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Original Research Article

A comparative study of the efficacy of intravenous magnesium sulphate and intravenous dexmedetomidine in attenuating haemodynamic response to laryngoscopy and endotracheal intubation

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ABSTRACT

Background: Both laryngoscopy and tracheal intubation elicit a sympathetic and parasympathetic response, which varies depending on the depth of anaesthesia, duration of laryngoscopy, and patient characteristics. Although different methods have been used to suppress the response, an ideal agent has yet to be discovered. This study compares and contrasts the effectiveness of intravenous dexmedetomidine and intravenous magnesium sulphate in reducing hemodynamic response during laryngoscopy and endotracheal intubation.

Materials and Methods: This 18-month prospective, randomised, double-blind, placebo-controlled comparative research was conducted in the Department of Anaesthesiology and Critical Care, Bokaro General Hospital, Bokaro Steel City, Jharkhand. One hundred twenty consenting study participants were randomly divided into three groups of forty. Before induction, Group A received IV normal saline as a placebo. Group B received 1 mcg/kg IV dexmedetomidine before induction, while Group C received 30 mg/kg IV 50% magnesium sulphate before induction.

Results: Gender distribution was consistent and equal among 120 patients. Gender, age, weight, ASA, and type of surgery did not differ significantly across groups. The three groups had no statistically significant difference in baseline hemodynamic parameters. When compared to the Control Group (A), there were statistically significant changes in hemodynamic parameters in the Dexmedetomidine (B) and Magnesium sulphate (C) groups. There was no hypotension, bradycardia, nausea, vomiting, dry mouth, or arrhythmias.

Conclusion: Dexmedetomidine and magnesium sulphate efficiently reduced the hemodynamic stress response to laryngoscopy and intubation, although dexmedetomidine attenuated the sympathetic response more effectively.

1. Introduction

Laryngoscopy and tracheal intubation have become essential components of anaesthesia management and critical care since their introduction in 1921. They trigger a momentary yet significant sympathetic response, leading to heightened heart rate and blood pressure. The intensity of this response is influenced by factors such as the depth of anaesthesia, the duration and complexity of laryngoscopy and intubation, and the patient's characteristics, like diabetes and cardiovascular disease.[1,2] While the exact mechanism behind this stress response remains unclear, it is widely accepted that it involves both sympathetic and parasympathetic elements. The transient effect typically occurs approximately 30 seconds after intubation and subsides within less than 10 minutes.[3] The sympathetic response follows a complex polysynaptic pathway, with the

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glossopharyngeal and vagus nerves forming the afferent arc to the sympathetic nervous system via the brain stem and spinal cord. As a result, a widespread autonomic response occurs on the efferent side, leading to an increased firing of cardio-accelerator fibres and the release of adrenergic mediators, such as norepinephrine, epinephrine, and vasopressin. This autonomic surge causes a rise in blood pressure (BP), heart rate (HR), pulmonary artery wedge pressure, and a decrease in ejection fraction. The parasympathetic reflex is a monosynaptic response that is more prevalent in children but can also occur in adults. Increased vagal tone at the SA node mediates the reflex.[4]

Approximately 5-10% of patients experience various cardiac dysrhythmias besides sinus bradycardia and tachycardia. However, most of these dysrhythmias are harmless and temporary.[5] While healthy individuals can typically tolerate this stress response, certain patient groups, such as those with ischemic heart disease, may be at risk of acute myocardial infarction. Patients with compromised heart function may also experience heart failure due to the increased heart rate. For individuals with cerebral aneurysms, this response could lead to hypertensive bleeding in the brain. Medical professionals have employed several approaches to mitigate these responses, including topical lignocaine spray, deep plane anaesthesia maintenance, intravenous (IV) opioids, calcium channel blockers, beta-blockers, alpha 2 agonists, and vasodilators. Despite using these methods, none have proven flawless, and the search for the ideal agent to manage the sympathetic response continues.[5,6]

