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Original Research Article

Comparative Study of IV Magnesium Sulphate Versus IV Esmolol in Attenuation of Hemodynamic Response During Extubation after General Anaesthesia

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Abstract

Introduction: The complications after tracheal extubation are three times more common than complications occurring during intubation and induction of anaesthesia (12.6% vs. 4.6%). Tracheal extubation is an important event in general anaesthesia which causes a modest (10% to 30%) and transient (lasting approximately 5 to 15 min) increase in blood pressure and heart rate. Several strategies are adopted to blunt the haemodynamic response to extubation. Esmolol leads to reduced heart contractility, slowed atrioventricular conduction and increased atrioventricular refractoriness, which ultimately results in decreased myocardial oxygen demand. Magnesium acts by inhibiting calcium channel mediated release of catecholamine from both adrenal glands and adrenergic nerve terminals in response to sympathetic stimulation. We undertook this randomized, prospective, double-blind study to compare IV esmolol and IV magnesium sulphate for attenuating haemodynamic response to extubation after general anaesthesia.

Methods: The present prospective, randomized double blind comparative study was conducted in a tertiary care hospital amongst 80 patients of either gender amongst ASA Grade 1 and 2 patients undergoing elective surgeries under general anaesthesia. Eighty consecutive patients undergoing elective surgery under general anaesthesia were enrolled and these patients were randomly allocated using computer generated randomization list into 2 groups with 40 patients in each group with allocation ratio 1:1 'Group M' were given IV magnesium sulphate (40 mg/kg) infusion in 100 ml normal saline over 5 minutes before extubation and 'Group E' were given IV esmolol (0.6 mg/kg) infusion in 100 ml normal saline over 5 minutes before extubation at the end of surgery.

Results: HR at extubation and 1, 3, 5, 10, and 15 minute after extubation reduced in both groups but it was statistically extremely significant in Esmolol group as compared to Magnesium group. MAP at extubation and 1, 3, 5, 10, 15 minutes after extubation was reduced in both groups but it was statistically extremely significant in Esmolol group as compared to Magnesium group. RPP at extubation and 1, 3, 5, 10, 15 minutes after extubation was recorded in both groups. It was statistically insignificant in Esmolol group as compared to Magnesium group.

Conclusion: We concluded that better hemodynamic stability was maintained by Magnesium sulphate without adverse effects, whereas Esmolol group showed fall in HR, SBP & MAP more than 20% of baseline.

Keywords: Magnesium, Esmolol, Extubation, Hemodynamic Response, Laryngoscopy.

Introduction

Laryngoscopy and tracheal intubation cause significant changes in the hemodynamics of patients.[1] The complications after tracheal extubation are three times more common than complications occurring during intubation and induction of anaesthesia (12.6% vs. 4.6%).[2] Tracheal extubation is an important event in general anaesthesia which causes a modest (10% to 30%) and transient (lasting approximately 5 to 15 min) increase in blood pressure and heart rate. A smooth emergence is preferable for all patients but is especially desired for those patients who would not tolerate any alteration in physiologic changes e.g., severe aortic stenosis, coronary artery disease, cerebral aneurysm clipping, carotid endarterectomy, thyroidectomy, craniotomies.[3]

Tracheal extubation is a critical step during anaesthetic care when cardiovascular and respiratory decompensations can occur, such as tachycardia, hypertension, arrhythmias, myocardial ischemia, bronchospasm, or laryngospasm. These potentially fatal complications related to extubation result from stimulation of the larynx, trachea, and bronchi, which increase the release of catecholamines. As a result, detailed monitoring of the cardiovascular stress response to extubation may be necessary, especially in high-risk patients.[4] Importantly, it has been demonstrated that the incidence of respiratory complications can be higher after extubation than during the induction of anaesthesia or tracheal intubation. While several strategies have been employed to control the cardiovascular and respiratory responses to airway manipulation during the intubation period, no standard therapy or guidelines have been established to prevent hemodynamic responses during the peri extubation period.[5] It has long been recognized that pharmacological strategies, such as local anaesthetics, N-methyl D-aspartate (NMDA) antagonists, alpha-2 agonists, and beta-blockers can significantly reduce the rate of serious outcomes related to tracheal intubation. In this respect, the prophylactic use of beta-blockers in the periextubation period has suggested a potential intervention to attenuate cardiovascular responses and decrease unfavourable events such as the reflexes of airway manipulation.[6]

