Original Article

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Effect of Nebulisation with Dexmedetomidine versus Magnesium Sulphate on Haemodynamic Response to Laryngoscopy and Intubation and Incidence of Postoperative Sore Throat: A Randomised Clinical Trial

Anaesthesia Section

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ABSTRACT

Introduction: Laryngoscopy and endotracheal intubation are essential procedures in general anaesthesia but can induce sympathetic hyperactivity, leading to transient increase in blood pressure and Heart Rate (HR). This can be particularly risky for patients with co-morbidities. Various agents, including dexmedetomidine and magnesium sulphate, have been studied for their potential to mitigate these responses.

Aim: To compare the effects of preoperative nebulisation with dexmedetomidine versus magnesium sulphate on haemodynamic responses during laryngoscopy and intubation and to determine the incidence of Postoperative Sore Throat (POST) in both groups.

Materials and Methods: This randomised clinical, double-blind trial was conducted at Dr. D. Y. Patil Medical College, Pune, Maharashtra, India over the period of two years. It involved 80 patients undergoing surgery under general anaesthesia, divided into two equal groups. Group A received nebulisation with dexmedetomidine (1 µg/kg) and Group B received magnesium sulphate (240 mg) diluted in 0.9% normal saline to make a 3 mL solution. Institutional ethical approval and Clinical Trials Registry India (CTRI) registration were obtained. Haemodynamic parameters including HR, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP) and POST were monitored. Statistical Package for the Social Sciences (SPSS) version 20.0 was used for statistical analysis. Data were analysed using unpaired t-tests for quantitative data and Pearson's Chi-square test for qualitative data, with significance set at p-value <0.05.

Results: Before nebulisation, group A had significantly higher HR and SBP than group B (p-value=0.003 and 0.009, respectively). Postnebulisation, there were no significant differences in HR or SBP between groups. However, group A had lower DBP and MAP during and after intubation and skin incision (p-value <0.001, 0.001, and <0.001 respectively for DBP and 0.030, 0.031 and 0.002 for MAP). Group A had a lower, though not statistically significant (p-value=0.36) incidence of POST compared to group B.

Conclusion: Nebulisation with dexmedetomidine and magnesium sulphate both provided effective management of haemodynamic responses during intubation. Both agents decreased the incidence of POST.

Keywords: Adrenergic, Adrenergic antagonists, Aerosols, Alpha-2, Receptors

INTRODUCTION

Laryngoscopy and endotracheal intubation are common procedures during general anaesthesia that can trigger significant sympathetic activity, causing the production of catecholamines, including norepinephrine and adrenaline, which causes a momentary increase in HR and blood pressure [1]. Even though these side-effects are usually benign for healthy persons, patients who suffer from illnesses like hypertension, coronary artery disease, or cerebrovascular disorders may be at risk for severe problems, including arrhythmias, strokes, or ischaemia [2]. Various pharmacological agents are used to mitigate these haemodynamic responses, including opioids, alpha-adrenergic blockers, alpha-2 adrenergic agonists, beta-blockers and calcium channel blockers [2]. Among these, dexmedetomidine and magnesium sulphate stand out for their sedative, analgesic and sympatholytic properties. Dexmedetomidine, an alpha-2 adrenergic agonist, reduces sympathetic outflow and inhibits norepinephrine release, providing sedation and analgesia without significant respiratory depression [3]. Magnesium sulphate acts as an N-methyl-D-aspartate (NMDA) receptor antagonist and calcium channel blocker, promoting vasodilation and reducing catecholamine release [4,5].

Nebulisation has emerged as an effective route for drug administration offering rapid action and targeted delivery to the respiratory tract, thus minimising systemic side-effects. Nebulised dexmedetomidine avoids first-pass metabolism and the potential bradycardia and hypotension seen with intravenous administration [2]. Similarly, nebulised magnesium sulphate can directly affect the respiratory mucosa, maintaining haemodynamic stability during airway procedures [4]. The POST is another common issue after intubation, with a prevalence of 6.6 to 90% [5]. It can be managed through various non pharmacological and pharmacological methods, such as using smaller tracheal tubes, careful airway management and topical anaesthetics or anti-inflammatory drugs [5,6].