Dexmedetomidine is a selective alpha 2 adrenergic receptor agonist and an imidazole derivative[7] α2-agonists cause noradrenergic neuron hyperpolarisation and suppression of neuronal firing in the locus coeruleus, resulting in decreased systemic noradrenaline release and attenuation of sympathoadrenal responses and hemodynamic stability during laryngoscopy and tracheal intubation.[8] Magnesium has long been recognised to decrease catecholamine release from both adrenergic nerve terminals and the adrenal gland, and intravenous magnesium sulphate reduces catecholamine release associated with laryngoscopy.[9] Endotracheal intubation and laryngoscopy-induced hemodynamic response have been impaired by magnesium sulphate.[10]

The study aims to evaluate and compare the efficacy of intravenous dexmedetomidine and intravenous magnesium sulphate to attenuate the hemodynamic response during laryngoscopy and endotracheal intubation.

2. Materials and Methods

This prospective, randomised, double-blind, placebo-controlled comparative study was conducted at the Department of Anaesthesiology and Critical Care, Bokaro General Hospital, Bokaro Steel City, Jharkhand, over 18 months (January 2020 to June 2021).

Inclusion criteria for the study comprised patients aged 18-60 years, weighing 45-65 kg, with ASA grades I and II, scheduled for elective non-cardiac surgery under general anesthesia. Patients who provided voluntary informed consent were included.

Exclusion criteria encompassed patients with hypertension (controlled and uncontrolled), systolic blood pressure < 90 mm Hg, heart rate < 60 beats/min, coronary artery disease, chronic obstructive pulmonary disease (COPD), morbid obesity, renal compromise, pregnant and lactating women, patients with physical characteristics indicative of difficult intubation (Mallampati grades III and IV), patients on significant drug therapy in the pre-operative period, and patients who refused to participate in the study. During the intubation, if the intubating attempt lasted>20 seconds, they were excluded from the study.

120 eligible study subjects who willingly consented to participate were enrolled and divided randomly into three groups, with 40 patients in each group following the approval of the hospital's ethical and scientific committee.

2.1. Study group

1. Group A received intravenous normal saline 50 ml as a placebo over 10 mins,10 mins before induction.
2. Group B received intravenous dexmedetomidine 1 mcg/kg made into 50ml over 10 mins,10 mins before induction.
3. Group C received intravenous 50% magnesium sulfate 30 mg/kg made into 50ml over 10 mins,10 mins before induction.

Before the surgery, all patients underwent a comprehensive pre-anesthetic checkup and assessment, including a detailed medical history of chronic illnesses, general and systemic examination, and routine investigations. Various parameters such as haemoglobin, total leukocyte count and differential leukocyte count, platelet count, blood sugar, blood urea and serum creatinine, coagulation profile, viral markers (HIV, HCV, HBsAg), ECG, and liver function tests were investigated.

The patients were pre-medicated with an oral Tab. Ranitidine 150 mg and Tab. Clonazepam 0.5 mg on the night before surgery. They were fasted for 8 hours before the surgery. After routine monitoring was instituted (ECG, NIBP, and pulse oximetry), an 18G intravenous cannula was inserted, and a lactated Ringer's solution infusion was started. Study drugs (50 ml) were administered over 10 minutes and 10 minutes before induction based on the respective group assignment. All patients were pre-oxygenated with 100% oxygen for 3 minutes using a tight-fitting face mask. Induction was performed with Inj. Propofol is given slowly until the loss of verbal commands. All groups received Inj. Vecuronium 0.1 mg/kg for tracheal

