

Compare the efficacy of IV clonidine, IV dexmedetomidine and IV magnesium sulfate for attenuation of pressor response during laryngoscopy and intubation under general anaesthesia

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Abstract

Aim & Objective: The present study is undertaken to compare the efficacy of Clonidine 1µg/kg, Dexmedetomidine 1µg/kg and Magnesium sulfate 30mg/kg in attenuating the sympathetic responses to laryngoscopy and tracheal intubation. **Methodology:** The present study was a prospective randomized non-blinded study. After approval from the institutional ethical committee, the study was conducted in 120 patients belonging to ASA I and II of either sex between 18 to 50 years of age undergoing elective surgeries under General anaesthesia in Government General Hospital, Kurnool, Andhra Pradesh. The study was conducted for two years in the Department of Anaesthesia in Kurnool medical college, Kurnool. **Results:** After informed consent was taken, patients were allocated into four groups - group D for Dexmedetomidine and group C for Clonidine, group M for Magnesium sulfate and group S for Control with 30 in each group. In Group D, 30 patients received 1mcg/kg Dexmedetomidine, in Group C, 30 patients received 1mcg/kg clonidine, Group M received 30mg/kg of Mgso4 and group S received normal saline after standard preoperative anaesthetic evaluation. The values for HR, SBP, DBP, and MAP were obtained just before the administration of the study drug, after the injection of study medications, after induction, just before intubation, immediately after intubation and 1, 3, 5 and 10 min post-intubation and compared among the groups. There was a decrease in HR after Dexmedetomidine administration. When compared among the four groups, we have observed that patients in the Dexmedetomidine group had a decrease in heart rate after study medication was given, after induction, before intubation, whereas, increase in heart rate was seen in groups of clonidine and Mgso4 which is statistically significant. Immediately after intubation, mean HR in all the groups was increased, but less increase is seen in Dexmedetomidine group. After 1min, 3 min, 5 min and 10 mins of intubation, the mean heart rate of the participants in each group was decreasing, but the decrease was more in Dexmedetomidine group than Clonidine and Mgso4 groups, which is statistically significant (p<0.05). When compared among the four groups, from baseline, after the infusion of study medication, after induction, before intubation there was a decrease in mean SBP values in the Dexmedetomidine and Mgso4 groups but remains the same in Clonidine and control groups. Whereas immediately after intubation, the mean SBP was increased in all the four groups, but in this, group D shows least increase in mean SBP followed by group M, C and S which is statistically significant (p<0.05). **Conclusion:** Dexmedetomidine (1mcg/kg), Clonidine (1mcg/kg) and Magnesium sulfate (30mg/kg) were effective in blunting the hemodynamic response to laryngoscopy in patients undergoing surgical procedures under general anaesthesia.

Keywords: Dexmedetomidine, Clonidine, Magnesium sulphate, Laryngoscopy, Hemodynamic parameters, Intubation

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Introduction

Direct laryngoscopy and endotracheal intubation are an integral part of general anaesthetic technique in modern-day anaesthesia. Significant improvement in equipment and development of new neuromuscular blockers combined with the technical skills of anaesthesiologist made the direct laryngoscopy and endotracheal intubation, a safe and common practice. It had been practised since its description by ROWBOTHAM and MAGILL in 1921.

Direct laryngoscopy and endotracheal intubation are always associated with hemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and aryngopharyngeal stimulation[1]. This increased sympathoadrenal activity results in tachycardia, hypertension[2] and arrhythmia[3,4], which are potentially dangerous. These changes are maximum at 1 minute after laryngoscopy and intubation and last for 5-10 min. This increase in blood pressure and heart rate are usually transitory, variable and unpredictable. Hypertensive patients are more prone to have a significant rise in blood pressure, whether they have been treated beforehand or not[5]. Transient hypertension and tachycardia may be hazardous to those with hypertension, myocardial diseases and cerebrovascular diseases. The laryngoscopy response in such individuals may predispose to pulmonary oedema, cerebrovascular accidents, intracerebral bleed myocardial insufficiency, and acute left ventricular failure in patients with end organ decompensation. A variety of agents have been used to attenuate this response. The techniques include topical anaesthesia of oropharynx - viscous Lignocaine, laryngotracheal installation of Lignocaine just before intubation, intravenous Lignocaine, adrenergic blocking drugs, either alpha[6] or beta blockers, alpha2 agonist like Dexmedetomidine,

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Clonidine, vasodilators like Hydralazine, Sodium nitroprusside, Nitroglycerine[7], deep inhalational anaesthesia, intravenous Opioids Magnesium sulfate etc. No single agent has been established as the most appropriate for this purpose.