While intravenous administration of dexmedetomidine and magnesium sulphate has been thoroughly studied, research on their preoperative nebulisation is scarce [1]. Studies assessing nebulisation as a non invasive route of administration are minimal and its comparative efficacy in controlling intubation-induced haemodynamic responses remains unclear [2]. The aim this study was to evaluate the impacts of magnesium sulphate and nebulised dexmedetomidine on haemodynamic responsiveness to intubation and laryngoscopy, as well as how they affect the likelihood of sore throat after surgery.

MATERIALS AND METHODS

The study was a prospective, double-blinded, randomised clinical trial conducted at Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India from September 2022

to September 2024. Institutional Ethics Committee (IEC) clearance (Ref. no. IESC/404/2022) was obtained and the trial was registered with CTRI (CTRI/2023/12/060483). All participants provided written informed consent.

Inclusion criteria: Eighty haemodynamically stable patients, aged 18 to 60 years, with American Society of Anaesthesiologists (ASA) grades I or II, undergoing surgery under general anaesthesia and with normal routine investigations and willing to participate in the study, were included in the study.

Exclusion criteria: ASA grade III or higher, age outside the specified range, emergency procedures, drug allergies, anticipated difficult intubation, obesity, or significant co-morbidities were excluded from the study.

Sample size: Comparing the mean and SD of SBP at 5 minutes between the dexmedetomidine group [2] and the magnesium sulphate group [7], the values were 109.50±16.83 mmHg and 120.64±10.25 mmHg, respectively. The minimum sample size needed, at 80% power and a 5% significance level, came to be 28 in each group. However, considering the drop-out rate and the need for an effective study, 40 patients in each group of patients were taken, making the total sample size 80. The formula used for sample size calculation was two-sample t-test sample size formula.

Study Procedure

Patients underwent preanaesthetic evaluation, including medical history, systemic examination and necessary investigations were instructed to fast for eight hours before surgery. Patients were randomised using a computer-generated random number sequence to assign them evenly across treatment groups. group A received 1 µg/kg dexmedetomidine [2] nebulisation and group B received 240 mg magnesium sulphate nebulisation [5], both diluted in normal saline to a 3 mL solution and administered over 15 minutes, ending 10 minutes before anaesthesia induction.

An independent investigator was responsible for administering nebulisation and closely monitoring haemodynamic parameters, including HR, SBP, DBP, MAP and Oxygen Saturation (SpO_2) at specific time intervals during the perioperative period. Baseline measurements were recorded prior to nebulisation, followed by subsequent recordings after nebulisation and before the induction of anaesthesia. Parameters were recorded during laryngoscopy and intubation, as well as every minute for 10 minutes following intubation. The investigator also documented the physiological response to the initial surgical skin incision and observed for adverse effects after no longer getting involved in this research.

An intravenous cannula measuring 20 G was implanted in the operating room and standard monitoring was established, including Non Invasive Blood Pressure (NIBP), SpO_2, Electrocardiogram (EKG) and End-tidal Carbon Dioxide ($EtCO_2$). Premedication included intravenous midazolam (20 µg/kg), fentanyl (1-2 µg/kg) and glycopyrrolate (4 µg/kg), after which 200% oxygen was used for three minutes of preoxygenation. Anaesthesia induction was achieved with propofol (2 mg/kg) and succinylcholine (2 mg/kg) for intubation, with haemodynamic parameters monitored every minute for 10 minutes postlaryngoscopy. Intubation was confirmed using $EtCO_2$ and bilateral air entry. Maintenance of anaesthesia involved oxygen and nitrous oxide combined (40:60), isoflurane (0.6-1%) and vecuronium (0.1 mg/kg). Ventilation was accordingly altered to keep $EtCO_2$ levels between 32 and 35 mm Hg. The response to skin incision was assessed through changes in HR and SBP. Following surgery, neostigmine (50 µg/kg) and glycopyrrolate (20 µg/kg) were used to reverse neuromuscular inhibition. After the patient was able to obey commands and had a Train-Of-Four (TOF) ratio of 0.9 or greater, they were extubated and taken to the Post-Anaesthesia Care Unit (PACU).

