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Original article

Magnesium Sulfate versus Nitroglycerin in Controlled Hypotensive Anesthesia in Middle Ear Surgeries

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ABSTRACT

Background: Controlled hypotension is required for middle ear surgeries to achieve a bloodless operative field and improve its quality, both magnesium sulfate and nitroglycerine used to produce deliberate hypotension.

Aim of the work: This study aimed to compare the efficacy of magnesium sulfate and nitroglycerin in inducing controlled hypotensive anesthesia as a primary outcome and using propranolol if tachycardia occurred as a secondary outcome, in middle ear surgeries**.**

Patients and Methods: The study was carried out on 40 adults' patients were randomly classified into two equal groups, twenty patients each: Group [M]: Received an intravenous [IV] bolus of magnesium sulfate 30 mg/ kg in 100 ml saline over 10 min followed by infusion of 10 mg/kg/h. Group [N]: Received nitroglycerin IV infusion 0.5-10 mcg/kg/min. Propranolol 1- 2.5 mg IV had been given to both groups if there was tachycardia.

Results: Both drugs induced hypotension with statistically significant difference in systolic and mean blood pressure [BP] and there was highly significant increase in heart rate [HR] in nitroglycerin more than magnesium sulfate and high doses of propranolol were administrated in nitroglycerine group. Postoperative pain was significantly increased in nitroglycerin than magnesium sulfate groups which had more analgesic effect.

Conclusion: Both drugs induced hypotension. However, magnesium sulfate was better as it provided optimum surgical field, less tachycardia, need less dose of propranolol with less post-operative pain in comparison to nitroglycerin.

Keywords: Nitroglycerin; Magnesium Sulphate; Hypotensive Agents; Middle Ear; Surgery.

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* Main subject and any subcategories have been classified according to the research topic.

INTRODUCTION

Deliberate hypotension is a procedure used to minimize intraoperative bleeding and enhance the consistency of the surgical field for improved vision during middle ear surgery and other head and neck surgeries[1]. However, regulated hypotension is needed for middle ear surgery to achieve a bloodless surgical field[2].

Magnesium is the fourth most common salt in the body after phosphorus, calcium and potassium. Magnesium has previously been used to cause deliberate hypotension and produces a hypotensive effect by reducing the release of calcium from the sarcoplasmic reticulum and produces a vaso-dilatation effect by increasing prostacyclin synthesis and inhibiting angiotensin-converting enzyme activity. The hypotension caused by magnesium during surgery is also explained by its strong analgesic effect, explained by its antagonism to N-methyl d-aspartate receptors[3].

Nitroglycerin is an organic nitrate that acts primarily on venous capacitance vessels to cause peripheral blood pooling and reduced cardiac ventricular wall stress. As the dose of nitroglycerin increases, the smooth muscle of the arterial vascular wall is relaxed. The most common clinical application of nitroglycerin is either sublingual or intravenous administration of angina pectoris due of coronary artery atherosclerosis or intermittent vasospasm of these arteries and to hypotension through infusion[4].

AIM OF THE WORK

In this study, we compared the efficacy of magnesium sulfate and nitroglycerin in induction of controlled hypotensive anesthesia and their effect on hemodynamics as a primary outcome and use of propranolol as adjuvant if tachycardia occurred with both drugs and recovery time and providing a better surgical field as a secondary outcome.

PATIENTS AND METHODS

This prospective randomized comparative clinical study had been performed in the faculty of medicine, Al-Azhar University [Assiut and Damietta]. It included 40 adult patients, aged from 21 to 40 years old admitted to Al-Azhar University Hospitals, scheduled for middle ear surgery.

Patients were selected according to the American Society of Anesthesiologists [ASA] physical status class I. The study took place from April to October 2019.

Exclusion criteria were: more than ASA status I, body mass index [BMI] > 35, patients have an allergy to the study medication, history of hypertension or diabetic patients, renal or hepatic patients, history of transient ischemic attacks [TIA], cerebrovascular strokes or valvular heart diseases, pregnant or menstruating women.

Patients were randomly divided by computer-generated numbers and sealed opaque envelops into two equal groups according to study medication each of 20 [n=20] and enrolled in elective surgery under general anesthesia.