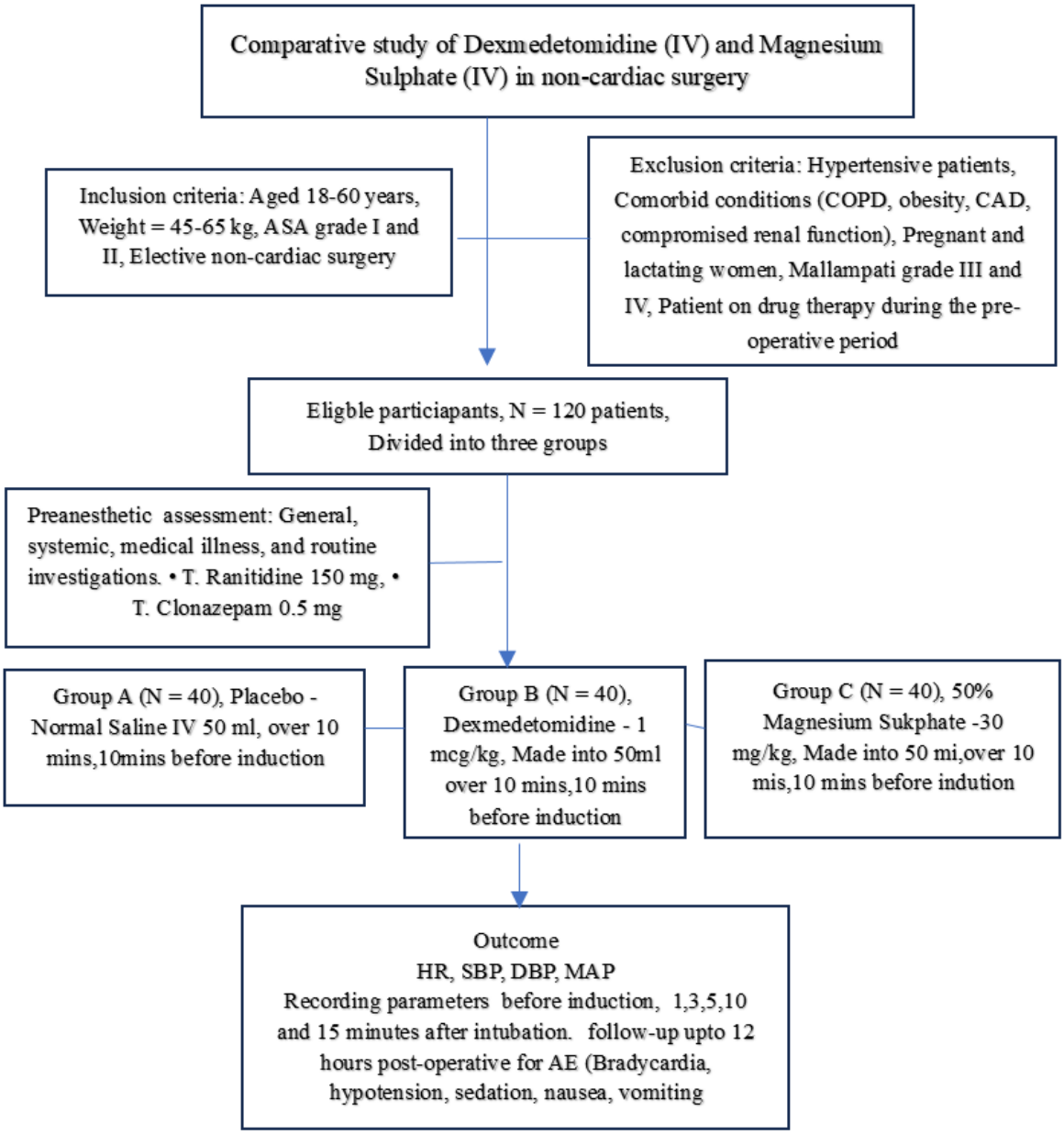

Diagram 1: Consort diagram

intubation facilitation. Laryngoscopy was performed using a rigid laryngoscope with a standard Macintosh blade, and intubation was carried out with an appropriately sized disposable, high-volume, low-pressure-cuffed endotracheal tube.

Anesthesia was maintained with O2, N2O, sevoflurane, and Inj. Vecuronium top-up. At the end of the surgery, reversal was achieved using Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 0.01 mg/kg IV. Extubation was performed after reversing the non-depolarizing muscle relaxant. Bradycardia (heart rate less than 40) was treated with Inj. Atropine hypotension (MAP less than 20% of pre-treatment value) was managed with Inj. Mephentermine. Any adverse effects related to drugs or anaesthesia were noted, and appropriate measures were taken.