The use of alpha-adrenergic agonists like Dexmedetomidine and Clonidine for the attenuation of hemodynamic response during laryngoscopy and intubation is increasing now.

Dexmedetomidine is a highly selective, specific and potent alpha-2 adrenergic agonist. Compared to Clonidine, it is said to be 7-10 times more alpha-2 selective & has a shorter duration of action than clonidine. Pre-treatment with Dexmedetomidine attenuates the hemodynamic response to tracheal intubation[8] and centrally decreases the sympathetic tone. Hence it is used in attenuating the intubation responses.

Clonidine is an alpha-adrenergic receptor agonist which is less potent than Dexmedetomidine and has a long duration of action. It is used to attenuate hemodynamic response to laryngoscopy and intubation[10]. Magnesium sulfate inhibits catecholamine release associated with tracheal intubation and produces vasodilation by directly acting on blood vessels[11].

Besides minimizing the cardiovascular responses to laryngoscopy and intubation during anaesthesia for patients at risk, these drugs must also satisfy the following requirements; they should be applicable to all patients of ASA I to II, should not alter the cerebral perfusion, should keep the patient in Guedel's stage II to III, and should not affect modality the ensuing anaesthesia.

IV Dexmedetomidine, Clonidine and Magnesium sulfate appear to fulfil the above mentioned criteria.

The present study is undertaken to compare the efficacy of Clonidine 1µg/kg, Dexmedetomidine 1µg/kg and Magnesium sulfate 30mg/kg in attenuating the sympathetic responses to laryngoscopy and tracheal intubation.

Materials and methods

The present study was a prospective randomized non-blinded study and was undertaken to compare the efficacy of Clonidine, Dexmedetomidine and Magnesium sulfate in attenuating the stress response to laryngoscopy and intubation.

After approval from the institutional ethical committee, the study was conducted in 120 patients belonging to ASA I and II of either sex between 18 to 50 years of age undergoing elective surgeries under General anaesthesia in Government General Hospital, Kurnool, Andhra Pradesh. The study was conducted for two years in the Department of Anaesthesia in Kurnool medical college, Kurnool.

Inclusion criteria

- Patients aged between 18-50yrs.
- ASA I and ASA II patients.
- Patients undergoing elective surgical procedures under General Anaesthesia.
- Weight between 30-80 kgs, BMI < 29.9 kg/m².
- Modified Mallampati grades I & II.
- Duration of Laryngoscopy and ET intubation being < 30seconds

Exclusion criteria

- Patients of ASA class III and above
- Patients on antihypertensive treatment.
- Age < 18yrs and > 50yrs.
- Pregnant or nursing women.
- Patient refusal to participate in the study
- Any history of drug reactions.
- Patients with anticipated difficult intubation and more than one intubation attempt.

Method of collection of data

Patients satisfying the inclusion and exclusion criteria were recruited to the study.

Patients and relatives were explained in detail regarding the nature of the study.

The study population was divided into four groups, with 30 patients in each group using the computerised randomisation technique.

1. GROUP D (N=30)

Received IV DEXMEDETOMIDINE in a dose of 1µg/kg diluted in 50ml of Normal saline (NS) infused over 10 minutes, administered 10 minutes before the induction of anaesthesia.

2. GROUP C (N=30)

Received IV CLONIDINE in a dose of 1µg/kg diluted in 50ml of Normal saline infused over 10 minutes, administered 10 minutes before the induction of anaesthesia.

3. GROUP M (N=30)

Received IV MAGNESIUM SULFATE in a dose of 30mg/kg diluted in 50ml of Normal saline infused over 10 minutes, administered 10 minutes before the induction of anaesthesia.

4. GROUP S (N=30)

Received IV Normal saline 50ml, 10 minutes before the induction of anaesthesia.

