Original Research Article

Comparison of esmolol versus magnesium sulfate for inducing controlled hypotension for functional endoscopic sinus surgery: a randomized double blinded interventional study

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Abstract

Background and Aims: Excessive bleeding during Functional endoscopic sinus surgery (FESS) can lead to poor visibility of surgical field which can be improved by controlled hypotension. Aim of this study was to compare hypotensive properties of esmolol and magnesium sulfate and to compare quality of surgical field during FESS.

Methods: A hospital based prospective randomized double blinded interventional study in which 130 patients undergoing FESS randomly allocated to two equal groups. Group A received inj. Esmolol 1mg/kg bolus diluted to 10ml in saline and maintenance infusion at 1mg/kg/hr. Group B received inj. Magnesium Sulfate 40mg/kg bolus in 10ml of saline followed by 15mg/kg/hr infusion. Hemodynamic parameters, quality of the surgical field (average category score), amount of blood loss, emergence time, time to first analgesic request and postoperative sedation were recorded. Outcome was analysed using appropriate statistical test. P value <0.05 was considered statistically significant.

Result: Mean Heart Rate and Mean Arterial Pressure were statistically significantly lower in group A compared to group B at all time intervals (P=0.001). Surgical field quality was found better in group A. Emergence time, postoperative sedation score and time to first analgesic request were significantly more in group B.

Conclusion: Esmolol provides comparatively better surgical field and better hemodynamic stability over magnesium sulfate without any significant side effect. Magnesium sulfate provides additional benefit of postoperative analgesia and sedation.

Keywords: Esmolol, Magnesium sulfate, Controlled hypotension, FESS, Surgical field visibility

Introduction

Functional endoscopic sinus surgery (FESS) is associated with high rate of success (approximately 90%) for symptomatic improvement in patients with chronic rhinosinusitis and polypous rhinosinusitis who were refractory to medical treatment.[1] Highly vascular nature of nasal and sinus mucosa makes it prone to bleeding during FESS. Even a small amount of bleeding during surgery may compromise vision of the surgical field.[2]

Anaesthesiologists play an important role in providing a bloodless surgical field and maintaining stable hemodynamic parameters. Certain techniques such as head elevation with reverse trendelenburg position,[3] nasal decongestion and local anaesthetics with vasoconstrictors have been tried since long but in modern era of better monitoring and controlled anaesthesia, controlled hypotension is a method of choice to limit intraoperative mucosal bleeding.

Controlled hypotension is defined as safely reducing baseline mean arterial pressure (MAP) by 30% or keeping MAP 65-70mmHg by using various agents like magnesium sulfate,[4] vasodilator (sodium nitroprusside[5]), nitroglycerine,[6] high dose of potent inhaled anaesthetic,[7] and beta blocker[8] either alone or in combination, while maintaining vital organ's perfusion adequately. Esmolol is an ultrashort acting selective β1 adrenoreceptor antagonist that has a rapid onset and reduces heart rate along with blood pressure. Esmolol produced desired hypotension without tachycardia and improved surgical condition by reducing operative field bleeding.[6] It has been reported that magnesium sulfate is a good agent for controlled hypotension, as it produces a vasodilating effect by increasing synthesis of prostacyclin and inhibits the release of norepinephrine by blocking the N-type Ca^{++} channels at nerve endings.[9]

The aim of this study was to compare hypotensive properties of esmolol and magnesium sulfate and to compare their effect on quality of surgical field during FESS. Primary objective of the study was to determine the haemodynamic parameters – heart rate and mean arterial blood pressure at different time intervals. Secondary objectives were to assess and compare the quality of surgical field by using average categorical scale, emergence time, sedation score, time to first rescue analgesic and the proportion of cases with complications in both the groups.