The following parameters were recorded,

1. Heart rate (per minute)
2. Systolic blood pressure (mmHg)
3. Diastolic blood pressure (mmHg)
4. Mean arterial pressure (mmHg)

Before the administration of the study drug baseline parameters were noted. Then, the parameters were noted just before intubation and then at 1 min,3 min,5

min,10 min and 15 min after intubation. All patients were observed intraoperatively and followed up for 12 hours postoperatively. Any adverse effects during the postoperative period such as bradycardia, hypotension, sedation, nausea, and vomiting, were also noted.

For statistical analysis, the collected data were organised, tabulated, and analysed using "MedCalc." Descriptive statistics such as mean with standard deviation or proportions were presented. Mean, median, standard deviation and variance were calculated. T-tests were used to compare two independent groups of continuous data, while the chi-square test was utilised for comparing categorical data. Student t-test and analysis of variance (ANOVA) were employed for comparing three continuous data at a time. The significance level was determined by comparing the calculated value with the tabulated value at a specific degree of freedom, with a p-value considered non-significant if $p > 0.05$ and significant if $p < 0.05$.

3. Results

Among 120 patients, the gender, age, mean weight, and ASA grading were comparable and equally distributed. There were statistically insignificant differences in gender among the three Groups ($p = 0.967$).

An average age of 40.12 ± 6.63 years in Group A, 39.22 ± 6.89 years in Group B and 40.32 ± 6.03 years in Group C. Among the three groups, most patients were between 30-40 and 40-50 years. There were statistically insignificant differences in age among the three Groups ($p = 0.640$).

Most patients were ASA grade 1 compared to grade 2 among the three groups.

The mean weight of Group A was 59.48 ± 4.80 kg, Group B was 57.40 ± 5.47 kg, and Group C was 57.73 ± 5.53. There were statistically insignificant differences in weight and ASA among the three Groups with a p-value of 1.79 and 0.905 respectively. (Table 1).

There was no significant difference in types of surgery between groups, with a p-value of >0.05 (Table 2).

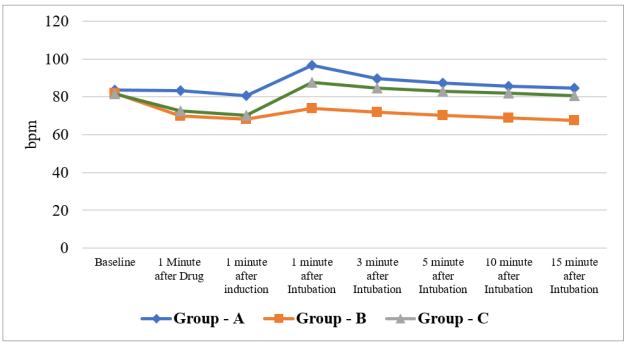

Figure 1: Mean heart rate between group

A change in heart rate was reported between the three groups, where Group A reported an increase in heart rate with a peak heart rate of 96-97 bpm, followed by Group C with a peak HR 87-88 bpm, and then Group b with peak HR 73-74 bpm, respectively (Figure 1).

After administration of the study drugs, changes in heart rate were observed in groups B and C (P 0.0045) from the control group A. Following induction, the mean heart rate was lower in Groups B and C than in Group A (P 0.0045). Heart rates at 1, 3, 5,10 and 15 min after intubation were lower in Group B compared with Groups C and A. Intubation caused an increase in the HR in all the groups. However, the increase in Groups B and C were less than the control group ($p<0.001$). Statistical evaluation between the groups showed that HR changes were significant at 1, 3, 5, 10, min and 15 minutes after intubation ($p<0.05$) (Figure 1).

Systolic blood pressure was statistically significantly lower in group B after induction and all-time observation after intubation compared to groups A and C ($p<0.001$). The reduction in SBP in Group B was higher than in Group C. All the groups had a rise in systolic BP one minute after intubation. The increase in BP was lower in Group B and Group C compared to Group A. The rise in BP was much lower in Group B compared to Group C (Figure 2).