Patients were evaluated for POST at intervals of 0,2,4,6,12 and 24 hours following extubation. An anaesthesiologist, who was unaware of the study details, performed these evaluations. The assessment involved inquiring about the presence of a sore throat, pain, voice changes, or any throat discomfort. POST severity was categorised using a 4-point scale (0-3), outlined in [Table/Fig-1] [8].

Grade	Severity of sore throat
Grade 0	No sore throat
Grade 1	Mild sore throat (complains of sore throat only on asking)
Grade 2	Moderate sore throat (complains of sore throat on his/her own)
Grade 3	Severe sore throat (change of voice or hoarseness, associated with throat pain)

[Table/Fig-1]: Grading and severity of Postoperative Sore Throat (POST) [8].

STATISTICAL ANALYSIS

Continuous variables, including age, height, weight, HR, systolic SBP, diastolic DBP, MAP and SpO_2, were expressed as mean±standard deviation and compared between the two groups using an unpaired t-test. Categorical variables, such as adverse effects, were presented as both the number and percentage of patients and comparisons between the two groups were made using Pearson's Chi-square test for independence. Statistical analysis was performed using SPSS version 20. An alpha level of 5% was set, meaning that p-values <0.05 were considered statistically significant. Paired t-tests were employed to compare the means of continuous variables.

RESULTS

Eighty patients were randomly divided into two groups. The study revealed comparable demographic data between the groups, including age, gender, ASA classification and body weight [Table/Fig-2]. Haemodynamic parameters, including HR, SBP, DBP, MAP and SpO_2, were measured at 14 intervals.

Variables		Group A Mean±SD	Group B Mean±SD	p-value	Significance
Age (years)		45.5±12.7	42.8±15.3	0.389	Not significant
Gender n (%)	Male	25 (62.5)	21 (52.5)	0.498	Not significant
	Female	15 (37.5)	19 (47.5)		
Body weight (kg)		61.2±9	59.2±12.6	0.423	Not significant
ASA grade n (%)	Grade 1	20 (50)	25 (62.5)	0.367	Not significant
	Grade 2	20 (50)	15 (37.5)		

[Table/Fig-2]: Demographic data, including age, gender, ASA classification and body weight, between the two groups.

Initially, group A had a significantly higher HR of 90±8.8 compared to group B, which had 84.3±8.2 (p-value=0.003). After nebulisation, HR became similar between the groups (p-value >0.05). Throughout the study, HR decreased from baseline in both groups, with no significant differences at later intervals [Table/Fig-3].

Heart Rate (HR)	Group A Mean±SD	Group B Mean±SD	p-value
Baseline before nebulisation	90±8.8	84.3±8.2	**0.003**
After nebulisation before induction	82.4±9.2	82.2±8.3	0.899
At the time of laryngoscopy and intubation	83.7±8.8	83.4±8.1	0.864
After intubation 1 min	83.7±8.6	83.3±8.1	0.841
2 mins	82.98±8.2	82.2±8.3	0.665
3 mins	82.1±8.4	81.98±8.6	0.969
4 mins	82.2±7.9	81.3±8.3	0.611
5 mins	81.7±8.1	81.2±8.02	0.793
6 mins	81.5±7.98	80.8±8.5	0.725
7 mins	81.1±7.9	79.9±8.4	0.521
8 mins	80.5±8.2	79.4±8.5	0.539
9 mins	80.4±8.2	79.7±7.9	0.710

10 mins	80.2±8.2	79.6±7.9	0.741
Response to skin incisions	81.95±7.9	84.6±8.6	0.157

[Table/Fig-3]: Comparison of Heart Rate (HR) in both groups at different time intervals.

Group A presented a significantly higher SBP of 118.8±8.2 mmHg before nebulisation compared to group B 113.7±8.8 mmHg (p-value=0.009). Postnebulisation and during subsequent measurements, SBP values between groups became comparable, remaining below baseline during laryngoscopy and intubation, with no significant differences observed (p-value >0.05) [Table/Fig-4].

