 individuals from the three mentioned groups (34.3%, 28.6%, and 25.7%, respectively) and the difference among three groups was not significant ($P = 0.73$). Five minutes after the surgery, the IOP was higher than 15 mm Hg for 7, 12, and 9 individuals of the three mentioned groups, (20%, 3.34%, and 7.25%, respectively) while the difference among three groups was not significant ($P = 0.4$).

In terms of medication, all patients in three groups received midazolam and fentanyl. The use of sodium thiopental in the three groups of mannitol, magnesium sulfate, and normal saline was 29, 26, and 14 cases, respectively, (85.3%, 74.3%, and 40%, respectively) and according to Chi-square test, the type of drug at three group had no significant difference ($P < 0.001$).

The level of sedation in 3 (8.6%) patients of mannitol and 1 (2.9%) case of magnesium sulfate was inappropriate. No case of unsuitable sedation was observed in the control group; however, according to the Fisher's exact test, there was no significant difference among the three groups ($P = 0.32$).

The mean score of surgeon satisfaction was 9.6 ± 1, 9.6 ± 0.92, and 9.3 ± 1.9, respectively, in mannitol, magnesium sulfate, and normal saline, respectively (based on 10), and according to one-way ANOVA, no significant difference was found between the three groups ($P = 0.66$). Furthermore, the mean score of patients satisfaction was 9.8 ± 0.55, 9.9 ± 0.31, and 9.7 ± 0.56, respectively, in the three mentioned groups, and according to the mentioned test, no significant difference was found between three groups ($P = 0.41$). Notably, during the study period, no patient suffered from a complication.

Discussion

The overall objective of the present study was to determine the effect of magnesium sulfate and mannitol on changes of the IOP in patients undergoing phacoemulsification surgery under local anesthesia and intravenous sedation and compare it with the control group.

In this study, three 35-member groups of patients undergoing cataract surgery with phacoemulsification were administrated by mannitol, magnesium sulfate, and normal saline. Patients in the three groups had no significant difference in terms of age, BMI, and ASA, but the gender distribution had a significant difference in the three groups. The investigation of variables mentioned in ANOVA showed that no variable had distortive effect on IOP and hemodynamic parameters. However, the investigation of hemodynamic parameters indicated that patients receiving normal saline have lower heart rate compared to patients in mannitol and magnesium sulfate groups and no case of bradycardia was seen in the mentioned patient and patients receiving mannitol had generally more stable hemodynamic than the other two groups.[7-10]

Assessing the changes of IOP in patients in three groups showed that patients in the mannitol group had higher level of IOP while there was no difference between the groups receiving mannitol and magnesium sulfate. On the other hand, the incidence of IOP >15 mm Hg for 5 min had no significant difference in the three mentioned groups. The surgeon and patient satisfaction were also not different in the three groups, and no complication was observed among them. In a study, patients who received 30 mg/kg of magnesium sulfate had a significant reduction in the IOP in comparison with normal saline group.[11] In the study by Ghaffaripour *et al*. conducted in Shiraz University of Medical Sciences in 2010, two groups of ninety patients receiving 30% magnesium sulfate and normal saline were studied and compared in terms of IOP during cataract surgery that the study results indicated the superiority of magnesium sulfate in the control of IOP.[12]

Conclusion

Therefore, according to the study results, it can be concluded that using magnesium sulfate had no effect on changes in the IOP and hemodynamic of patients during the surgery. Using mannitol may be effective in reducing IOP while no effect of magnesium sulfate on IOP was found. Since some other studies have suggested a positive effect of magnesium sulfate on IOP, it is recommended that another study with larger sample size and in a broader level be conducted in the future.

Due to old age of our patients, we used low doses of magnesium sulfate so that it may be a cause of ineffectiveness of magnesium sulfate on IOP.

The main limitation of the study was inaccessibility of operated eye after surgery and both eyes during operation.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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