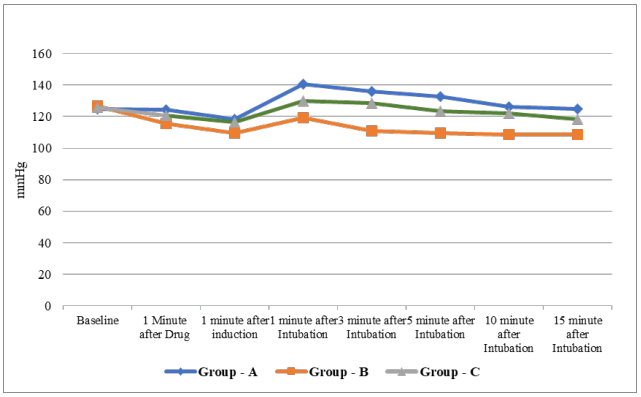

Figure 2: Mean systolic blood pressure between groups

A statistically significant difference among groups was observed ($p<0.001$) at all the time intervals after the study drug. Diastolic blood pressure was significantly lower in group B after induction and all observations after intubation compared with groups A and C ($p<0.001$). The reduction in DBP in Group B was higher than in Group C. There was a rise in diastolic BP one minute after intubation in all the groups. The increase in DBP was lower in Group B and Group C compared to Group A, and the increase in DBP was much lower in Group B compared to Group C (Figure 3).

A statistically significant difference among groups was observed ($p<0.001$) at all the time intervals after the study drug. Mean arterial pressure followed the same trend as systolic and diastolic blood pressure. Mean arterial pressure was significantly lower in group B after induction and all observations after intubation compared to groups A and C ($p<0.001$). The amount of reduction in MAP in Group B

Table 1: Demographic data between groups

		Group -A (n=40)	Group - B (n=40)	Group - C (n=40)
Gender	Male	20 (50%)	21 (52.5%)	20 (50%)
	Female	20 (50%)	19 (47.5%)	20 (50%)
Age (in years)	20-30	5 (12.5%)	5 (12.5%)	1 (2.5%)
	30-40	17 (42.5%)	18 (45%)	22 (55%)
	40-50	17 (42.5%)	15 (37.5%)	16 (40%)
	50-60	1 (2.5%)	2 (5%)	1 (2.5%)
Mean weight		59.48 ± 4.80 kg	57.40 ± 5.47 kg	57.73 ± 5.53 kg
ASA Grading	1	21 (52.5%)	22 (55%)	20 (50%)
	2	19 (47.5%)	18 (45%)	20 (50%)

Table 2: Type of surgery among the three groups

Surgery	Group -A	Group - B	Group - C	P value
Abdominal Hysterectomy	3 (7.5%)	4 (10%)	3 (7.5%)	0.9048
Appendicectomy	4 (10%)	3 (7.5%)	4 (10%)	0.9131
Breast Lump Excision	0.00%	2 (5%)	0.00%	0.1547
Excision Biopsy	4 (10%)	3 (7.5%)	4 (10%)	0.9131
Fibroadenoma Excision	2 (5%)	1 (2.5%)	2 (5%)	0.8187
Hemithyroidectomy	2 (5%)	2 (5%)	2 (5%)	1
Humerus Plating	1 (2.5%)	2 (5%)	1 (2.5%)	0.7788
Implant Removal	1 (2.5%)	1 (2.5%)	1 (2.5%)	1
Incisional Hernia Repair	4 (10%)	1 (2.5%)	3 (7.5%)	0.4169
Inguinal Hernia Repair	0.00%	0.00%	1 (2.5%)	0.3173
Laminectomy L4-L5	3 (7.5%)	4 (10%)	3 (7.5%)	0.9048
Laparotomy	4 (10%)	2 (5%)	4 (10%)	0.6703
Lipoma Back Excision	0.00%	1 (2.5%)	0.00%	0.3173
Mastectomy	2 (5%)	1 (2.5%)	2 (5%)	0.8187
Mastoidectomy	1 (2.5%)	1 (2.5%)	1 (2.5%)	1
Myomectomy	0.00%	1 (2.5%)	0.00%	0.3173
Open Cholecystectomy	5 (12.5%)	6 (15%)	5 (12.5%)	0.9394
Pyelolithotomy	2 (5%)	1 (2.5%)	2 (5%)	0.8187
Ranula Excision	0.00%	1 (2.5%)	0.00%	0.3173
Submandibular Gland Excision	0.00%	1 (2.5%)	0.00%	0.3173
Split Skin Graft	1 (2.5%)	0.00%	1 (2.5%)	1
Thyroidectomy	1 (2.5%)	2 (5%)	1 (2.5%)	0.7788