Patients were assigned to receive magnesium sulfate [M group] and nitroglycerin [N group].

In group [M], patients received an intravenous [IV] bolus of magnesium sulfate 30 mg/ kg in a total volume of 100 ml saline over 10 min followed by infusion of 10 mg/kg/h until the end of the operation.

On the other side, in group [N], patients were received nitroglycerin IV infusion 0.5-10 mcg/kg/min [dosage based on hemodynamic parameters]. Propranolol 1- 2.5 mg IV were given to both groups if there was a tachycardia [heart rate [HR] >100 bpm].

Every patient was subjected to a careful pre-anesthesia assessment, which was formed of history taking [current medical illness, drug therapy and previous experience with general or regional anesthesia], thorough clinical examination and laboratory investigations [Complete blood picture, serum creatinine, prothrombin time, international normalized ratio [INR], fasting blood sugar, serum glutamic oxaloacetic transaminase [SGOT], serum glutamic-pyruvic transaminase [SGPT]].

In the operating room, the ECG electrodes were placed, an IV cannula was introduced, and an infusion of Ringer's solution was started approximately 10 min before induction of anesthesia. HR, non-invasive arterial BP, oxygen saturation, end-tidal carbon dioxide, and respiratory parameters were monitored approximately 5 minutes before induction of anesthesia for baseline recording.

After pre-oxygenation via face mask, anesthesia was induced with propofol 1-2 mg/kg, IV fentanyl [2 mcg/kg] In all groups and then study drugs were given.

In all groups after the loss of eyelid reflex, patients were ventilated with one minimum alveolar concentration [MAC] isoflurane and tracurium [atracurium besylate] 0.5 mg/kg IV was given to facilitate tracheal intubation.

Muscle relaxation was reversed with atropine 0.02 mg/kg and neostigmine 0.04 mg/kg IV. Anesthesia was maintained with one MAC isoflurane and lungs were ventilated with oxygen and medical air at a ratio of 1:1.

Systolic blood pressure, diastolic blood pressure and mean blood pressure [MAP] and HR were registered before induction of anesthesia [baseline], one minute before intubation, one minute after intubation, then every 5 min intraoperatively and one minute before extubation, then after admission to post-anesthesia care unit [PACU], and after 15 min and 30 min after admission to PACU, and the total dose of propranolol given in both drugs when tachycardia occurred was calculated.

The surgeons who were not aware of the selected hypotensive agent were asked to assess the quality of the surgical field according to the quality scale recorded by the surgeon [0= no bleeding, 1= slight bleeding blood evacuation not necessary, 2= slight bleeding sometimes blood has to be evacuated, 3= low bleeding blood has to be often evacuated, the operative field is visible for some seconds after the evacuation, 4= average bleeding blood has to be often evacuated, the operative field is visible only right after evacuation, and 5= high bleeding constant blood evacuation is needed].

Sometimes, bleeding exceeds evacuation. Surgery is hardly possible. Assessment of the quality of the surgical field was recorded 15, 30 and 45 minutes after skin incision.

Post-operative pain was evaluated using a visual analog scale [VAS] starting from 0 for no pain to 10 for the worst pain[5]. If VAS was >4, ketorolac 30 mg IV was administered. VAS was recorded on admission to the PACU and then 15 and 30 minutes later.

Statistical Analysis: Data entry and statistical analyses were performed using SPSS [statistical package of social sciences] version 21 [SPSS Inc., Chicago, IL, USA]. Continuous, normally distributed data is expressed in mean and standard deviations. Quantitative data were analyzed by the Kolmogorov Smirnov data normality test Individual sample t-test [student t-test] was used for continuous data normally distributed. Statistical significance was considered when the likelihood value [P] was less than or equal to 0.05.

RESULTS

The mean age of Magnesium sulphate group was 32.30 ± 5.33 and 60% was female, and in the Nitroglycerin group the mean age was 34.90 ± 7.52 and 40% was female. Without significant differences between the two groups concerning age and gender [p=0.314, 0.670] respectively.

