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Comparison of Magnesium Sulphate and Esmolol In Attenuating the Cardiovascular Responses to Tracheal Extubation –A Prospective, Randomized, Comparative Indian Study

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ABSTRACT

Tracheal extubation is known to cause a rise in systolic, diastolic and arterial blood pressure. Present study was conducted to compare MgSO4 and Esmolol with regards to their effects on haemodynamic extubation stress response in patients after general anaesthesia. Study population comprised of 60 patients aged between 20 and 50 years, with ASA grade I and II scheduled for elective surgery under general anesthesia with intubation. Group M received IV magnesium sulphate-40mg/kg and Group E received IV esmolol-0.6 mg/kg, both diluted in 100 ml NS started 5 minutes before extubation. Intergroup comparison of heart rate, mean arterial pressure, systolic and diastolic blood pressure was done before extubation, at time of extubation, 3mins, 5mins and 10mins after extubation. Quality of extubation was evaluated and compared between groups with extubation quality score and modified Ramsay sedation score. Demographic details were statistically comparable between study groups in terms of age, weight, sex, ASA grade. Mean HR after extubation was significantly lower in group E ($p<0.05$). MAP, SBP and DBP after extubation were significantly lower in esmolol group ($p<0.05$). Mean EQS was significantly higher in group E ($p<0.05$) after extubation. Mean MRS was higher in group M after extubation ($p<0.05$).Mean extubation time in group E was lower than group M ($p<0.05$) Haemodynamic parameters were well controlled with both esmolol and MgSo4 and the readings were in clinically normal range for both groups. However quality of extubation and sedation was superior with MgSo4.

Keywords: BP, HR, MAP, SBP, DBP, Esmolol, MgSO4, EQS, MRS

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INTRODUCTION

Tracheal extubation is a critical step during anaesthetic care when cardiovascular and respiratory decompensations can occur, such as tachycardia, hypertension, arrhythmias, myocardial ischaemia, bronchospasm, or laryngospasm.[1,2] It is an integral and crucial part during general anaesthesia. Extubation is known to cause irritation of the airways, leading to cough or strain, both of which are known to raise systolic, diastolic as well as arterial pulse pressure. Coughing can cause an elevation in intrathoracic pressure that can interfere with venous return to heart. Reflex sympathetic discharge occurring because of epipharyngeal and laryngopharyngeal stimulation leads to significant rise in heart rate and arterial pressure that may persist into recovery period.[3-6]

A variety of pharmacological agents have been recommended for the control of haemodynamic events during extubation. Documented beneficial effects of magnesium, as a selective blocker for calcium channels and N-methyl-d-aspartate (NMDA) receptor antagonist, have been the basis for multiple studies that have reported protective effects of this medication regarding haemodynamic responses, in patients undergoing general anaesthesia.[7,8] Studies have noted that magnesium has an important role as a vasodilator in arterioles, whereas this effect is minimal on venules, which result in improvement in cardiac output.[9]This function is regulated mainly by blocking sympathetic system via inhibiting the release of catecholamines from the adrenal, as well as peripheral nerve endings.[10] In addition, magnesium has beneficial effects on maintaining diastolic function and regulating sinus rhythm, during arrhythmias.[11] Since magnesium is a vasodilator, it has been used in general anaesthesia to decrease BP and prevent its elevation.

Esmolol is a unique selective β1-adrenoceptor antagonist leading to reduced heart contractility, slowed atrioventricular conduction, and increased atrioventricular refractoriness, which ultimately results in decreased myocardial oxygen demand.[10] Besides its cardio-selectivity, this beta-blocker has become an attractive therapeutic choice in the peri-extubation period due to its rapid onset of action as well as its effects with a short duration. However, few trials have assessed whether the administration of esmolol could improve patient safety and outcomes after extubation.[11-13]The rapid onset and short duration of action (T1/2 = 9 min) of esmolol make it an ideal agent to prevent acute increases in heart rate and arterial pressure which occur at extubation.[14,15]

Literature search revealed that there is a dearth of scientific evidence which have compared intravenous magnesium sulphate and intravenous esmolol in attenuating haemodynamic extubation stress response after general anaesthesia, especially in Indian context. Hence, present study was planned to compare the two pharmacological agents with regards to their effects on haemodynamic extubation stress response in Indian patients after general anaesthesia.