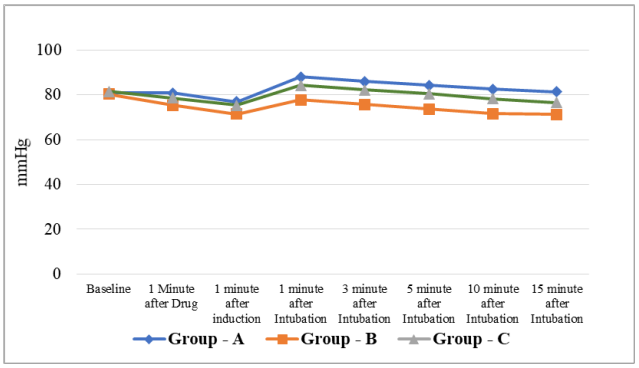

Figure 3: Mean diastolic blood pressure between groups

was higher than in Group C. All the groups had a rise in mean arterial BP one minute after intubation. The increase in MAP was lower in Group B and Group C compared to Group A. The increase in MAP was much lower in Group B compared to Group C (Figure 4).

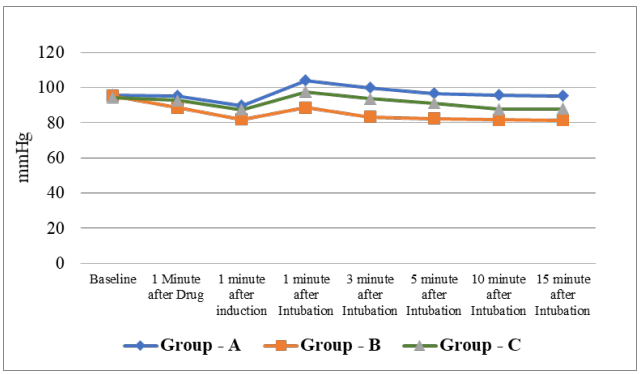

Figure 4: Mean arterial pressure between groups

Bradycardia and hypotension have been reported in studies concerning the effect of dexmedetomidine and magnesium sulphate on perioperative hemodynamics. In contrast to these studies, we did not detect any excessive reduction in HR or BP. There was no incidence of other side effects like nausea, vomiting, dry mouth, or excessive sedation.

4. Discussion

There was no significant difference in gender, age, weight, ASA, or type of surgery across groups in our study. In all groups, intubation induced an increase in HR. Nonetheless, the rise in Groups B and C was smaller than in Group A. Statistical analysis revealed substantial HR increases at 1, 3, 5, 10 and 15 minutes after intubation. The change in mean HR was more in Group A, then Group C, then group b; group A reported the highest elevation from 83 to 96-97, followed by group C from 72 to 87-88 and then group C from 70 to 73—74.

According to Krishna Chaithanya et al.'s study, Dexmed and MgSO4 substantially influenced heart rate compared to the control group. These data suggest that both Dexmed and MgSO4 have a statistically significant effect on heart rate.[11] In research by Chhaya Joshi et al., there was no significant change in heart rate before induction but a significant difference between the three groups at intubation, 2, and 5 minutes after intubation (p<0.0001).[12]

According to Chandrakala et al., the MgSO4 group had the highest mean heart rate of 99.27 3.96 bpm at 0 minutes after intubation, showing a significant difference. Similar to our study, a significant difference was seen between the groups after 1 and 3 minutes of intubation (p0.001).[13] Dexmedetomidine and magnesium sulphate groups demonstrated a statistically significant drop in HR compared to pre-drug values up to 30 min, according to Lakshmi Mahajan et al. In contrast, the dexmedetomidine group had a statistically significant reduction in HR compared to MS for up to 9 minutes.[14]