As illustrated in table [1], there was a statistically significant difference between the two groups in mean systolic blood pressure [higher in M group in 1, 5, 25 min after intubation and 30 min in PACU], and there was no statistically significant difference between both groups all through the study in mean diastolic blood pressure.

There was a statistically significant difference between the groups in MAP after 5,10,15, 20, 25, 30, 35, 40, 45 minutes from intubation as seen in **table [2].**

As shown in **table [3],** there was a statistically significant difference between both groups according to heart rate from 5 to 45 min after intubation.

Considering the dose of propranolol, it was higher with N group [1.28 ±0.55] than M group [0.67 ± 0.26] with a statistically significant difference.

There was no significant difference in the quality of the surgical field during operation as shown in **table [4]**

According to the results of the heart rate the total dose of propranolol for tachycardia given is higher with nitroglycerin than magnesium sulfate. As shown in **table [5**].

Table [1]: Arterial blood pressure [mm/Hg].

	Systolic blood pressure			Diastolic blood pressure		
	M group	**N group**	**P-Value**	**M group**	**N group**	**P-Value**
1 min before intubation	118.00 ± 7.8	121.00 ± 7.37	0.391	72 ± 11.53	73 ± 8.23	0.824
1 min. after intubation	106 ± 6.99	90.00 ± 4. 08	**0.00***	60 ± 8.17	56 ± 4.60	0.194
After 5 min of intubation	96 ± 4.59	88.50 ± 4.74	**0.002***	55 ± 4.72	53 ± 4.74	0.487
After 10 min of intubation	94.5 ± 4.97	91.00 ± 5.16	0.14	52.5± 4.25	53 ± 4.83	0.809
After 15 min of intubation	90.5 ± 4.97	87.50 ± 4.24	0.164	52.5± 3.54	52.5± 3.54	1
After 20 min of intubation	88 ± 2.58	91.00 ± 5.16	0.118	54 ± 4.60	53 ± 4.83	0.641
After 25 min of intubation	92.5 ± 5.89	87.50 ± 4.24	**0.043***	52 ± 3.50	52.5± 3.54	0.754
After 30 min of intubation	92 ± 5.37	91.00 ± 5.16	0.143	54.5± 4.97	52.5± 4.25	0.346
After 35 min of intubation	91 ± 3.94	87.50 ± 4.24	0.764	54.5± 4.97	52.5± 3.54	0.314
After 40 min of intubation	90 ± 4.33	88.33 ± 5.00	0.331	56 ± 4.6	53 ± 4.83	0.172
After 45 min of intubation	88.50 ± 4.74	92.00 ± 5.37	0.14	53.5± 4.74	54.5± 4.97	0.651
After 50 min of intubation	91 ± 5.16	91.00 ± 3.94	1	53 ± 4.83	54.5± 4.97	0.503
After 55 min of intubation	87.50 ± 4.24	90.00 ± 4.08	0.196	52.5± 3.54	56 ± 4.60	0.072
After 60 min of intubation	88.50 ± 4.74	88.50 ± 4.74	1	52.5± 4.25	53.5± 4.74	0.626
After 65 min of intubation	91.50 ± 3.32	91.50 ± 5.29	1	52.5± 3.53	52 ± 3.5	0.754
After 70 min of intubation	87.78 ± 5.06	92.00 ± 5.37	0.097	53 ± 4.83	54.5± 4.97	0.503
1 min before Extubation	103 ± 8.23	106.00 ± 6.99	0.391	57.5± 4.25	60 ± 8.17	0.402
15 min PACU	111 ± 7.37	114.00 ± 5.16	0.306	66 ± 6.99	72 ± 11.35	0.172
30 min PACU	124 ± 5.16	91.00 ± 5.16	**<0.001***	78 ± 11.35	80 ± 9.43	0.673

*Significant at P-value < 0.05. **SD = Standard Deviation. *** PACU = Post anesthetic care unit.

Table [2]: Mean arterial blood pressure [mm/Hg].