Pre-anaesthetic checkup and preparation

The pre-anaesthetic evaluation was done a day prior to surgery. It included the following assessments,

- The general condition of the patient
- Airway assessment using Modified Mallampati grading and the Rule of 1-2-3.
- A general physical examination including the height, weight and BMI.
- A detailed systemic examination.
- Complete blood profile
- Blood sugars: FBS/PPBS
- Blood urea, serum creatinine and electrolytes.
- Urine examination for Albumin, Sugar and Microscopy
- A standard 12 lead ECG and
- A screening Chest X-Ray

The procedure of general anaesthesia was explained to the patient and written informed consent was taken. Preparation included an overnight fast of 8 hours before the surgery, premedication with Tab Alprazolam 0.25 mg PO in the night before surgery.

Preparation of the operation theatre

The anaesthesia machine was checked. Appropriate sized ET tubes, working laryngoscope with medium and large-sized blades and working suction apparatus were kept ready before induction. All anaesthetic and emergency drugs were loaded into labelled syringes and kept ready for use.

Anaesthetic technique

On arrival of the patients to the operating room, they were connected to a multichannel monitor which measures the HR, SBP, DBP, MAP, EtCO₂, SpO₂ and performs continuous ECG monitoring and the HR, SBP, DBP and MAP were recorded. The Cardiac rate and rhythm were also monitored by a continuous visual display of the lead II ECG. A peripheral line was secured, and an infusion of normal saline was started. Patients were randomly assigned to receive either IV Normal Saline or IV clonidine 1µg/kg or IV Dexmedetomidine 1µg/kg or IV magnesium sulphate 30mg/kg.

At the end of the surgery, the patients were reversed with Inj Neostigmine 0.05mg/kg and Inj. Glycopyrrrolate 0.01mg/kg IV. The patients were extubated when awake and breathing adequately and shifted to the recovery unit. Any untoward effects related to the drug and anaesthesia were noted and attended to appropriately.

Monitoring

The following parameters were monitored

- HR in beats/min,
- SBP,
- DBP and
- MAP in mmHg.

These parameters were recorded at the following intervals

- Basal before giving the study drug
- After study drug infusion
- Post induction
- Before intubation
- Immediately after intubation and 1, 3, 5, and 10minutes

following endotracheal intubation

Statistical analysis

The Statistical Package for the Social Sciences [SPSS] Version 24 was used for the analysis of the data. Microsoft Word 2016 and Excel 2016 have been used to generate graphs, tables etc.

All the values observed were analysed and expressed as mean+/-SD. Unpaired Student t-test was employed for quantitative data analysis. Repeated ANOVA test was employed for qualitative data analysis. Intergroup comparison was done by POST HOC test. Significance is assessed at 5 % level of significance.

A probability value(P) less than 0.05 is considered as significant.

- ANOVA test (two-tailed, independent) has been used to find the significance of study parameters on a continuous scale between four groups (Intergroup analysis) on metric parameters.
- Chi-square/ Fisher Exact test has been used to find the

significance of study parameters on a categorical scale between two or more groups.

- ANOVA POST HOC test has been used for the comparison of p values among the groups.

Results and observations

Demographic data comparison

Age distribution

Mean age of the patients in the groups was compared using ANOVA 't' test. The average age in group D was 39.03 years, group C was 36.6 years, group M was

36.6 years, and group S was 36.03. Therefore, we conclude that the difference between these groups was statistically insignificant (p value: 0.595). This is shown in Table no.1.

Table 1: Age distribution of patients studied

	N	Mean	SD	P Value
DEXMEDETOMIDINE	30	39.03	8.364	.595
CLONIDINE	30	36.60	9.825	
MGSO4	30	36.60	9.825	
CONTROL	30	36.03	8.743	

Gender distribution:The percentage of males in group D was 63.3%, GROUP C was 60.0%, GROUP M was 60.0%, and GROUP S was 60.0% which were comparable. The percentage of females in group D was 36.7%, GROUP C was 40.0%, GROUP M was 40.0%, and GROUP S was 40.0%. Chi-square test is used for comparison. The Gender distribution is shown in table no. 2.