MATERIALS AND METHOD

Study Design

A single centre, hospital based prospective, randomized comparative study after Ethical Committee approval.

Study site

Department of Anaesthesiology, Government Medical College, Kota

STUDY PERIOD- MAY 2021-JULY 2022

Study Subjects

60 patients scheduled for elective surgery under general anaesthesia with intubation

Inclusion criteria

- ASA class I and II
- Age group of 20-50 years
- Both sex

Exclusion criteria

- ASA grade III and IV
- Emergency surgeries
- Pregnant and lactating women
- Preoperative hypotension(MAP<60 mm Hg)
- Preoperative bradycardia (PR<60)
- Patient on drug and alcohol abuse
- Patient on drug like beta blocker and calcium channel blocker

SAMPLE SIZE CALCULATION

Sample size was calculated using MedCalc Software version 11.5.0.0. (MedCalc Software bvba Acacialaan 22, 8400 Ostend, Belgium). Based on minimum mean difference of 25% in parameters (mean heart rate and mean blood pressure) with α =0.01 and β =0.20, sample size for each group was estimated as 28. Rounding up this figure, a sample size of 30 per group was required to detect a significant difference between the groups.

Statistical Analysis

After data collection, data entry was done in Microsoft Excel. Data analysis was done with the help of statistical software Graph pad In Stat v3.0 Quantitative data was presented with the help of Mean and Standard deviation. Qualitative data was expressed in terms of frequency and percentages. Quantitative data were analyzed using t-test for normally distributed data. The qualitative data were compared between groups using chi-square test or Fischer's exact test. A p value of less than 0.05 was statistically significant.

After inclusion of patients, following steps were followed in-line with the study and hospital protocol:

Pre-operative assessment

A thorough preoperative evaluation of each patient was done. All routine biochemical, hematological, and radiological investigations (Hb, blood sugar, blood urea, serum creatinine, BT, CT, HIV, HBsAg, X-ray chest PA view) was done as per our hospital protocol. A baseline ECG was obtained. All patients were examined on the day before surgery and explained about the anaesthetic technique and perioperative course. Informed written consent was taken from each patient.

Preparation and premedication

Routine preoperative preparation consisted of fasting for 6-8 hours prior to surgery. All the patients were premeditated with tablet alprazolam 0.25 mg night before surgery. Confirmation of the following was done: nil by mouth status as per ASA guidelines, investigations, and standard anesthetic trolley including drugs and airways.

Monitoring

The parameters monitored at the time of laryngoscopy, intubation and intraoperative period consisted of:

- Heart rate and rhythm by three lead ECG.
- Non-invasive blood pressure (systolic, diastolic, and mean arterial pressure).
- Oxygen saturation by pulse oximeter.
- End tidal concentrations of anaesthetic agents and CO2 level by capnograph.

Anaesthesia technique

After arrival in OT, all patients were attached to standard monitor, secured an IV line with 18/20 G cannula and maintenance infusion of RL/NS was started.

All the patients were pre-medicated with IV midazolam -0.02mg/kg, IV Fentanyl- 2 microgram/kg.

Patients were induced with propofol (2.5mg/kg), after 3 min of preoxygenation intubation with appropriate size tube was facilitated by nondepolarizing muscle relaxant succinylcholine (1-1.5 mg/kg).

After proper relaxation a short and careful larygoscopy, was done and patient was intubated.

After fixing of ETT & connecting it to anaesthesia ventilator, anaesthesia was maintained with sevoflurane (0.6-1 MAC) in oxygen and intermittent IV atracurium.