	M group	N group	P-Value
1 min before intubation	82.3 ± 6.96	82.6 ± 5.87	**0.918***
1 min. after intubation	83.8 ± 4.94	86 ± 4.29	**0.302***
After 5 min of intubation	79.4 ± 5.68	88.1 ± 4.06	**0.001***
After 10 min of intubation	78.4 ± 6.31	88.8 ± 4.44	**<0.001***
After 15 min of intubation	76.8 ± 6.40	87.9 ± 6.62	**0.001***
After 20 min of intubation	74.9 ± 6.15	87.2 ± 8.23	**0.001***
After 25 min of intubation	72.8 ± 6.07	86.4 ± 7.26	**<0.001***
After 30 min of intubation	71 ± 4.59	85.5 ± 7.29	**<0.001***
After 35 min of intubation	71.1 ± 9.25	83.6 ± 6.45	**0.003***
After 40 min of intubation	71 ± 9.05	81.7 ± 4.97	**0.003***
After 45 min of intubation	72.9 ± 9.46	80.1 ± 4.97	**0.047***
After 50 min of intubation	75.7 ± 11.36	77.8 ± 6.69	0.621
After 55 min of intubation	75.6 ± 6.41	78.6 ± 5.86	0.29
After 60 min of intubation	78 ± 5.53	80.4 ± 3.86	0.276
After 65 min of intubation	80 ± 5.07	82 ± 2.66	0.285
After 70 min of intubation	81 ± 6.68	83.7 ± 3.65	0.277
1 min before Extubation	84.5 ± 4.45	85.9 ± 3.14	0.427
15 min PACU	84.6 ± 3.23	85.8 ± 2.65	0.377
30 min PACU	85.9 ± 3.66	85.7 ± 3.02	0.896

*Significant at P-value < 0.05. **SD = Stander Deviation. *** PACU = Post anesthetic care unit.

Table [3] Heart rates [beat/ min] among studied groups.

	Magnesium sulphate group	Nitroglycerin group	P-Value
1 min before intubation	82.3 ± 6.96	82.6 ± 5.87	0.918
1 min. after intubation	83.8 ± 4.94	86 ± 4.3	0.302
After 5 min of intubation	79.4 ± 5.68	88.1 ± 4.07	0.001*
After 10 min of intubation	78.4 ± 6.31	88.8 ± 4.44	0.00*
After 15 min of intubation	76.8 ± 6.41	87.9 ± 6.63	0.001*
After 20 min of intubation	74.9 ± 6.16	87.2 ± 8.23	0.001*
After 25 min of intubation	72.8 ± 6.07	86.4 ± 7.26	0.00*
After 30 min of intubation	71 ±4.6	85.5 ± 7.29	0.00*
After 35 min of intubation	71.1 ± 9.26	83.6 ± 6.45	0.003*
After 40 min of intubation	71 ± 9.06	81.7 ± 4.3	0.003*
After 45 min of intubation	72.9 ± 9.47	80.1 ± 4.98	0.047
After 50 min of intubation	75.7 ± 11.36	77.8 ± 6.7	0.621
After 55 min of intubation	75.6 ± 6.42	78.6 ± 5.89	0.290
After 60 min of intubation	78 ±5.54	80.4 ± 3.87	0.276
After 65 min of intubation	80 ± 5.08	82 ± 2.67	0.285
After 70 min of intubation	81 ± 6.68	83.7 ± 3.65	0.277
1 min before Extubation	84.5 ± 4.45	85.9 ± 3.14	0.427
15 min PACU	84.6 ± 3.24	85.8 ± 2.66	0.377
30 min PACU	85.9 ± 3.67	85.7 ± 3.02	0.896

Table [4]: The quality of the surgical field during operation among sampling time

	Group M	**Group N**	**P-value**
15 min after skin incision	2.0 ± 0.78	2.1 ± 0.62	0.656
30 min after skin incision	2.0 ± 0.65	2.0 ± 0.83	1.000
45 min after skin incision	1.8 ±0.67	1.6 ± 0.58	0.319

Table [5]: Amount of propranolol

	Group M	Group N	[Total [M+N
[Amount of propranolol [Mg	4	23	27
Median	0.5	1.25	1
Mean ± SD	0.67 ± 0.26	1.28 ±0.55	1.13 ± 0.56
P-value			<0.001*

*SD = Stander Deviation. ** Group M= Magnesium sulphate. *** Group N= Nitroglycerin group.
****Significant at P-value < 0.05

DISUCSSION

Middle ear surgery is a surgical procedure during which all necessary manipulations can be performed by using a fiberoptic camera. Bleeding must be reduced during surgery, because only a small amount of blood will completely block vision through the endoscope. Various methods have been used to establish a dry area of operation [6].