Subject and Methods

After getting approval from institutional ethical committee and clinical trial registration, this hospital based, prospective, randomized, double blinded, interventional study was conducted on a total of 130 patients of either sex, aged 20–50 years, weighing 45–65 kg and of American Society of Anaesthesiologists (ASA) physical status I–II, undergoing FESS under general anaesthesia. Patients having a history of hypertension, coronary arterial disease, renal dysfunction, hepatic dysfunction, cerebral insufficiency, coagulation abnormalities, recurrent sinus surgery, rhinorrhoea and allergy to study drugs were excluded. Patients were randomized by simple randomisation technique via chit-in-box method. Concealment of randomisation was done by using sealed envelope method. Sample size was calculated to be 63 subjects for each of two groups at an alpha error 0.05 and power 80% expecting minimum detectable difference of 2±4 mmHg in mean blood pressure in both groups from base line, 5 minutes after intubation as per the study done by *Jangra et al.*[12] So, for study purpose, 65 cases were taken in each group. Group A (n=65) received

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inj. Esmolol 1mg/kg (diluted to 10ml in normal saline) bolus over 10 minute before induction followed by an infusion of 1mg/kg/hr through infusion pump. Group B (n=65) received inj. Magnesium sulfate 40mg/kg (diluted to 10ml in normal saline) bolus over 10 minute before induction followed by an infusion of 15mg/kg/hr through infusion pump. Double blinding was done as the anaesthesiologist who administered anaesthesia was different from the anaesthesiologist who recorded study parameters.

After confirming patient identification, Pre-anaesthetic evaluation, consent and Nil per Oral (NPO) status, standard ASA monitoring applied. Electrocardiogram, Pulse oximeter, Non-invasive blood pressure (NIBP) were attached and we recorded the baseline vital parameter- Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation(SPO2). Study drug was given and GA was induced. Inj Fentanyl 2µg/kg used for analgesia. Intraoperative haemodynamic parameters (HR, SBP, DBP, MAP, SPO2) were recorded after the loading dose, after induction, 1 min after intubation, 5 min after intubation and then every 10 min. The surgical site was observed for the severity of bleeding and the need for frequent suctioning.

We used the average category score (0-5) proposed by Fromme and Boezaart[10] (score 0=no bleeding, score 1=slight bleeding, no suctioning of blood required score 2=slight bleeding, occasional suctioning required, surgical field not threatened, score 3=slight bleeding, frequent suctioning required, bleeding threatens surgical field a few seconds after suction is removed, score 4=moderate bleeding, frequent suctioning required, bleeding threatens surgical field directly after suction is removed, score 5= severe bleeding, constant suctioning required, bleeding appears faster than can be removed by suction, surgical field severely threatened and surgery not possible).

We stooped the study drug infusion at 5 min before the completion of surgery. Emergence time, the time between discontinuation of anaesthetic agent and response of eye opening to verbal command, was noted. GA was reversed with inj. Neostigmine 0.05 mg/kg and inj. Glycopyrrolate 0.01 mg/kg. Extubation was done when patient was fully awake and have adequate muscle power. Post-operative sedation was assessed by using Ramsay Sedation Score. Severity of pain was scored using Visual analogue scale (VAS). Intravenous diclofenac 75mg (aqueous) was given as rescue analgesic on VAS score of 3. The time to first administration of rescue analgesic was also noted. This was the end point of our study, however occurrence of any adverse effects (nausea, vomiting, hypotension and bradycardia) were recorded until postoperatively 24 hours.

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) software version 21. We used the Student's't' test to evaluate the significance of difference in normally distributed variables, whereas the Mann–Whitney test was used otherwise. Chi-square test was used to compare proportions. P value <0.05 was considered statistically significant.

Results

All enrolled patients were received the study drug without any dropout and outcome analysis was done on the collected data of 130 patients. Both the study groups were comparable with respect to demographic data (Table 1).