Table 2: Gender distribution of patients studied

	Male		Female	
	Frequency	Percent (%)	Frequency	Percent (%)
DEXMEDETOMIDINE	19	63.3	11	36.7
CLONIDINE	18	60.0	12	40.0
MGSO4	18	60.0	12	40.0
CONTROL	18	60.0	12	40.0

Weight distribution:Weight of the patients in the groups was compared using ANOVA 't' test. Average weight in group D was 58.83 kgs; group C was 58.90 kgs, group M was 59.43 kgs and group S was 61.43 kgs. Therefore, it can be concluded that the difference between these groups was statistically not significant. (p value: 0.067).this is shown in Table no.3 .

Table :3 Weight distribution of the patients studied

		N	Mean	SD	P VALUE
Weight	DEXMEDETOMIDINE	30	58.83	4.332	.067.
	CLONIDINE	30	58.90	3.763	
	MGSO4	30	59.43	3.549	
	CONTROL	30	61.43	4.485	

Vital parameter data: 1) heart rate:The basal (BL) mean heart rate of group D was 83.27+/-7.16, group C was 86.67+/-5.39, group M was 84.90+/-3.80 and group S was 86.57+/-7.01, and the difference in the mean heart rate at baseline among the groups is not statistically significant (p>0.05). After study drug infusion (ADI), after induction (AI), before intubation (BI), the mean heart rate starts decreasing in group D, but increasing in group M and C, but in group S, it was at and around the baseline value.Immediately after intubation (IAI), and at 1 minute after intubation (T1), the mean heart rate increased in all the groups, but less increase was seen in group D compared to other groups, which was statistically significant (p <0.05). After 3, 5 and 10 min of intubation, mean heart rate starts decreasing in all the groups, but considerable decrease was seen in group D, followed by group M, C and S. By ANOVA test and Post hoc test, the p-value is <0.05 (significant) The table no.4 shows the trend of HEART RATE from baseline to over a period of 10 min after intubation.

Table 4: Comparison of heart rate (bpm) in the study groups at different time intervals

	Group	Mean	SD	P value	Inter group comparison of P values (POSTHOC TEST)					
					D- C	D-M	D- S	C- M	C- S	M- S
BL	D	83.27	7.163	.097	.181	1.00	.212	1.000	1.000	1.000
	C	86.67	5.390							
	M	84.90	3.809							
	S	86.57	7.011							
ADI	D	74.60	7.356	.000	.0001	.0001	.0001	1.000	.001	.023
	C	91.40	5.110							
	M	89.93	4.209							
	S	85.60	5.612							
AI	D	68.83	5.615	.000	.000	.000	.000	.154	1.00	.379
	C	89.37	5.027							
	M	92.30	4.419							
	S	89.87	4.967							
BI	D	67.77	3.757	.000	.000	.000	.000	.000	1.00	.000
	C	89.40	4.917							

	M	95.73	4.741							
	S	89.80	4.221							
IAI	D	80.37	3.189	.000	.000	.000	.000	.000	1.000	.000
	C	127.73	2.935							
	M	107.17	4.654							
	S	127.37	4.694							
T1	D	84.17	3.323	.000	.000	.000	.000	.000	.000	.000
	C	123.93	3.194							
	M	103.87	4.614							
	S	129.77	4.415							
T3	D	74.87	2.837	.000	.000	.000	.000	.000	.000	.000
	C	109.33	3.387							
	M	98.10	3.448							
	S	130.03	3.864							
T5	D	69.23	2.459	.000	.000	.000	.000	.000	.000	.000
	C	98.13	3.246							
	M	93.17	3.384							
	S	123.10	3.960							
T10	D	69.20	2.469	.000	.000	.000	.000	.000	1.000	.000
	C	97.63	3.264							
	M	92.50	3.560							
	S	98.53	3.776							

The mean difference is significant When P value is <0.05.

Systolic blood pressure

At baseline, the mean systolic blood pressure (SBP) of group D was 128.40+/- 7.02, group C was 128.10+/-3.41, group M was 127.87+/-4.718 and group S was 124.73+/-8.57, and the difference in mean SBP at baseline among the groups is not statistically significant (p>0.05). After study drug infusion (ADI), after induction (AI), before intubation (BI), the mean SBP starts decreasing in group D and M, but the considerable decrease is seen in group D, and it remains at and around the baseline in group C and S.

