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Original Research Paper

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COMPARING MAGNESIUM SULFATE AND DEXMEDETOMIDINE IN CONTROLLED HYPOTENSION DURING ENDOSCOPIC SINUS SURGERY: A PROSPECTIVE RANDOMIZED STUDY

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ABSTRACT

BACKGROUND: Functional endoscopic sinus surgery (FESS) has been proposed as a selected treatment used in patients with chronic sinusitis. Due to the nature of the location of endoscopic sinus surgery, even a small amount of bleeding can reduce the operative visibility and thus cause surgeon dissatisfaction and prolong the operation trauma. The aim of the work was to compare dexmedetomidine and magnesium sulfate regarding their efficacy as a hypotensive agent in FESS to obtain a bloodless surgical field.

METHODS: A randomized, prospective comparative study and was conducted in the Department of Anesthesia, Government Medical College, Jammu, J&K, for a period of 6 months, on sixty patients, aged between 18 and 60 years, of both genders, and assigned into two equal groups: magnesium sulfate group and dexmedetomidine group.

RESULTS: Dexmedetomidine controlled blood pressure better than magnesium sulfate as nitroglycerin was added to achieve the targeted MAP in the Group M. There was a statistically significant decrease in the MAP among Dexmedetomidine Group 58.07 ± 3.83 mmHg compared to Magnesium Sulfate Group 66.58 ± 3.96 mmHg at 30 minutes and similarly at 60 minutes, post-extubation and postoperatively. There was a statistically significant decrease in the HR at 30 minutes and later, as also in the amount of blood loss ($p = 0.019$). The surgeon satisfaction was significantly higher in Group D than in Group M.

CONCLUSION: Dexmedetomidine can provide more effective controlled hypotension and thus contribute to improved visibility of the surgical site.

KEYWORDS : Dexmedetomidine, Magnesium sulfate, Controlled hypotension, Functional endoscopic sinus surgery

INTRODUCTION

Functional endoscopic sinus surgery (FESS) has been proposed as a selected treatment method for patients with chronic rhinosinusitis, and is widely used in patients that have not responded to medical therapy. However, due to the nature of such surgeries, intra-operative bleeding, of even a small amount, can leave a negative effect on the vision of the surgeon leading to many problems in establishing a proper surgical field; thus, surgery becomes harder and longer.[1] This may further lead to an increased rate of complications like cerebrospinal fluid (CSF) leak, intracranial infection, orbital complications or hemorrhage.

Improving the visibility of the surgical site by reducing bleeding during FESS is an important issue for anesthesiologists. Therefore, controlled hypotension, which is a technique in which the arterial blood pressure is lowered in a controlled manner to minimize blood loss and associated complications, and also to enhance the operative field visibility, is used.[2,3] The ideal agent used for controlled hypotension must have the characteristics, such as: ease of administration, short onset time, effect that disappears quickly when administration is discontinued, rapid elimination, nil or negligible effects on vital organs, and predictable, dose-dependent effects.[3-5]

Dexmedetomidine is a highly selective α_2-adrenoceptor agonist with sedative, anxiolytic, and analgesic characteristics. It binds to trans-membrane G protein-binding adreno-receptors and has a unique property among sedatives, as it produces sedation without causing respiratory depression, analgesic effects known as opioid-sparing, anxiolytic, and sympatholytic property in anesthesia.[6] The sympatholytic performance of dexmedetomidine is manifested by reduced arterial blood pressure, heart rate, cardiac output, and reduced release of norepinephrine.[7]

Magnesium sulfate, on the other hand, is a good agent for controlled hypotension; it stabilizes the cell membrane and intracytoplasmic organelles by interceding the activation of Na^+-K^+ ATPase and Ca^{++} ATPase enzymes.[5,8] Mg^{2+} also inhibits the release of norepinephrine by blocking the N-type Ca^{++} channels at nerve endings and thus decreases the blood pressure.[8]

Several studies determining the effectiveness of dexmedetomidine and magnesium sulfate in controlled hypotension, have compared them with other hypotensive agents, but very less number of studies have compared these two agents with each other.[9,10] The aim of the present study was to compare the efficacy of magnesium sulphate and dexmedetomidine in inducing controlled hypotension to obtain a bloodless surgical field for better exposure and surgeon satisfaction during functional endoscopic sinus surgery (FESS) and their effects on postoperative recovery, discharge, and postoperative analgesia.