SBP (mmHg)	Group A	Group B	p-value
Before nebulisation	118.8±8.2	113.7±8.8	**0.009**
After nebulisation before induction	112.6±8.2	111.8±8.5	0.679
At the time of laryngoscopy and intubation	113.9±8.03	113.7±8.2	0.901
After intubation 1 min	113.5±7.7	113.5±8.7	0.989
2 mins	112.4±8.03	112.3±7.5	0.931
3 mins	111.7±8.6	112.2±7.7	0.785
4 mins	111.1±8.4	111.6±7.3	0.798
5 mins	111.3±8.2	110.9±7.5	0.821
6 mins	111.3±8.2	109.98±6.97	0.457
7 mins	111.05±8.5	109.7±6.91	0.438
8 mins	110.95±8.4	110.2±6.4	0.644
9 mins	111.03±8.5	110.4±6.9	0.730
10 mins	110.95±8.5	110.1±6.5	0.608
Response to skin incisions	112.1±8.8	115.05±6.9	0.100

[Table/Fig-4]: Comparison of Systolic Blood Pressure (SBP) between two groups at various time intervals.

While group A had a slightly higher baseline DBP, it was significantly lower during laryngoscopy and intubation at 73.8±5.6 mmHg compared to group B 78.2±5.3 mmHg (p-value=0.001). This trend continued postintubation, with significant differences observed for up to 8 minutes after intubation and during skin incision responses (Group A: 74.3±6.6 mmHg vs. Group B: 79.3±5.1 mmHg, p-value <0.001) [Table/Fig-5].

DBP (mmHg) (bpm)	Group A	Group B	p-value
Before nebulisation	78.3±5.9	75.9±6.75	0.095
After nebulisation but before induction	73.03±5.9	75.3±5.5	0.080
At the time of laryngoscopy and intubation	73.8±5.6	78.2±5.3	**0.001**
After intubation 1 min	73.5±5.4	77.65±5.3	**0.001**
2 mins	73.2±5.2	77.05±5.6	**0.002**
3 mins	72.9±5.3	77.5±5.6	**<0.001**
4 mins	72.5±5	77.4±5.8	**<0.001**
5 mins	73.1±5.6	77.5±5.6	**0.001**
6 mins	73±5.3	77.2±5.2	**0.001**
7 mins	73.6±6.3	77.1±4.5	**0.005**
8 mins	73.9±5.9	76.4±4.6	**0.034**
9 mins	74.4±6.2	76.5±4.6	0.093
10 mins	74.8±6.9	75.8±5.04	0.473
Response to skin incisions	74.3±6.6	79.3±5.1	**<0.001**

[Table/Fig-5]: Comparison of Diastolic Blood Pressure (DBP) between both groups at various time intervals.

Group A exhibited higher initial MAP values of 91.8±5.9 mmHg, which were statistically significant compared to group B 88.5±6.9 mmHg (p-value=0.025). During laryngoscopy, intubation and the first five minutes postintubation, group A consistently demonstrated lower MAP values than group B, with statistically significant p-values ranging from 0.008 to 0.046. However, from six minutes post-intubation through the ten-minute interval, the differences in MAP between the two groups were no longer statistically significant, with p-values ranging from 0.058 to 0.521 [Table/Fig-6].

MAP (mmHg)	Group A	Group B	p-value
Before nebulisation	91.8±5.9	88.5±6.9	**0.025**
After nebulisation but before induction	86.2±6.04	87.5±6.1	0.356
At the time of laryngoscopy and intubation	87.2±5.75	90±5.6	**0.030**
After intubation 1 min	86.8±5.6	89.6±5.8	**0.031**
2 mins	86.3±5.5	88.8±5.6	**0.046**
3 mins	85.8±5.6	89.05±5.6	**0.013**
4 mins	85.4±5.5	88.8±5.6	**0.008**
5 mins	85.8±5.8	88.6±5.4	**0.027**
6 mins	85.7±5.8	88.1±5.1	0.058
7 mins	86.1±6.3	87.9±4.7	0.132
8 mins	86.2±6.2	87.7±4.5	0.230
9 mins	86.6±6.4	87.8±4.8	0.352
10 mins	86.9±6.8	87.76±5.8	0.521
Response to skin incisions	86.9±6.76	91.2±5.1	**0.002**

[Table/Fig-6]: Comparison of Mean Arterial Pressure (MAP) between both groups at various time intervals.