At the end of surgery patients were randomly allocated into two groups i.e., 30 subjects in each group using computer generated randomization list with allocation ratio 1:1.

To summarize the distribution of patients:

Group M

Received IV Magnesium Sulphate 40 mg/kg started 5 minutes before extubation and

Group E

Received IV Esmolol 0.6mg/kg started 5 minutes before extubation.

Both the drugs were diluted in 100 ml normal saline and were administered over 5 minutes. The infusion was stopped if patient developed any adverse event like hypotension/ bradycardia etc. and were treated as standard protocol. Neuromuscular blockade was reversed with IV neostigmine (0.05 mg/kg) and glycopyrrolate (0.01mg/kg). Patients were extubated after confirming adequate reversal of neuromuscular block.

Demographic details were noted for all included cases. The mean extubation time was compared between study groups. The intergroup comparison of various variables like heart rate (HR), mean arterial pressure (MAP), systolic blood pressure (SBP), diastolic blood pressure (DBP), was done before extubation, at time of extubation, 3 mins, 5 mins and 10 mins after extubation. Additionally, the quality of extubation was evaluated at the abovementioned time-points and compared between groups with help of extubation quality score (EQS)[16] and modified Ramsay sedation score (MRS) [17].

RESULTS AND DISCUSSION

Both the groups were comparable with regards to demographic data (Table 1)

Table 1: Demographic details of enrolled cases in study groups

Variables	**Group M (n=30)**	**Group E (n=30)**
Age (years)	36.27±9.70	39.53±9.14
Weight (kg)	60.31±6.23	58.23±5.98

The mean HR at 5 min and 10 mins after extubation was significantly lower in the Esmolol group versus the MgSO4 group ($p<0.05$). (Table 2)

Table 2: Mean heart rate (beats per min)

Time of assessment	***Group M (n=30)***	***Group E (n=30)***
Preoperative	90.73 ± 5.19	90.6 ± 5.46
Before induction	87.67 ± 4.8	86.13 ± 5.16
Just before study drug administration	84.33 ± 4.5	80.80 ± 6.16
1 min after extubation	80.47 ± 4.44	75.87 ± 5.84
3 mins after extubation	76.77 ± 4.43	70.80 ± 7.12
5 mins after extubation	73.4 ± 4.33	66.2 ± 7.70
10 mins after extubation	70.63 ±4.35	61.70 ± 7.47

P<0.05 Group M vs Group E

The MAP, SBP and DBP all were statistically comparable between the two study groups till 1 minute of extubation. (P>0.05) However, the mean MAP, SBP and DBP at 3 min, 5 min and 10 min after extubation were significantly lower in the esmolol group versus the MgSO4 group (p<0.05). (Table 3-5)

Table 3: Mean Arterial Pressure (mm Hg)

Time of assessment	Group M (n=30)	Group E (n=30)
Preoperative	93.03 ± 4.09	93.23 ± 3.92
Before induction	93.03 ± 4.09	93.23 ± 3.92
Just before study drug induction	88.7 ± 4.71	90 ± 4.65
1 min after extubation	86.94 ± 4.12	84.73 ± 4.07
3 mins after extubation	85.93 ± 3.96	80.47 ± 4.15
5 mins after extubation	82.8 ± 4.18	78 ± 4.34
10 mins after extubation	78.63 ± 4.57	74.13 ± 4.01

P<0.05 Group M vs Group E

Table 4: Systolic Blood Pressure (mm Hg)

Time of assessment	Group M (n=30) Mean± SD	Group E (n=30) Mean± SD
Preoperative	138.58±7.06	137.48±6.55
Before induction	137.57 ± 7.06	137.47 ± 6.55
Just before study drug administration	130.83 ± 6.89	131.93 ± 6.01
1 min after extubation	127.85 ± 5.73	127.13 ± 5.61
3 mins after extubation	126 ± 5.5	119.73 ± 5.91
5 mins after extubation	119.1 ± 6.49	113.83 ± 7.89
10 mins after extubation	115.2 ± 7.74	110.53 ± 8.73