Several strategies are adopted to blunt the haemodynamic response to extubation like extubation under deeper plane of anaesthesia, administration of various drugs like lignocaine, esmolol, propofol, labetalol, fentanyl, calcium channel blockers and nitro glycerine.[7]

Esmolol is a unique selective 1-adrenoceptor antagonist leading to reduced heart contractility, slowed atrioventricular conduction and increased atrioventricular refractoriness, which ultimately results in decreased myocardial oxygen demand.[8]

Besides its cardioselectivity, it has become an attractive therapeutic choice in the periextubation period due to its rapid onset of action as well as its effects with a short duration.

Esmolol in doses of 1.5 mg/kg showed better results to control haemodynamic response during extubation. It is more effective to prevent haemodynamic response to laryngoscopy, intubation and extubation compared to fentanyl and lidocaine.[8] Esmolol is rapidly metabolized by plasma esterase.[7]

Magnesium sulphate has been used for many years as an anti arhythmic and for prophylaxis against seizures. Magnesium a naturally occurring calcium channel antagonist and non-competitive antagonist of N-methyl D-aspartate (NMDA) receptor acts by inhibiting calcium channel mediated release of catecholamine from both adrenal glands and adrenergic nerve terminals in response to sympathetic stimulation.[9]

The role of magnesium sulphate in blunting the haemodynamic response to endotracheal intubation is evolving. It has been shown to inhibit catecholamine release from adrenal medulla & adrenergic nerve endings.[10]

We undertook this randomized, prospective, double-blind study to compare IV esmolol and IV magnesium sulphate for attenuating haemodynamic response to extubation after general anaesthesia (GA).

Materials and Methods

The present study prospective, randomized double blind comparative study was conducted in a tertiary care hospital amongst 80 patients of either gender. Adult patients belonging to ASA Grade 1 and 2 undergoing elective surgeries under general anaesthesia were enrolled in the study.

Baseline screening process and recording: Patients detailed clinical history was recorded, also breath holding time, mouth opening, MPC grade, Hb, CBC, LFT, KFT, RBS, ECG, Chest x- ray, Urine examination was noted.

Study Procedure:

Eighty consecutive patients undergoing elective surgery under general anaesthesia were enrolled and these patients were randomly allocated using computer generated randomization

list into 2 groups with 40 patients in each group with allocation ratio 1:1 'Group M' were given IV magnesium sulphate (40 mg/kg) infusion in 100 ml normal saline over 5 minutes before extubation and 'Group E' were given IV esmolol (0.6 mg/kg) infusion in 100 ml normal saline over 5 minutes before extubation at the end of surgery.

Detail procedure of study:

A detailed pre-anesthetic evaluation of each case was done day before surgery. All patients were kept nil by mouth 6-8 hours before surgery. In the operating room baseline pre-operative heart rate, SBP, DBP, MAP, RR, ECG, SPO2 were recorded. All the patients were pre-medicated with IV Midazolam- 0.02 mg/kg IV, IV Glycopyrrolate 0.04, IV Fentanyl 2 mcg /kg, IV Ondansetron- 4 mg IV. Induction of general anaesthesia was done using IV Propofol 2 mg/kg till the loss of eyelid reflex & Suxamethonium- 2 mg/kg IV given, patient was intubated with appropriate size endotracheal tube, position of ETT confirmed & tube secured. Anaesthesia was maintained with oxygen, nitrous oxide, Isoflurane and IV Vecuronium 0.08 mg/kg. Fluids & blood loss was replaced with IV fluid or blood as appropriate. At the end of surgery Group M received IV magnesium sulphate – 40 mg/kg started 5 minutes before extubation and Group E received IV esmolol – 0.6 mg/kg started 5min before extubation. Both drugs diluted in100 ml normal saline & administered over 5 mins. Neuromuscular blockade reversed with IV neostigmine (0.05 mg/kg) and glycopyrrolate (0.08 mg/kg). Patient extubated after confirming adequate reversal of neuromuscular block. Study vitals (HR, SBP, DBP, SPO2, MAP) were recorded at baseline, at intubation, before extubation, 1 min, 3 mins, 5 mins,

10 mins, 15 mins after extubation. Patients observed in post anaesthesia care unit for complications like arrhythmias, bradycardia, respiratory depression, muscle weakness, nausea/vomiting for 2 hrs. Sedation was measured by Ramsay sedation score as

Ramsay Sedation Scale: Score Responsiveness

1. Patient is anxious and agitated or restless, or both.
2. Patient is cooperative, oriented and tranquil.
3. Patient responds to commands only.
4. Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
5. Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus.
6. Patient exhibits no response.

Withdrawal / Discontinuation criteria (s):

Those patients who refuse to participate in the study were excluded. The drug infusion was stopped if patient develops any significant side effect.

Data analysis:

Data was coded and analyzed in statistical software IBM SPSS Statistics Version 25. Quantitative variables were expressed in terms of mean and SD whereas categorical variables in frequency and percentage. Inferential statistics included a test of significance for comparing difference in two groups and within the group difference by unpaired test. Two independent sample test was used to compare mean change from baseline in two groups. Within the group difference of mean was compared using paired t test. Chi square test was used to compare difference in proportion in two groups. $P<0.05$ was considered statistically significant for all comparison.

Results:

A prospective, randomized, double blind clinical comparative study was designed for comparison of IV Magnesium Sulphate and IV Esmolol in attenuating haemodynamic extubation response after general anaesthesia.

Table 1: Comparison of Mean Heart Rate (per min) in two groups.

Time (Min.)	Esmolol Group		$MgSO_4$ Group		P Value	Summary
	Mean	SD	Mean	SD		
Baseline	92.85	±15.40	91.95	±14.43	0.788	N.S
Before Extubation	86.02	±13.99	88.30	±13.87	0.467	N.S
AtExtubation	81.35	±13.93	88.35	±13.90	0.027	Significant
1 min	77.25	±14.05	84.20	±14.04	0.029	Significant
3 min	73.37	±13.64	80.37	±13.59	0.024	Significant
5 min	69.62	±13.28	76.62	±13.70	0.021	Significant
10 min	66.80	±12.50	73.80	±12.48	0.014	Significant
15 min	64.70	±11.98	71.70	±12.00	0.011	Significant

*N.S – Not Significant

HR at extubation and 1, 3, 5, 10, and 15 minute after extubation reduced in both groups but it was statistically extremely significant in Esmolol group as compared to Magnesium group.