Immediately after intubation (IAI) then mean SBP of group D was 116.10+/- 3.45, group C was 160.20+/-5.28. group M was 132.90+/-4.80 and group S was 164.93+/-4.1, which shows that group D shows less increase in SBP followed by group M, C and S. From 1 minute to 10 minutes after intubation, the mean SBP starts decreasing in all the groups, but considerable decrease is seen in group D, followed by group M, C and S. By ANOVA test and POST HOC test, the p-value is <0.05 (significant) The table no.5 and graph no.5 shows the trend of SYSTOLIC BLOOD PRESSURE from baseline to over a period of 10 min after intubation.

Table 5: Comparison of sbp (mm hg) among the studygroups at different time intervals

	Group	Mean	SD	P Value	Inter group comparison of P values(POST HOC TEST)					
					D-C	D-M	D-S	C-M	C-S	M-S
BL	D	128.40	7.025	.088	1.000	1.000	.151	1.000	.237	.330
	C	128.10	3.418							
	M	127.87	4.718							
	S	124.73	8.578							
ADI	D	120.33	5.713	.001	.001	.280	.007	.347	1.000	1.000
	C	125.87	3.246							
	M	123.17	4.403							
	S	125.00	7.520							
AI	D	110.77	5.900	.000	.000	.000	.000	.000	.001	1.000
	C	127.33	2.746							
	M	120.47	4.117							
	S	122.20	7.136							
BI	D	106.43	4.125	.000	.000	.000	.000	.000	.000	.272
	C	130.10	2.746							
	M	120.90	4.802							
	S	123.20	5.473							
IAI	D	116.10	3.546	.000	.000	.000	.000	.000	.001	.000
	C	160.20	5.288							
	M	132.90	4.802							
	S	164.93	4.177							
T1	D	109.97	3.449	.000	.000	.000	.000	.000	.000	.000
	C	158.53	1.889							
	M	128.90	4.802							
	S	165.93	3.383							
T3	D	100.00	4.533	.000	.000	.000	.000	.000	.000	.000
	C	137.23	4.174							
	M	122.03	4.327							

T5	S	165.27	3.443	.000	.000	.000	.000	.000	.000
	D	94.93	3.629						
	C	132.50	3.803						
	M	119.30	3.975						
T10	S	158.07	2.982	.000	.000	.000	.000	.000	.000
	D	96.23	3.213						
	C	128.73	3.051						
	M	119.30	3.879						
	S	134.87	3.014						

The mean difference is significant when P is < 0.05

Diastolic blood pressure

At baseline, the mean Diastolic blood pressure (DBP) of group D was 74.70+/-3.12, group C was 75.77+/-2.60, group M was 74.33+/-3.29 and group S was 75.77+/-5.04, and the difference in mean DBP at baseline among the groups is not statistically significant (p>0.05). After study drug infusion (ADI), after induction (AI), before intubation (BI), the mean DBP starts decreasing in group D but remains at and around the baseline values in group C, M and S. Immediately after intubation (IAI) the mean DBP of group D was 79.67+/- 4.42, group C was 106.10+/-2.53, group M was 84.93+/-3.14 and group S was 116.03+/-4.49, which indicates that group D shows less increase in DBP. From 1 minute to 10 minutes after intubation, the mean DBP starts decreasing in all the groups, but the considerable decrease is seen in group D, followed by group M, C and S. By ANOVA test and POST HOC test, the p-value is <0.05 (significant). The table no.6 and graph no.6 shows the trend of DIASTOLIC BLOOD PRESSURE from baseline to over a period of 10 min after intubation.