METHODS

A randomized, prospective comparative study and was conducted in the Department of Anaesthesia, SMGS hospital, Jammu, J&K, for a period of 6 months, on sixty patients, aged between 18 and 60 years, duly enrolled in the study after fulfilling the inclusion criteria. All the participants were randomly assigned into two equal groups: Group M and Group D i.e. Group M (n=30) for patients administered 40 mg/kg magnesium sulfate in 100 mL saline solution over 10 min as the intravenous loading dose 10 min before induction, with a subsequent 10 to 15 mg/kg/h infusion during surgery; and Group D (n=30) for patients administered 1 µg/kg dexmedetomidine in 100 mL saline solution as the loading dose 10 min before surgery and 0.5 to 1 µg/kg/h dexmedetomidine during surgery.

After approval of the Institutional Ethical Committee, written informed consent was obtained from all participants. Randomization was done using sequentially numbered, opaque, sealed envelopes containing computer generated random allocations in a ratio of 1:1. The study participants, operation nurse and the otorhinolaryngologist constituted the 'blind' study group.

Inclusion Criteria:

The study included patients with grades I and II according to the American Society of Anesthesiology physical status (ASA-PS) of either sex, who were scheduled for FESS under general anesthesia.

Exclusion Criteria:

The study excluded patients who refused or were in the age group lower than 18 years or more than 60 years. Pregnant women, patients with hypertension, ischemic heart diseases, cerebrovascular insufficiency, neuromuscular diseases, diabetic neuropathy, peripheral vascular diseases, renal impairment, hepatic impairment were also excluded from the study. Patients receiving calcium channel blockers or receiving drugs influencing blood coagulation were also excluded.

Routine preoperative assessment was done for each patient including routine history taking, clinical examination, and laboratory investigations, which included complete blood picture, kidney function tests, liver function tests, prothrombin time, and partial thromboplastin time.

Patients were informed for verbal numerical rating scale (NRS) (0: no pain, 10: severe pain). All patients' body weights were recorded in their files. All patients were administered a 5 mL/kg/hour intravenous isotonic solution (Lactated Ringer) infusion 2 hours before the induction, which was continued during the surgery.

After the patients were taken into the operating room, mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2) and end tidal carbon dioxide were monitored; and hemodynamic data was recorded at the initial phase, after the induction, 5, 10, 15, 30 and 45 min after intubation, and 1 and 5 min after extubation.A solution containing 40 mg/2 mL lidocaine hydrochloride + 0.025 mg/2 mL epinephrine was applied directly or through soaked cotton to the nasal side of both the medial and lateral conchae, for topical vasoconstriction/ local anesthesia.

The dosages and infusion rates of magnesium sulphate and dexmedetomidine were so chosen to sustain the target MAP and avoid the serious hemodynamic side effects. All patients received standard anesthetic technique with propofol 1–2 mg/kg and tramadol 1mg/kg; endotracheal intubation was facilitated with atracurium 0.5 mg/kg with suitable size cuffed tube. Anesthesia was maintained with 50% nitrous oxide and 50% oxygen, and 1% isoflurane.

Volume-controlled mechanical ventilation was per- formed with an end-tidal carbon dioxide pressure between 35 and 40 mmHg.