In the current prospective randomized trial, nitroglycerin or magnesium sulfate was used to cause hypotension in an effort to provide a successful surgical area. The findings of the present study showed that both magnesium and nitroglycerin had a hypotensive effect appropriate for middle ear surgery. The study demonstrated the potential of magnesium sulfate and nitroglycerin to cause intentional hypotension in patients undergoing middle ear surgery. Magnesium sulfate has more benefits during onset and postoperative times, and its use has been associated with more stable perioperative hemodynamics [smaller changes in MAP and HR] and improved recovery profiles [less postoperative pain] than remifentanil.

In a study **Bayram et al.** [7] controlled hypotension of magnesium sulfate and dexmedetomidine were compared during functional endoscopic surgery to examine the effects of magnesium sulfate and dexmedetomidine used for managed hypotension on the vision of the surgical site. Magnesium sulfate was administered as IV 40mg/kg in this study. Bolus and 15 mg/kg/hour IV infusion provided the target mean arterial blood pressure and equal surgical area, but the satisfaction of the surgeon was better in the dexmedetomidine community. In the present analysis, magnesium sulfate was administered as I.V. 30 mg / kg, bolus and 10 mg / kg / hour infusion and can sustain deliberate hypotension during the process.

The reduction of MAB was followed by an increase in HR and rebound hypertension following the cessation of infusion. These findings are consistent with the study conducted by Srivastava et al. [8], which compared nitroglycerin with esmolol and noted that when hypotension is induced, it induces the release of endogenous catecholamines. Nitroglycerin has a strong effect on the smooth muscles of the vascular. The vasodilator effect has created more oozing in the surgical field. Reflex tachycardia can lead to increased surgical bleeding by increasing cardiac output.

In a study done by **Elsharnouby and Elsharnouby**[9], there were 2 groups, one group getting magnesium sulfate and the other as a control group. This research showed that magnesium sulfate contributed to a reduction in arterial pressure, heart rate, blood loss and length of surgery, as in our research, magnesium sulfate provided strong hypotensive anesthesia with a decent surgical area.

With an agreement to this study, a study conducted by **Khalifa and Awad** [10], the comparison of dexmedetomidine, magnesium sulfate and nitroglycerine during functional endoscopic sinus surgery revealed that there was a substantial difference between the groups in the analysis of the time required to restore the basal values of mean arterial pressure with a longer period in the dexmedetomidine group.

Moreover, Hamed[11] included eighty adult patients with patients' ASA I and II [age 20-50 years] who scheduled for fundus endoscopic sinus surgery [FESS] and randomly divided to receive lidocaine 2 mg/kg/h with maximum of 200 mg/h or iv bolus of magnesium sulfate 50mg/kg in a total of 100ml saline over 10 min followed by infusion of 15mg/kg/h until the end of surgery. They concluded that, both lidocaine and magnesium sulfate successfully induced controlled hypotension in FEES, with superiority for lidocaine.

In addition, **Chhabra et al.[12]** concluded that, both dexmedetomidine and magnesium sulphate were effective in achieving target mean arterial pressure, with superiority of target MAP in lesser time with minimum infusion dose.

Finally, Shoukry and Mahmoud[13] compared nitroglycerin to magnesium sulphate as the current work and conclude that, both nitroglycerin and magnesium sulphate are safe for production of controlled hypotension during fundus endoscopic sinus surgery. But magnesium sulphate was superior than nitroglycerin as it provides optimum surgical conditions and low tachycardia.

CONCLUSION

We concluded that both drugs induced hypotension. However, MGS was better as it provided optimum surgical field, less tachycardia, need less dose of propranolol in comparison to Nitroglycerin.

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