Table 6: Comparison of dbp (mm hg) among the study groups at different time intervals

	Group	Mean	SD	P value	Inter group comparison of p values (POSTHOC TEST)					
					D-C	D-M	D-S	C-M	C-S	M-S
BL	D	74.70	3.120	.311	1.000	1.000	1.000	.776	1.000	.776
	C	75.77	2.609							
	M	74.33	3.294							
	S	75.77	5.042							
ADI	D	71.07	3.172	.001	.014	.000	.000	.017	.586	1.000
	C	74.37	3.146							
	M	77.60	4.576							
	S	76.13	5.124							
AI	D	65.13	4.032	.000	.000	.000	.000	1.000	.065	.004
	C	76.87	2.862							
	M	77.77	3.607							
	S	74.27	4.799							
BI	D	69.27	3.787	.000	.000	.000	.000	.627	.009	.672
	C	77.50	3.637							
	M	75.93	2.852							
	S	74.40	4.391							
IAI	D	79.67	4.428	.000	.000	.000	.000	.000	.001	.000
	C	106.10	2.537							
	M	84.93	3.140							
	S	116.03	4.491							
T1	D	72.77	3.431	.000	.000	.000	.000	.000	.000	.000
	C	99.97	2.646							
	M	82.40	3.616							
	S	116.53	4.740							
T3	D	67.57	3.319	.000	.000	.000	.000	.000	.000	.000
	C	87.03	4.303							
	M	76.07	3.290							
	S	114.93	4.331							
T5	D	72.43	3.025	.000	.000	.000	.000	.027	.000	.000
	C	82.87	4.424							
	M	80.10	3.273							
	S	105.97	3.935							
T10	D	69.43	3.025	.000	.000	.000	.000	.448	.000	.000
	C	78.03	4.004							
	M	76.43	3.530							
	S	95.80	3.134							

The mean difference is significant when P value is <0.05

Mean arterial pressure

At baseline, the average mean arterial pressures (MAP) in group D was 92.63+/-3.32, group C was 93.20+/-2.32, group M was 92.07+/-2.53 and group S was 92.03+/-4.52, and the difference in mean MAP at baseline among the groups is not statistically significant (p>0.05).

After study drug infusion (ADI), after induction (AI), before intubation (BI), the mean MAP starts decreasing in group D but remains at and around the baseline values in group C, M and S.

Immediately after intubation (IAI) the MAP values of group D was 91.93+/- 3.36, group C was 124.27+/-2.69, group M was 100.97+/-

2.65 and group S was 132.27+/-3.14, which indicates that group D shows less increase in MAP. From 1 minute to 10 minutes after intubation, the mean MAP starts decreasing in all the groups, but the considerable decrease is seen in group D, followed by group M, C

and S. By ANOVA test and POST HOC test, the p-value is <0.05 (significant). The table no. 7 shows the trend of MEAN ARTERIAL PRESSURE from baseline to over a period of 10 min after intubation.

Table 7: Comparison of map (mm hg) in the study groups at different time intervals

	Group	Mean	SD	P value	Inter group comparison of p values (POSTHOC TEST)					
					D-C	D-M	D-S	C-M	C-S	M-S
BL	D	92.63	3.327	.474	1.000	1.000	1.000	1.000	1.000	1.000
	C	93.20	2.325							
	M	92.07	2.532							
	S	92.03	4.522							
ADI	D	87.47	2.991	.001	.0001	.0001	.0001	.949	1.000	1.000
	C	91.57	2.763							
	M	92.87	3.371							
	S	92.80	4.723							
AI	D	80.33	3.698	.000	.000	.000	.0001	.336	.001	.336
	C	93.67	2.454							
	M	91.93	2.840							
	S	90.20	4.536							
BI	D	81.70	3.053	.000	.000	.000	.000	.000	.000	1.000
	C	95.10	2.893							
	M	90.93	2.288							
	C	90.70	3.888							
IAI	D	91.93	3.362	.000	.000	.000	.000	.000	.000	.000
	C	124.27	2.690							
	M	100.97	2.659							
	S	132.27	3.140							
TI	D	85.07	2.677	.000	.000	.000	.000	.000	.000	.000
	C	119.50	1.996							
	M	97.90	2.708							
	S	133.07	3.503							