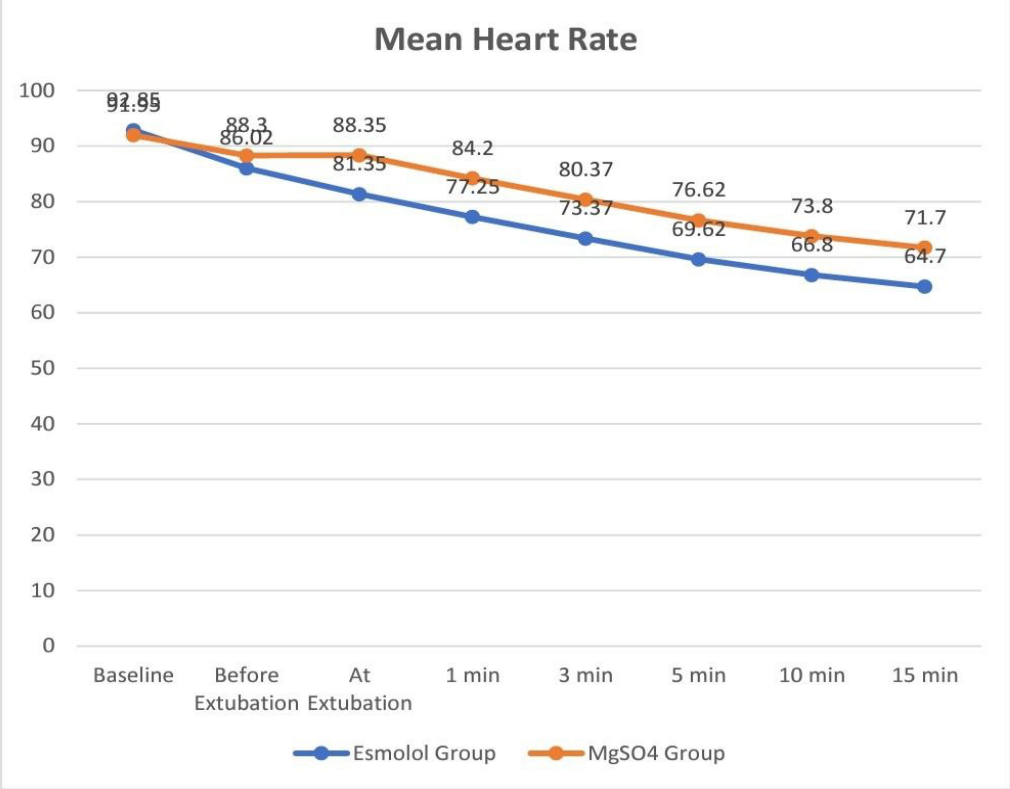

Chart 1: Mean Heart Rate of Esmolol and $MgSO_4$ Groups

Table 2: Comparison of Mean Systolic Blood Pressure (mmHg) in two groups

Time (Min.)	Esmolol Group		$MgSO_4$ Group		P Value	Summary
	Mean	SD	Mean	SD		
Baseline	131.32	±11.88	131.07	±13.03	0.929	N.S
Before Extubation	125.72	±10.98	126.00	±12.05	0.915	N.S
At Extubation	121.92	±10.65	128.92	±10.63	0.004	Significant
1 min	116.97	±10.17	123.87	±10.07	0.003	Significant
3 min	113.35	±9.38	120.36	±9.36	0.001	Significant
5 min	109.40	±9.13	116.39	±9.12	0.001	Significant
10 min	106.05	±8.66	113.04	±8.64	0.001	Significant
15 min	103.65	±7.58	110.62	±7.54	0.001	Significant

Systolic blood pressure at extubation and 1, 3, 5, 10, 15 minutes after extubation was reduced in both groups but it was statistically extremely significant in Esmolol group as compared to Magnesium group.

Table 3: Comparison of Diastolic Blood Pressure (mmHg) in two groups

Time (Min.)	Esmolol Group		$MgSO_4$ Group		P Value	Summary
	Mean	SD	Mean	SD		
Baseline	83.15	±9.48	81.02	±9.66	0.335	N.S
Before Extubation	79.65	±8.80	78.02	±9.37	0.427	N.S
At Extubation	76.47	±7.78	83.46	±7.78	0.001	Significant
1 min	73.02	±7.53	80.02	±7.51	0.001	Significant
3 min	70.05	±7.28	77.05	±7.25	0.001	Significant
5 min	67.22	±6.87	74.22	±6.89	0.001	Significant
10 min	65.22	±6.85	72.22	±6.88	0.001	Significant
15 min	64.17	±6.46	71.17	±6.48	0.001	Significant

DBP at extubation and 1, 3, 5, 10, 15 minutes after extubation was reduced in both groups but it was statistically extremely significant in Esmolol group as compared to Magnesium group.