Deliberate hypotension, defined as a mean arterial pressure of 60 to 70 mmHg,[7] was treated by increment doses of ephedrine 10 mg I.V. Bradycardia was defined as HR < 50 beats/ min and was treated by atropine 0.01 mg/kg, patients who have nausea and vomiting were given additional 1 mg granisetron I.V., and patients who were shivering were warmed with heated blankets.

Magnesium sulfate and dexmedetomidine infusions were discontinued at the end of the surgery. Then, 0.02 mg/kg atropine and 0.04 mg/kg neostigmine was applied in order to antagonize the neuromuscular block- age.

If there was an increase in the arterial blood pressure above the targeted MAP (55–65 mmHg), nitroglycerine infusion was started by 0.5 μg/kg/min. The drug infusion rate decreased when the targeted MAP was achieved. Patients were extubated when they open their eyes in response to verbal commands.

The total blood loss was measured, and bleeding score assessed using scores: 0 = no bleeding; 1 = slight bleeding, no aspiration required; 2 = minor bleeding, aspiration required; 3 = minor bleeding, frequent aspiration required; 4 = moderate bleeding, visible only with aspiration; and 5 = severe bleeding, continuous aspiration required.[11] The surgeon satisfaction was scored for quality of the surgical field and was rated using a 4-point Likert scale at the end of surgery: 1 = bad, 2 = moderate, 3 = good, and 4 = excellent.[12]

All statistical analyses were performed on Microsoft Excel 2010 software. Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Student's t-test was used for the comparison of hemodynamic parameters and duration of anesthesia, operation. Chi-square (χ^2) test was used to compare surgeon satisfaction and visibility of the surgical site, while Fisher's exact test was used in comparison of bradycardia, hypotension, and other parameters. $p < 0.05$ was considered statistically significant.

The primary outcome was to measure bleeding score, and secondary outcomes were: mean arterial blood pressure and heart rate, to reach bloodless surgical field by controlled hypotension. All intra-operative and postoperative complications were recorded.

RESULTS

Demographically, there were no statistically significant differences among the two groups. Similarly, not much difference was there in the ASA-PS, duration of operation, and other parameters too. (Table1)

Table 1: Comparison Between Both Groups According To Demographic Data

Demographic data	Group M (n = 30)	Group D (n = 30)	p-value
Gender: Male (n, %) Female (n, %)	12 (40.0%) 18 (60.0%)	10 (33.3%) 20 (66.7%)	0.629
Age in years (Mean ± SD)	42.87 ± 11.96	42.15 ± 10.82	0.404
Weight in kg (Mean ± SD)	75.92 ± 11.63	76.08 ± 10.78	0.468
ASA-I (n, %)	21 (70.0%)	22 (73.3%)	0.330
ASA-II (n, %)	9 (30.0%)	8 (26.7%)	
Duration of operation (minutes) (Mean ± SD)	97.06 ± 18.03	86.42 ± 16.43	0.149

Mean arterial pressure(MAP) at baseline was similar in two groups, before loading dose; at induction then at 15minutes after induction, but there was a statistically significant decrease in the MAP among Dexmedetomidine Group58.07 ± 3.83mmHg compared to Magnesium SulfateGroup66.58 ± 3.96mmHg at 30 minutes and similarly at 60 minutes, post-extubation and postoperatively (p = 0.021) also. (Table 2)

Table 2: Comparison Regarding The Mean Arterial Blood Pressure (map) (mmhg)

MAP (mmHg)	Group M (n = 30)	Group D (n = 30)	t test	pvalue
Baseline	88.55 ± 9.63	86.59 ± 7.82	2.23	0.380
After induction	78.24 ± 7.47	75.21 ± 5.93	0.734	0.402
After 15 min	70.51 ± 5.63	64.22 ± 4.96	0.654	0.258
After 30 min	66.58 ± 3.96	58.07 ± 3.83	1.918	0.047*
After 60 min	67.09 ± 4.11	56.82 ± 3.92	2.951	0.029*
After 90 min	62.38 ± 3.98	59.46 ± 3.59	1.741	0.083
End of surgery	68.56 ± 6.47	60.09 ± 4.79	1.976	0.038*
Post-extubation	75.44 ± 5.84	66.22 ± 4.89	2.012	0.041*