Both groups maintained SpO_2 levels above 98%, with no significant differences throughout the study (p-value >0.05). Postoperatively, a lower incidence of sore throat was noted in Group A, with only one patient (2.5%) reporting symptoms at four hours compared to two patients (5%) at four and six hours in group B. However, this difference was not statistically significant (p-value=0.36), indicating a low overall incidence of POST [Table/Fig-7].

POST	Group A	Group B	Grade of POST	Chi-square	p-value
After extubation	0	0	0	0.83	0.36
2 hours	0	0	0		
4 hours	1 (2.5%)	2 (5%)	2		
6 hours	0	2 (5%)	2		
12 hours	0	0	0		
24 hours	0	0	0		

[Table/Fig-7]: Comparison of Postoperative Sore Throat (POST) between two groups at various time intervals.

DISCUSSION

The study compared 80 patients, equally divided into two groups undergoing elective surgery under general anaesthesia. Preoperatively, group A was nebulised with dexmedetomidine (1 µg/kg), while group B received nebulised magnesium sulphate (240 mg). The haemodynamic response to laryngoscopy and intubation was noted and incidence of POST was also compared. Both groups showed comparable HR and SBP throughout the study after the initial measurements. However, the dexmedetomidine group exhibited significantly lower MAP and DBP during laryngoscopy and intubation and at various time intervals after intubation. The results were comparable to various studies, including the study performed by Grover N et al., where a comparison was done between nebulised fentanyl, dexmedetomidine and magnesium sulphate for attenuating the haemodynamic response to laryngoscopy and intubation. It concluded that dexmedetomidine and magnesium led to a more significant reduction in pressor response after intubation [9].

In another study comparing nebulised magnesium sulphate with normal saline, conducted by Elmeligy M and Elmeliegy M, it was concluded that preoperative nebulisation with magnesium sulphate effectively attenuates the stress response to endotracheal intubation [5]. The study by Paul NS et al., revealed that nebulised dexmedetomidine effectively blunted the increase in HR and blood pressure associated with laryngoscopy and intubation [10]. The

systematic review and meta-analysis by Gupta M et al., examined the effectiveness of nebulised dexmedetomidine in attenuating the haemodynamic response to laryngoscopy and intubation, concluded that nebulised dexmedetomidine significantly reduces HR and blood pressure during these procedures [11].

The current study suggests a lower DBP and MAP at various time intervals, including during laryngoscopy and intubation and even response to skin incision, can be attributed to the centrally acting, alpha-2 agonistic action of dexmedetomidine, leading to a sympatholytic response [9]. In this study, the overall incidence of POST was lower in the dexmedetomidine group compared to the magnesium sulphate group, but this difference was statistically non significant. The results were comparable with a study conducted by Yadav M et al., who concluded that nebulisation with magnesium sulphate significantly reduces the incidence and severity of POST compared to a control group [4]. Another study by Thomas D et al., also showed similar results while investigating the efficacy of nebulised dexmedetomidine in reducing POST in patients undergoing thyroidectomy, comparing it with nebulised ketamine [8]. The results demonstrated that dexmedetomidine significantly decreased both the incidence and severity of POST compared to ketamine.

Limitation(s)

A key limitation of this study was the absence of a control group, which would have provided a baseline comparison for evaluating the efficacy of nebulised dexmedetomidine and magnesium sulphate more robustly. Further studies incorporating a control group would offer a more detailed assessment and clearer evidence of the relative benefits of dexmedetomidine and magnesium sulphate.

CONCLUSION(S)

The study demonstrated that both nebulised dexmedetomidine and magnesium sulphate effectively decreased the sympathetic responses associated with laryngoscopy and intubation, though the dexmedetomidine group showed a statistically significant decrease in DBP and MAP, which can be attributed to its highly specific alpha-2 adrenergic agonistic action. Both groups experienced a lower incidence of POST, indicating that these interventions may help enhance recovery after surgery. Importantly, there were no reported side-effects in either group, suggesting that both agents are safe for use in this context.

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