Table 4: Comparison of Mean Arterial Pressure (mmHg) in two groups

Time (Min.)	Esmolol Group		$MgSO_4$ Group		P Value	Summary
	Mean	SD	Mean	SD		
Baseline	99.25	±9.39	97.77	±9.95	0.498	N.S
Before Extubation	94.97	±8.32	93.94	±9.44	0.612	N.S
At Extubation	91.65	±7.61	98.64	±7.45	0.001	Significant
1 min	87.70	±7.31	94.69	±7.30	0.001	Significant
3 min	84.52	±6.75	91.50	±6.77	0.001	Significant
5 min	81.32	±6.29	88.29	±6.30	0.001	Significant
10 min	78.84	±5.93	85.85	±5.90	0.001	Significant
15 min	77.32	±5.11	84.32	±5.09	0.001	Significant

MAP at extubation and 1, 3, 5, 10, 15 minutes after extubation was reduced in both groups but it was statistically extremely significant in Esmolol group as compared to Magnesium group.

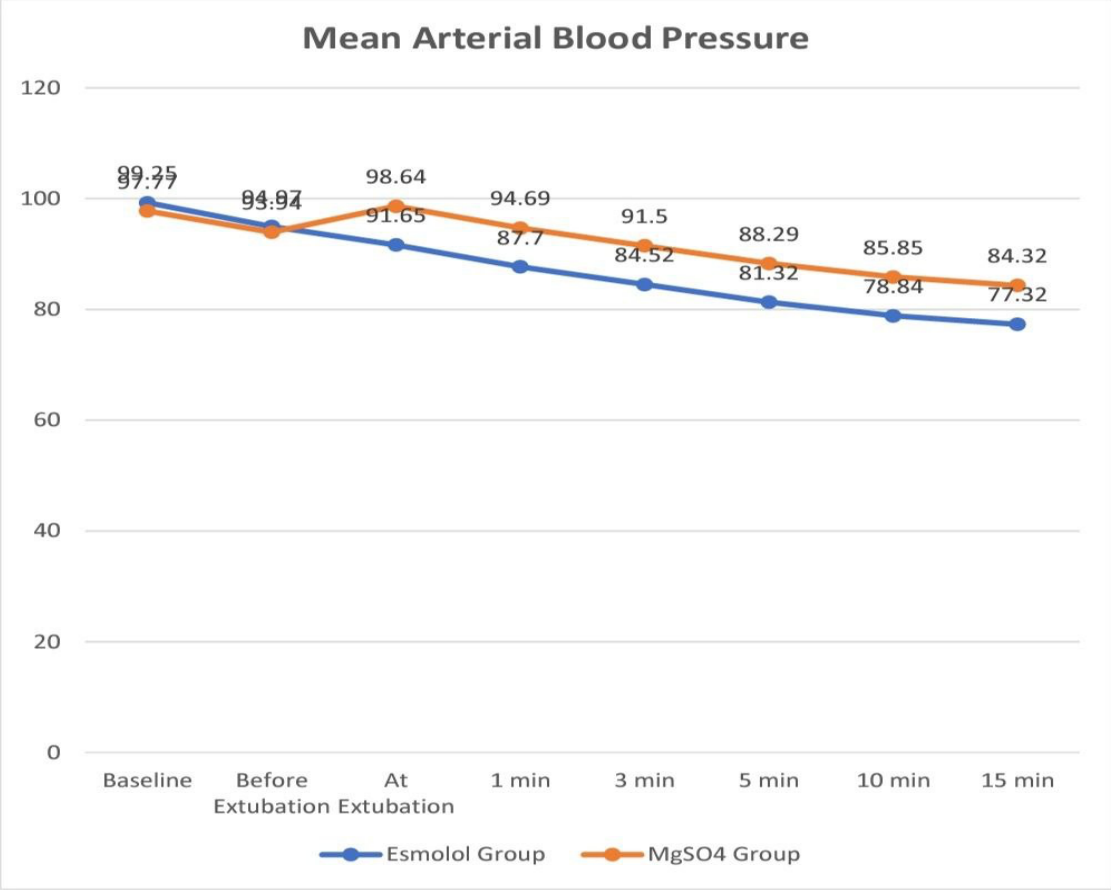

Chart 2: Mean Arterial Pressure of Esmolol and $MgSO_4$ Groups

Table 5: Comparison of Mean RSS Score in two groups