Post-operative 30 min	78.50 ± 6.43	66.46 ± 5.90	2.922	0.021*

*p-value <0.05 = significant

There were no statistically significant differences between the two groups regarding HR at baseline and 15 minutes after induction, but there was a statistically significant decrease in the HR after anesthetic induction and at 30, 60 and 90 minutes, intra-operatively, post-extubation; and post-operatively; among the Group D as compared to the Group M.(Table 3)

Table 3 Comparison Regarding The Heart Rate (beats/minute)

Heart rate (beat/min)	Group M (n = 30)	Group D (n = 30)	t test	p-value
Baseline	82.33 ± 6.42	83.06 ± 6.93	0.687	0.457
After induction	79.76 ± 5.22	75.49 ± 5.05	1.429	0.109
After 15 min	76.91 ± 6.89	68.13 ± 5.24	1.863	0.067
After 30 min	67.25 ± 5.49	60.02 ± 4.60	2.528	0.041*
After 60 min	64.76 ± 4.54	57.90 ± 4.15	3.908	0.023*
After 90 min	67.29 ± 4.16	58.37 ± 4.98	7.704	0.005*
End of surgery	74.18 ± 5.73	65.86 ± 5.03	6.233	0.021*
Post-extubation	81.19 ± 6.66	71.19 ± 5.48	4.996	0.017*
Post-operative 30 min	78.72 ± 5.31	66.40 ± 4.27	3.218	0.011*

*p value < 0.05 significant

There was a statistically significant decrease in the amount of blood loss among Group D as compared to the Group M (p = 0.019). The surgeon satisfaction was significantly higher in Group D than in Group M. (Table 4)

Table 4: Assessment Of Intra-operative Surgical Field And Surgeon Satisfaction Score

Variable	Group M (n = 30) (%)	Group D (n = 30) (%)	χ^2	p-Value
Bleeding score 0	1 (0.33)	3 (10.0)	15.33	0.006**
1	9 (30.0)	19 (63.3)		
2	9 (30.0)	7 (23.3)		
3	6 (20.0)	1 (3.3)		
4	5 (16.7)	0 (0)		
5	0 (0)	0 (0)		
Satisfaction score 1	4 (13.3)	0 (0)	21.46	0.003**
2	11 (33.3)	3 (6.6)		
3	10 (26.6)	9 (26.6)		
4	5 (26.6)	18 (66.6)		

*p value < 0.05 significant, ** p value < 0.001 highly significant

Two cases of nausea and vomiting were recorded among the magnesium group. The number of patients who required nitroglycerine was significantly lower in Group D (p=0.012). Nitroglycerin was used only in 7 cases in the Group M, while it was used in 4 cases in Group D. There was no difference between the two groups in terms of recovery room verbal numerical rating scale.

DISCUSSION

Functional endoscopic sinus surgery (FESS) is performed using a fiber-optic endoscope with magnificent powerful camera. In such a surgical procedure, even a drop of blood may obscure the surgical field completely. Various approaches have been used to secure a dry operating field with minimal bleeding; among them are topical vasoconstrictors, alpha and beta adrenergic blockade and preoperative steroids. But these methods are associated with significant side effects.

Studies have been conducted using oral nifedipine as a premedication for induced hypotension in FESS.[13] However, in the current study, dexmedetomidine and magnesium sulphate were used, where dexmedetomidine was found more effective in performing controlled hypotension during FESS and that it provided a better surgical site and surgeon satisfaction and a lower necessity of additional hypotensive agent than magnesium sulfate. Similar to our study, a a study assessing the hypotensive effects of dexmedetomidine administered as a 0.4 µg/kg/hour i.v. infusion following a 1 µg/kg i.v. bolus dose in middle ear surgery, has reported that surgeon satisfaction was increased and inhalation agent necessity to decrease the MAP was lessened upto 30% in the dexmedetomidine administered patient group.[14] These results were also similar to the Faranak et al. study, in which bleeding score was lower and the surgeon's satisfaction score was higher, besides less analgesic was required in the dexmedetomidine group than the magnesium group. Dexmedetomidine controlled blood pressure better than magnesium sulphate as nitroglycerin was added to achieve the targeted MAP in the Group M.