P<0.05 Group M vs Group E

Table 5: Diastolic Blood Pressure(mm Hg)

Time of assessment	Group M (n=30) Mean± SD	Group E (n=30) Mean± SD
Preoperative	82.17±5.3	80.7±5.16
Before induction	82.17 ± 5.3	81.7 ± 5.15
Just before study drug administration	79.87 ± 4.9	79.17 ± 4.9
1 min after extubation	78.24 ± 4.85	76.87 ± 4.66
3 mins after extubation	77.53 ± 4.51	71.83 ± 5.81
5 mins after extubation	76.47 ± 4.32	71.57 ± 4.85
10 mins after extubation	71.90 ± 4.33	67.03 ± 5.31

P<0.05 Group M vs Group E

The mean extubation quality score was significantly higher in Group E as compared to Group M (Figure 1) and Modified Ramsay Sedation score was significantly higher in Group M as compared to Group E. (Figure 2)

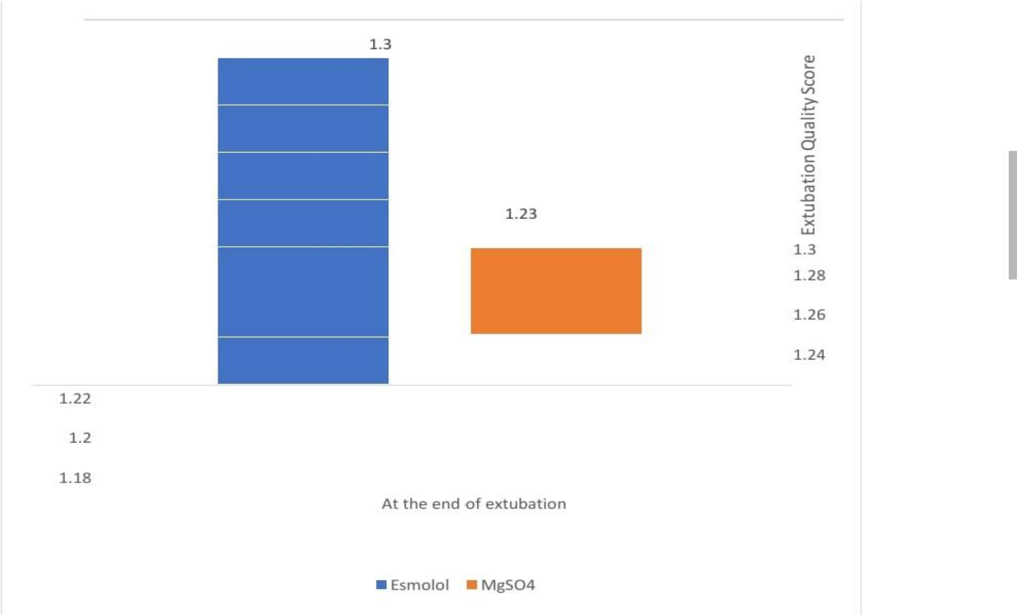

Figure 1: Extubation Quality Score at the end of extubation

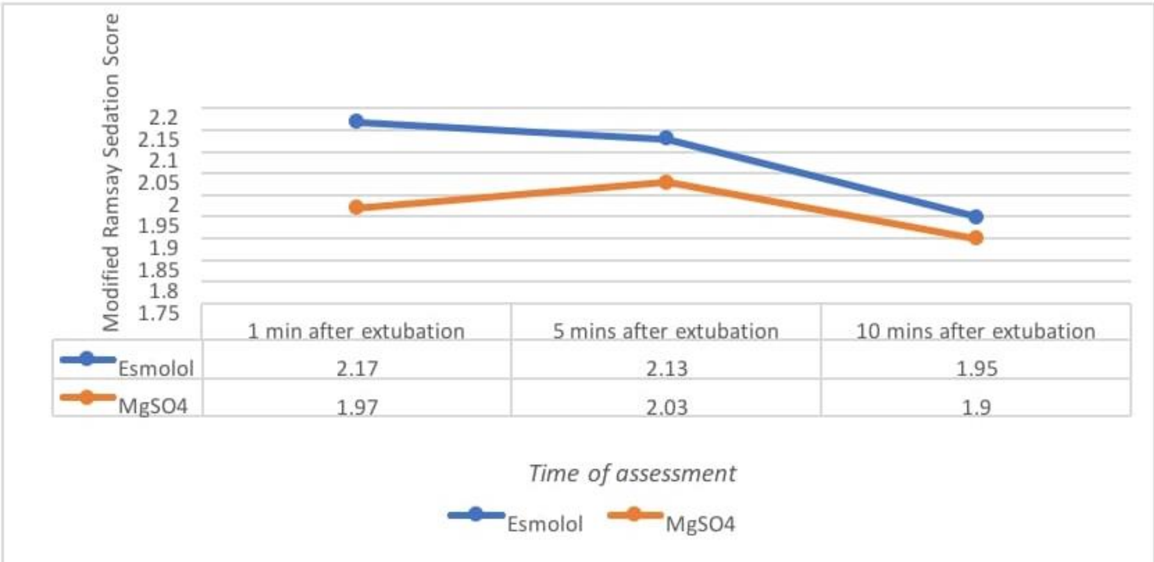

Figure 2: Mean Modified Ramsay Sedation Score at various time points in study groups

The mean extubation time in the esmolol group was noted to be 9.83 ± 1.95 minutes, which was significantly lower than the time in the MgSO4 group (13.57 ± 2.13 minutes.

DISCUSSION

Hypertension and tachycardia are well-documented events during extubation. This rise in blood pressure and heart rate (HR) is typically transitory, variable, and unpredictable. The development of postoperative hypertension necessitates immediate assessment and treatment to lessen the risks of myocardial infarction, arrhythmias, congestive heart failure, stroke, bleeding, and other end-organ damages[18]. Lowrie and colleagues showed a significant rise in the plasma concentration of adrenaline during the process of tracheal extubation, after major elective surgery.[6] If precise measures are not adopted to avert hemodynamic response, the heart rate can rise from 26% to 66% and systolic blood pressure from 36% to 45%, in susceptible patients.[19] As a result, detailed monitoring of the cardiovascular stress response to extubation may be necessary, especially in high-risk patients.[19,20] Scientific data reveals that cardiopulmonary adverse events resulted from tracheal extubation (12.6%) are three times more common when compared to those of endotracheal intubation and induction of general anaesthesia (4.6%).[1]

In present study, esmolol attenuated the tachycardia and hypertensive response of extubation more effectively than MgSO4. In the similar study by Arar et al.,[21]HR and blood pressure were significantly lower in esmolol group compared to magnesium sulphate group ($p<0.05$). In the study by Agrawal et al.,[22] at time of Extubation, the significant reduction was observed in HR and BP, which was more in esmolol group as compared to Magnesium group ($P=0.018$). Ray et al.[23] as well as Verma et al.[24] showed a greater reduction in heart rate in esmolol group versus magnesium group, findings similar to our study and other similar studies. In the study by Juhi Sharma et al.,[25] though esmolol led to greater reduction and control of heart rate as compared to MgSO4.