Time (Min.)	Esmolol Group		$MgSO_4$ Group		P Value	Summary
	Mean	SD	Mean	SD		
Baseline	1.97	±0.15	0.95	±0.22	0.562	N.S
Before Extubation	1.92	±0.26	1.90	±0.30	0.697	N.S
At Extubation	2	±0.00	1.92	±0.26	0.075	N.S
1 min	1.95	±0.22	2	±0.00	0.161	N.S
3 min	1.97	±0.15	1.95	±0.22	0.560	N.S
5 min	1.9	±0.30	1.97	±0.15	0.170	N.S
10 min	1.8	±0.40	1.82	±0.38	0.778	N.S
15 min	1.95	±0.22	1.87	±0.33	0.241	N.S

RPP at extubation and 1, 3, 5, 10, 15 minutes after extubation was recorded in both groups. It was statistically insignificant in Esmolol group as compared to Magnesium group.

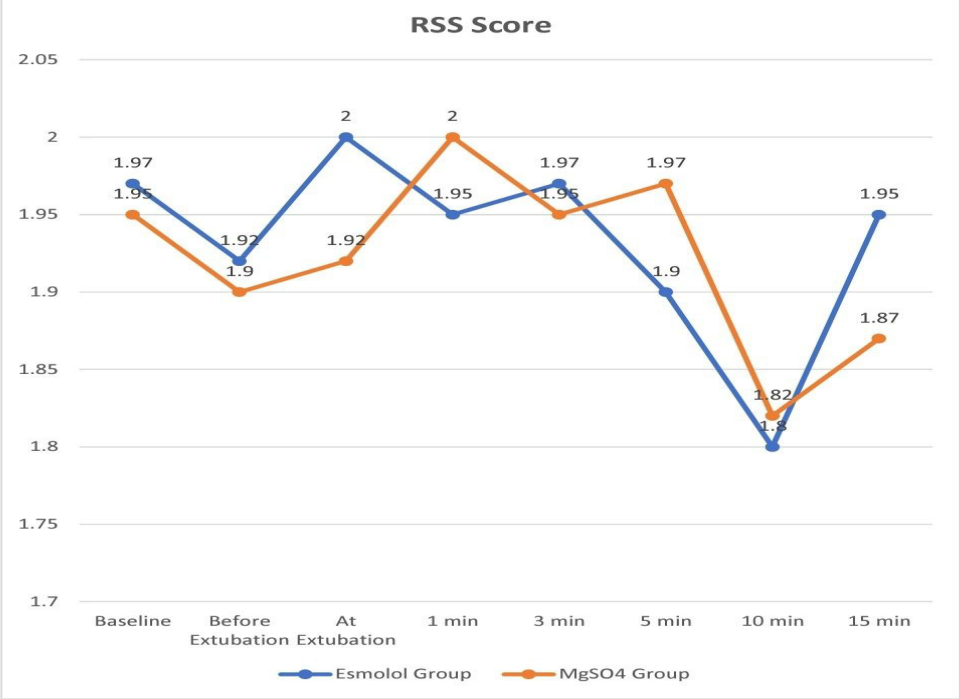

Chart 3: Mean RSS Score of MACKINTOSH AND C-MAC Groups

Discussion

Out of the total 80 study subjects, 42 were females (52.50%) and 38 were males (47.50%). Both the groups were comparable with respect to the baseline parameters like Age, Weight and ASA grade (p>0.05).