We also observed that bleeding at the surgical site was decreased and surgeon satisfaction improved, in the dexmedetomidine study group, similar to the finding of Shams et al.[15] & Ayoglu et al [16] The analgesic effects of dexmedetomidine can be due to the activation of α_{2B}-adrenoceptors at the level of the dorsal horn of the spinal cord and the inhibition of substance P release.[17]

Dexmedetomidine is a highly selective and potent central $_2$-receptor agonist; it has a central and peripheral sympatholytic property manifested by reduced arterial blood pressure, heart rate, cardiac output, and release of norepinephrine. In addition, it has a unique sedative property among other sedatives as it causes sedation without respiratory depression. Magnesium sulphate, on the other hand, induces deliberate hypotension by intervention of the activation of membrane Ca^{2+} ATPase and Na–K ATPase involved in the transmembrane ion exchanges during depolarization and repolarization phases. Also, Mg^{++} inhibits the release of norepinephrine.

Kalra et al.[18] compared magnesium sulfate with clonidine, which is another α_2 receptor antagonist, in patients undergoing laparoscopic surgery; it was stated that the duration until achieving a reply to verbal stimulus was longer in the magnesium sulfate patient group compared to the 1 µg/kg i.v. and 1.5 µg/kg i.v. clonidine groups, which was attributed to the depressor effects of magnesium sulfate on the central nervous system.

Patel et al.,[19] compared dexmedetomidine with nitroglycerin to produce controlled hypotension; dexmedetomidine had the advantage of maintaining better cardiovascular stability as compared to nitroglycerine. In Ghodraty et al.[20] study, magnesium was compared with remifentanil, finding both drugs similar in terms of providing controlled hypotension; also, similar hemodynamic properties were reported.

In a study the incidence of bradycardia occurred in 4 patients in the dexmedetomidine group versus one patient in the magnesium group.[12] In our study two cases of hypotension (MAP < 50 mmHg) were recorded among the dexmedetomidine group and treated by mephtermine increments 12 mg, but this was statistically insignificant. Five cases of bradycardia (HR<50b/m) occurred in the dexmedetomidine group and one case in the magnesium group and were treated with atropine 0.5 mg with no statistically significant difference.

As for bleeding score, it was lower among the Group D when compared with the Group M. Surgeon's satisfaction score for operative field visibility was higher among patients in the Group D. Peripheral vasoconstriction might be another reason for less bleeding and better surgical field among patients in the Group D besides the decrease in BP and HR effects.

Yu et al.[21] studied the use of intravenous magnesium sulphate on postoperative analgesia in orthopedic surgery and concluded that perioperative intravenous administration of magnesium sulfate could reduce postoperative analgesic consumption and reduce postoperative pain.

Limitation of this study is absence of controlled group and a small sample size. We may not have been able to detect other adverse events that could occur with a low frequency. Furthermore, postoperative magnesium sulfate level was not measured, but no patients showed any signs of excessive neuromuscular blocks or toxicity.

CONCLUSION

Dexmedetomidine is more effective than magnesium sulfate to achieve controlled hypotension, higher surgeon satisfaction and less bleeding in patients undergoing FESS. Dexmedetomidine controlled blood pressure better than magnesium sulfate which needed additional nitroglycerin providing a favorable quality of the surgical field. Dexmedetomidine also has a potent analgesic effect than magnesium with decreased duration of analgesic requirement postoperatively.

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