Table 1: Demographic data comparison of both groups

Variables		Group A (n=65)	Group B (n=65)	P value
Age (yrs) Mean±SD		33.98 ± 6.57	33.74 ± 5.44	0.81* (NS)
Weight (kgs) Mean±SD		56.74 ± 4.28	56.14 ± 3.28	0.36* (NS)
Gender	Male	45 (69.23%)	44 (67.70%)	0.85# (NS)
	Female	20 (30.77%)	21 (32.30%)	
ASA Physical Status	I	55 (84.61%)	56 (86.15 %)	0.80# (NS)
	II	10 (15.39%)	9 (13.85%)	
Duration Of Surgery (min) Mean±SD		65.05 ± 2.96	65.67 ± 3.24	0.25* (NS)

*student unpaired t-test, #chi-square test, SD= Standard deviation, NS=Non-significant

Baseline values of HR and MAP were comparable in both the groups (p=0.11). Target BP was achieved in both the groups after administering the study drug. Intra group comparison was done using repeated measure ANOVA with Bonferroni post hoc analysis. Mean HR and mean MAP were statistically significantly lower (p<0.001) in group A than group B after giving loading dose of study drugs and at all times intraoperatively (Table-2, Table-3).

Table 2: Mean Heart Rate (Beats per minute)

Time point	Group A		Intra group p value	Group B		Intra group p value	Intergroup P value
	Mean	SD		Mean	SD		
Baseline	84.17	6.818	--	86.14	7.237	--	0.11*
After Loading	68.08	5.475	0.001$ (S)	81.35	6.674	0.001$ (S)	0.001* (S)
After Induction	68.37	6.446	0.001$ (S)	80.48	6.055	0.001$ (S)	0.001* (S)
1 min	71.52	7.047	0.001$ (S)	78.97	6.172	0.001$ (S)	0.001* (S)
5 min	68.68	6.394	0.001$ (S)	76.75	6.101	0.001$ (S)	0.001* (S)
10 min	67.69	6.581	0.001$ (S)	75.63	6.244	0.001$ (S)	0.001* (S)
20 min	68.68	7.007	0.001$ (S)	74.78	5.840	0.001$ (S)	0.001* (S)
30 min	68.55	5.850	0.001$ (S)	73.58	5.903	0.001$ (S)	0.001* (S)
40 min	69.23	5.711	0.001$ (S)	73.15	6.055	0.001$ (S)	0.001* (S)
50 min	70.26	6.849	0.001$ (S)	73.92	6.178	0.001$ (S)	0.002* (S)
60 min	69.02	6.224	0.001$ (S)	77.08	6.003	0.001$ (S)	0.001* (S)
70 min	71.94	5.318	0.001$ (S)	81.29	5.870	0.01$ (S)	0.001* (S)

*Student unpaired't' test, $Repeated ANOVA, SD= Standard deviation, S = Significant

Table 3: Mean Arterial Pressure (mmHg)

Time point	Group A		Intra group P value	Group B		Intra group P value	Intergroup P value
	Mean	SD		Mean	SD		
Baseline	92.886	6.4695	--	90.931	6.3378	--	0.08*
After Loading	74.606	5.2667	0.001$ (S)	78.495	4.9547	0.001$ (S)	0.001* (S)
After Induction	73.757	5.4862	0.001$ (S)	76.495	4.5014	0.001$ (S)	0.002* (S)

1 min	74.495	4.5266	0.001$ (S)	78.672	4.6048	0.001$ (S)	0.001* (S)
5 min	70.858	4.0282	0.001$ (S)	74.966	3.8112	0.001$ (S)	0.001* (S)
10 min	69.274	4.3286	0.001$ (S)	73.345	3.5042	0.001$ (S)	0.001* (S)
20 min	69.391	4.3173	0.001$ (S)	73.414	3.4951	0.001$ (S)	0.001* (S)
30 min	69.362	4.3545	0.001$ (S)	73.843	3.1244	0.001$ (S)	0.001* (S)
40 min	69.412	4.4664	0.001$ (S)	73.900	3.0053	0.001$ (S)	0.001* (S)
50 min	70.297	3.9435	0.001$ (S)	74.494	2.8252	0.001$ (S)	0.002* (S)
60 min	72.695	3.9429	0.001$ (S)	75.443	2.6639	0.001$ (S)	0.001* (S)
70 min	77.472	4.4424	0.001$ (S)	78.354	3.1386	0.001$ (S)	0.19*

*Student unpaired't' test, $Repeated ANOVA, SD= Standard deviation, S = Significant

Average category score (for assessment of quality of surgical field) was between 1-2 in group A and 2-3 in group B (Figure-1).There was no significant difference in the blood loss intraoperatively in both groups also no excessive blood loss presented in any patient. Blood transfusion was not required in any of the patient in either group.