In our study, mean baseline heart rate per minute was comparable between both groups (P=0.788). After drug administration the mean HR was slightly reduced in both groups (Esmolol: from 92.85 to 86.02 beats/ min; Magnesium sulphate: from 91.95 to 88.30 beats/ min) which decreased further at the time of extubation, from 86.02 to 81.35 beats/ min in Esmolol group and from 88.30 to 88.35 beats/min in Magnesium sulphate group.

After extubation, heart rate was gradually decreased in both groups and reached below baseline levels (77.25 beats/min in Esmolol and 84.20 beats/ min in Magnesium). There is significantly reduced in HR in esmolol group than magnesium sulphate group from baseline to 15 minutes after extubation so when patient shifted to postoperative care unit monitored till heart rate came to baseline value in esmolol group. Thus, the control of HR was

significantly better in Group E than in Group M from extubation to 15 min after extubation.

Chetan et al (2020) [12] in their study found that HR was significantly reduced in esmolol group compared with magnesium sulphate group at before extubation, at extubation and 1, 3, 5, 10, 15 minutes after extubation

There was 21.82% fall in heart rate observed in group M with a plateau at 10 - 15 minutes compared to a 37.07% in group E with a peak at 15 minutes (p=0.0150).

Similar findings observed in other study like C. Arar et al (2007) [10] they observed that there is decrease in HR in esmolol group compared to magnesium group ($p < 0.05$) and control group ($p < 0.001$) which was a very significant. Whereas there was increase in HR in magnesium sulphate group at the time of extubation ($p<0.001$) and 1 minute after extubation ($p<0.05$) which was significant compared to before drug administration. While magnesium sulphate compared to control group there was significantly increase in HR at the time of extubation and 1 minute after extubation. As they found increase in HR in magnesium sulphate group it could be because of inadequate dose that's why we selected a 40 mg/kg for our study.

There were some other studies done using esmolol and magnesium sulphate, but they are at the time of intubation like-

Indu et al (2018) [12] they found significantly decrease in HR in esmolol group compared to magnesium sulphate group after intubation when esmolol and magnesium sulphate given after premedication. They recorded HR after intubation and 1, 3, 5, 10, 15 minutes after intubation and found there was significant decrease in heart rate in both groups.

Lais constante Machado et al (2017) [13] they found group who received esmolol were more haemodynamically stable compared to group who received magnesium sulphate and placebo drug before intubation.

Nagrale M H et al (2016) [14] they studied comparison of esmolol, propofol and lignocaine while extubation. They found group who received esmolol 1.5 mg/kg show significant decrease in HR compared to who received propofol 0.5 mg/kg and lignocaine 1 mg/kg after intubation.

When SBP of both groups compared before extubation which is not significant. At the time of extubation and 1, 3, 5, 10, 15 minute was significant. The fall of SBP in esmolol group is 21.07% from baseline which is very significant compared to magnesium sulphate group in which 18.48% fall from baseline.

Similarly, when DBP of both groups compared before extubation show nonsignificant findings. But at the time of extubation and 1, 3, 5, 10, 15 minutes was significant. There was fall in DBP in esmolol group is 22.82% which is significant than magnesium sulphate group having 12.21% fall from baseline. In MAP there is significant finding in esmolol group compared to magnesium sulphate. We got decrease in MAP in esmolol group by 22.09% whereas in magnesium sulphate group by 13.75 % from baseline MAP.

Chetan et al (2020) [11] they found fall in SBP in esmolol group was significant than magnesium sulphate group. But in DBP and MAP was lower in esmolol group than magnesium sulphate group though it was statistically not significant ($p>0.05$).