Group B had considerably lower systolic blood pressure after intubation than Groups A and C, with a reduced rise in SBP one minute after intubation in our research. After intubation, Chhaya Joshi et al. found substantial changes in systolic blood pressure across groups. These data imply that administering dexmedetomidine may assist in preserving systolic blood pressure stability during intubation, but administering magnesium sulphate may result in higher systolic blood pressure levels.[12]

Dexmedetomidine and magnesium sulphate groups exhibited a substantial drop in mean SBP value before intubation, with dexmedetomidine having the lowest SBP value, according to Lakshmi Mahajan et al.[14] Similar to our findings, research by Krishna Chaithanya et al. and Chandrakala et al. found no significant variation in systolic blood pressure across groups from pre-induction to 5 minutes.[11,13]

Diastolic blood pressure was considerably lower in Group B during induction and all observations following intubation in our research. At the same time, Group B had a lesser rise in DBP than Group C. At any time interval (>0.05), no significant variations in diastolic blood pressure between the control and Dexmed groups. However, at 2 and 5 minutes after intubation, the MgSO4 group had substantially higher diastolic blood pressure values than the control and Dexmed groups (p0.0001). According to the study by Lakshmi Mahajan et al., dexmedetomidine plus magnesium sulphate had a substantial (p0.001) drop in DBP but no significant change in DBP in the control group. At all periods, the comparison of both groups was significant.[14]

Mean arterial pressure was considerably lower in Group B during induction and all observations following intubation in our research. In Group B, however, the rise in mean arterial BP one minute after intubation was smaller. A significant change in mean arterial pressure at 2 and 5 minutes after intubation (p0.0001), consistent with our findings.

In our research, both Dexmedetomidine and Magnesium sulfate were found to be effective in controlling the rise in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) during laryngoscopy and intubation. However, dexmedetomidine demonstrated superior attenuation of the sympathetic response, as the hemodynamic parameters remained below the baseline throughout the study period. Importantly, neither drug exhibited adverse effects, such as hypotension, bradycardia, nausea, vomiting, dry mouth, or arrhythmias.

Even though different studies exist, the search for an ideal agent to blunt the hemodynamic response to laryngoscopy and intubation without any significant adverse effects continues.[15] The current study highlights the various parameters, including HR, blood pressure, and intubation time after the administration of dexmedetomidine in patients. The study also assessed the hemodynamic stability in patients who underwent anaesthesia. The study highlights using both medications to maintain hemodynamic stability for laryngoscopy and intubation. The evaluation was of various parameters, and MAP was reported by this study, which was not seen in the majority of the studies.

5. Conclusion

Our study's findings indicate that dexmedetomidine and magnesium sulphate effectively controlled the hemodynamic stress response during laryngoscopy and intubation. Dexmedetomidine demonstrated a more significant reduction in the sympathetic response, as evidenced by hemodynamic parameters remaining below baseline throughout the entire study period. Importantly, both drugs showed no adverse effects during

and immediately after the surgery.

6. Limitations

Due to the age range of 18-60 years in our study, the generalisation of results to patients outside this age range may not be applicable. Additionally, all patients included had ASA I & II physical status, which limits the assessment of drug effects on patients with significant comorbidities. It's essential to note that this study was conducted solely on elective surgical cases and may yield different results in emergencies. Monitoring adequate depth of anaesthesia and neuromuscular relaxation relied solely on clinical observations, which may not provide a comprehensive evaluation.

Furthermore, it's important to consider that various drugs in this study can influence hemodynamic changes, but these effects should have been specifically evaluated. We did not separately analyse hemodynamic changes associated with the two distinct stages of direct laryngoscopy and tracheal tube insertion. Additionally, the post-operative observation period was limited to 12 hours, preventing evaluating any potential long-term effects of the study drugs.

7. Recommendations

This study highly recommends dexmedetomidine to attenuate hemodynamic stress response to laryngoscopy and intubation in patients undergoing surgery under general anaesthesia. Magnesium sulphate also attenuates hemodynamic stress response to laryngoscopy and intubation. So it can be used when other alternative drugs are not available.

8. Source of Funding

None.

9. Conflict of Interest

None.

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