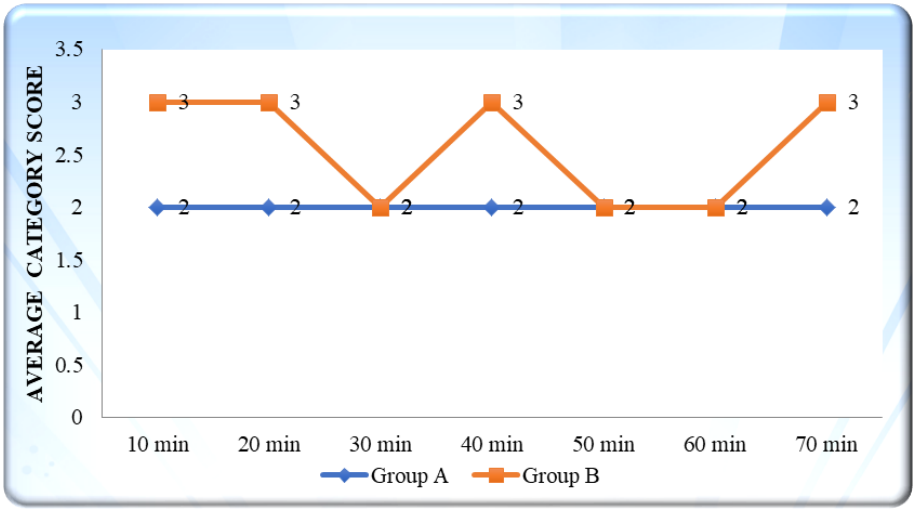

Figure 1: Average category score

Emergence time was significantly lower in group A (4.42 ± 0.87 min) than group B (7.22 ± 0.74 min). The mean postoperative sedation scores were statistically significantly higher in group B than in group A at 0 min (3.03 vs. 2.6), at 30 min (2.43 vs. 2.14) min. and at 60 min. (1.78 vs.1.55) min (P<0.01). (Figure-2)

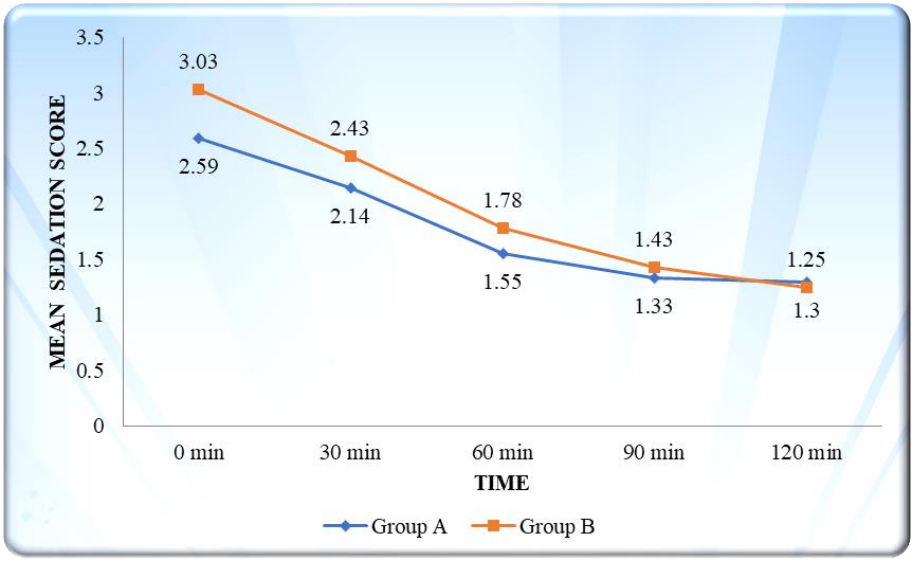

Figure 2: Mean Sedation Score

Time to first analgesic request was significantly more in group B (74.30 ± 8.36 min) than group A (30.0 ± 5.06 min) respectively (p<0.01). Table-4 depicts proportion of complications. There was no statistically significant difference between the two groups with

regards to postoperative complications.