C Arar et al (2007) [10] - They found group receiving esmolol show fall in SBP significant than who receiving magnesium sulphate and normal saline ($p<0.001$) during extubation. While DBP was high in normal saline group than esmolol and magnesium sulphate group. And MAP low in esmolol than magnesium sulphate and normal saline group after extubation.

R. Vachhani et al () [8] they study the effect of esmolol and nitro glycerine on

hemodynamic response during extubation. They observed that group who received esmolol show DBP and MAP significantly low than nitro glycerine group at extubation and 1, 3 minutes after extubation.

Azim Honarmand et al (2015) [15] they given different doses of magnesium sulphate and there was control group who received normal saline before intubation. They found Systolic, diastolic and mean arterial pressures were statistically significant less at 1, 3, and 5 minutes after intubation in comparison with other times of following up in the three groups received $MgSO_4$ than the control group. And they conclude that use of $MgSO_4$ in doses less than 50 mg/kg can be effective to reduce cardiovascular instability related to laryngoscopy and tracheal intubation.

Arshdeep sing et al (2015) [7] they divided cases in 3 group which they given esmolol, diltiazem and normal saline during extubation. The group receiving diltiazem show that attenuating effect on changes of SBP and DBP was greater with diltiazem than esmolol. And Diltiazem is more effective than Esmolol in attenuating the SBP changes.

Lais Constante Machado et al (2017) [13] they given esmolol and magnesium sulphate during intubation and group Magnesium sulphate had the highest mean systolic blood pressure. The systolic blood pressure of the Magnesium sulphate group was higher than the group Esmolol at different times. They found a bolus of 1.5 mg/kg esmolol three minutes before intubation was able to attenuate the hypertensive response to orotracheal intubation, being more effective than 30 mg/kg of magnesium sulphate infused ten minutes before anaesthetic induction.

The saturation level in both group is comparable. The finding after comparison is insignificant. So, the change in spo2 has no any relation with esmolol and magnesium sulphate.

There is insignificant finding come after statistically comparison between esmolol and magnesium sulphate. Few patients after extubation are anxious and agitated or restless or both while remaining all are cooperative, oriented and tranquil. It was observed that Magnesium causes insignificant sedation as we studied low dose i.e., 40 mg/kg

Patients observed intra operative and post anaesthesia care unit for any ECG changes like bradycardia, tachycardia, arrythmias and ST-T changes. There was no such finding noted in any patients in this study in any drug.

There were no any side effects noted to any drug intraoperative or postoperative in any case, like nausea, vomiting, respiratory depression and muscle weakness. In this study we got good hemodynamic stability with Magnesium sulphate and there was insignificant postoperative sedation. And Esmolol group showed significant fall in Heart rate (more than 20% of baseline), SBP, DBP, MAP. Though there are few studies done in this direction, but still more studies are required to set protocol while extubation and also to rule out role of Magnesium sulphate in attenuation of hemodynamic response after extubation.

Conclusion

After comparison of IV Esmolol and IV Magnesium in attenuating. Haemodynamic extubation response after general anaesthesia following conclusions were drawn: Both drug shows there is decrease in HR, SBP, DBP and MAP after extubation but more with esmolol than magnesium sulphate. Saturation was comparable in between both groups. Ramsay sedation score was comparable in between both groups. Thus, we conclude that better hemodynamic stability was maintained by Magnesium sulphate without adverse effects, whereas Esmolol group showed fall in HR, SBP & MAP more than 20% of baseline.

Abbreviations:

ASA- American Society of Anaesthesiologist
HR- Heart rate
SBP- Systolic blood pressure
DBP- Diastolic blood pressure
MAP- Mean arterial pressure
MPC- Mallampati Grading Score
CBC- complete blood count
KFT- Kidney function test
RBS- Random blood sugar
ECG- Electrocardiogram
SPO2- Saturation pulse oximetry
SD- Standard deviation

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