The mean EQS was significantly higher in the Esmolol group as compared to MgSO4 group at the time of extubation ($p<0.05$). The mean MRS was noted to be significantly lower in the Esmolol group at the time of extubation, 5 mins and 10 mins after extubation ($p<0.05$).In the study by Agrawal et al.,[22] sedation score was comparable between esmolol and magnesium groups except at 1 minute after extubation where it was increased in magnesium group by 13.63% as compared to 8.88% ($p<0.05$) in esmolol group. The sedation score remained at < 2 for rest of the observation period in both the groups & was comparable to baseline in each group. This was similar to a trend noted in our study, albeit at 5 min and 10 min post extubation. The advantage of magnesium sulphate is attributed to the fact that it does not result in bradycardia & provide postoperative analgesia.

Extubation time was shorter and quicker with esmolol usage. The reason for longer extubation time with MgSO4 might be due to the interference of MgSO4 with neuromuscular blockade, well highlighted in scientific literature. Magnesium lowers acetylcholine release due to inhibition of calcium-dependent channels, reduces the sensitivity to acetylcholine in the motor plate, and directly attenuates the excitability of the muscle fiber.[26]

Esmolol is an ultra-short acting beta blocker with a transient effect and short half life. However, the side effects of beta blockers i.e, asthma in susceptible individuals and bradycardia compounded with pre disposing factors may at times preclude its uses.[27] Esmolol is more effective in checking the rise in systolic blood pressure as compared to diastolic as it decreases cardiac contractility more than its effect on peripheral vascular resistance. MgSO4 has a good control over blood pressure. Besides it is also known that MgSO4 is useful in treating various arrythmias which are otherwise resistant. Magnesium has been shown to inhibit catecholamine release during tracheal intubation.[28] Calcium exerts major role in the release of catecholamines in response to sympathetic stimulation. Magnesium has been described as physiological calcium antagonist.[29]It has been used to control hypertension in obstetric patients of pre eclamptic toxaemia to attenuate the pressor response[30].The anti-adrenergic activity of magnesium has recently been advanced as rationale for its use in patients undergoing resection of phaeochromocytoma[31.] Vasodilator effects of magnesium are characterized by the decrease in blood pressure associated with peripheral vasodilatation and consistent increase in cardiac index[32]. It has been studied by James et al in 1992 that MgSO4 in patients of PIH provides a good control over hypertensive response as compared to alfentanil and lignocaine. However, he also suggested that the combination of MgSO4 and alfentanil may be superior. Magnesium sulphate being NMDA antagonist protects against pathological events after ischemia of neural tissue. Esmolol though is being used to attenuate the pressor response, its effect is short lived, and it may not be able to provide a sustained control. On the other hand, MgSO4 although has a renal elimination but large initial doses of 40 to 60mgkg-1 maintain serum magnesium levels 2-4mmols/l.[33]

Our study did have a few limitations. The sample size was limited, and data was collected at only one study centre. Hence, the generalization of the results should be done with caution. Future studies with a larger sample size and multi centre study design will help in validation of present study findings.

CONCLUSION

To conclude, the haemodynamic parameters were controlled well with both esmolol as well as MgSO4, and the readings were in clinically normal range for both groups. The quality of extubation and sedation was superior with MgSO4. Extubation time was significantly shorter in esmolol group. Hence in our opinion we conclude that magnesium sulphate in dose of 40mg/kg in 100 ml normal saline infusion transfused over 5 minutes prior extubation can be used regularly to attenuate haemodynamic responses to extubation because of its properties like efficacy in controlling blood pressure and heart rate with good quality and sedation.

ABBREVIATIONS:

IV: Intravenous

EQS: Extubation Quality Score

MRS: Modified Ramsay Sedation score

ICU: intensive care unit

ASA: American Society of Anesthesiologists

SD: Standard deviation

HR: heart rate

SBP: Systolic blood pressure

DBP: Diastolic blood pressure

MAP: Mean arterial pressure

RR: Respiratory rate

ECG: Electrocardiogram

HIV: Human immunodeficiency virus

ETT: endotracheal tube

MAC: Minimum alveolar concentration

NIBP: Non-invasive Blood Pressure

BT: Bleeding time

CT: Clotting time

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