Table 4: Proportion of Complications in both groups

Complications	Group A (n=65)		Group B (n=65)		P value
	N	%	N	%	
Bradycardia	15	23.1	12	18.5	0.51* (NS)
Hypotension	10	15.4	9	13.8	0.80* (NS)
Tachycardia	0	0	3	4.6	0.08* (NS)
Nausea/vomiting	9	13.8	11	16.9	0.62* (NS)

*Chi-square test, NS= Non-Significant

Discussion

Functional endoscopic sinus surgery is a minimal invasive nasal surgery in which a bloodless surgical field is prerequisite. Among many other approaches used to provide a bloodless surgical field, controlled hypotension has been widely used in view to control bleeding during FESS to improve the quality of surgical field.[8] In our study both the groups achieved the target MAP (65–70 mmHg) and improved the surgical field visibility with reduced blood loss. The decrease in HR and MAP after giving loading dose of esmolol and at most of times during surgery, is attributed to its cardio-selective β receptor antagonism.

Esmolol lowers mean arterial pressure through a decrease in cardiac output secondary to negative chronotropic and ionotropic effects of β adrenergic antagonism. The decreased heart rate seen with esmolol decreases metabolic demand, whereas the protracted diastolic time potentially increases blood supply to the myocardium.

Magnesium stabilize the excitable myocardium, slowing the rate of SA (sino-atrial) node and prolonging the rate of conduction by controlling the movement of calcium, sodium and potassium ions across the cell membrane. It limits the outflow of calcium from sarcoplasmic reticulum and produces a vasodilating effect by increasing synthesis of prostacyclin and inhibiting angiotensin converting enzyme activity. It also inhibits the release of norepinephrine by blocking the N-type Ca++ channels at nerve endings and thus decreases the blood pressure.

N.M Elsharnouby et al[11] concluded that magnesium sulfate led to a reduction in mean arterial pressure, heart rate, blood loss and duration of surgery and also observed that magnesium sulfate alters anaesthetic dose requirements and emergence time. Kiran jangra et al[12] concluded that MAP was significantly lower in both magnesium sulfate and esmolol group. During esmolol induced hypotension, unopposed α-adrenergic effects (as a result of β-blockade by esmolol) causes vasoconstriction of arterioles & pre-capillary sphinctors leading to less oozing at the operative site thus better quality of surgical field.[13] U.Srivastava et al[6] also found esmolol better as it provided optimum surgical condition with only mild reduction in blood pressure and less intra operative bleeding and less occurance of tachycardia were added advantages. Guney et al[14] have also shown that esmolol can be safely used as an alternative to nitroglycerine for controlled hypotension. In our study, Emergence time was significantly prolonged in Magnesium sulfate group because of its property of potentiation of opioids and neuromuscular blockers leading to delayed emergence.[15] we also found that the time to first rescue analgesia request was more in magnesium sulfate group. M R Tramer et al [16] found that magnesium-treated patients consumed less analgesic during the first 48 h. The analgesic property of Magnesium sulfate is associated with its calcium channel blocking property and it also noncompetitively blocks NMDA (N-Methyl-D-Aspartate) receptors. Sedative property of magnesium is due to its CNS depressant action.

Limitation of our study was that we didn't use control group as not providing controlled hypotension and allowing surgical field flooded with blood would be unethical.

Conclusion

We concluded that esmolol provides better hemodynamic stability and better quality of surgical field in comparison to magnesium sulfate without any significant adverse effect. Magnesium sulfate provides additional benefit of postoperative analgesia and sedation.

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