Discussion

A haemodynamic response of increased HR and BP to manipulation in the area of the larynx, by means of laryngoscopy and intubation[11], has been well recognized for 60 years. Stimulation of mechanoreceptors in the pharyngeal wall, epiglottis, and vocal cords is thought to be the cause for the haemodynamic response. The receptors are abundant over arytenoid cartilage, vocal cords, epiglottis and hypopharynx. Transitory hypertension and tachycardia are probably of no consequence in healthy individuals, but either one or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases. The transient changes can result in potentially deleterious effects like cerebral haemorrhage, myocardial ischemia leading to left ventricular failure and pulmonary oedema. Several protective measures against haemodynamic and catecholamine responses to laryngoscopy and intubation have been described, but no single anaesthetic technique has become generally accepted as being effective in preventing or attenuating these responses. Several agents like Lignocaine, Nitroglycerine, Esmolol, Labetalol, Fentanyl, Diltiazem, Verapamil etc. have been used in various studies to attenuate the haemodynamic responses to laryngoscopy and intubation with positive results and varying efficacies. Recent studies show Dexmedetomidine, Clonidine, Magnesium sulfate has been used in several clinical trials to attenuate the pressor responses to laryngoscopy and intubation with proven efficacy. Hence in this study, we compared Dexmedetomidine, Clonidine and Magnesium sulphate, which are proved to be effective in decreasing the haemodynamic responses to laryngoscopy and intubation in various clinical trials. In this study, 120 patients undergoing elective surgeries under general anaesthesia were grouped into four groups of 30 each- Group D (Dexmedetomidine), group C (Clonidine), group M (Magnesium sulfate) and group S (control). All the patients were comparable with respect to the demographic parameters: age, gender and weight. All the patients were comparable

with respect to the ASA physical status grading. All the patients were clinically and statistically comparable with respect to Pre-intubation and post-intubation haemodynamic parameters: HR, SBP, DBP and MAP. In this study, Dexmedetomidine 1µg/kg was used according to the study done by **Singh D et al[12]**, who demonstrated beneficial effects of the drug inattenuating intubation response. Clonidine was used at a dose of 1 µg/kg according to a study done by **Arora S et al[10]**. Magnesium sulfate 30mg/kg was used based on the study done by **Bidyut borah et al[13]**. Dexmedetomidine (1 mcg/kg), clonidine(1mcg/kg) and Mgso4 (30mg/kg) were administered 10 minutes prior to induction after recording baseline parameters (HR, SBP, DBP, MAP) and these parameters were recorded after drug infusion, after induction, before intubation, immediately after intubation, 1,3,5 and 10 minutes after intubation and compared among the groups 'D', 'C', 'M' and 'S' in concurrence with other studies.

Bidyut borah et al[13], compared the effects of Dexmedetomidine, Clonidine and Magnesium sulfate in prevention of haemodynamic responses to intubation and concluded that Dexmedetomidine (1mcg/kg) in comparison to Clonidine (1mcg/kg) and Magnesium sulfate (30mg/kg) was far more effective in blunting the hemodynamic response to laryngoscopy in patients undergoing surgical procedures under general anaesthesia.

Heart rate

From the results of our study, On Comparison among the groups D, C, M and S, there was a statistically insignificant difference between the mean HR values of the four groups at baseline. After infusion of study medication, after induction, before intubation mean HR was decreased in group D and increased in group C, M and group S. Immediately after intubation and at 1min after intubation, the mean HR was increased in all the four groups, but in this, group D shows least increase in mean HR followed by group M, C and S which is statistically significant. (p<0.05). From 3rd xmin to 10th minute

after intubation, the increased heart rate starts decreasing in all the groups but, the considerable decrease is seen in group D, followed by group M, C and S. By ANOVA test and POST HOC test, the p-value is <0.05 (statistically significant). This is in correlation to the study done by **Bidyut borah et al[13]**. In the study done by **Bidyut Borah et al[13]**, the mean HR recorded was below the baseline values in the Dexmedetomidine group at all measurement times but mean HR was increased in Group C, M and S immediately after intubation which concurred with our study results.

Our study results were also in accordance with the results of **Chhaya Joshi et al[14]** who observed that Dexmedetomidine 1µg/kg given before induction was able to suppress the HR response better compared with Mgso4 (30mg/kg).

Our study results were also in accordance with the results of **Arindam Sarkar et al[15]**, who observed that the effect of intravenous dexmedetomidine infusion 0.5 mcg/kg given 10 min prior to induction suppresses the heart rate response better compared with Clonidine 3mcg/kg.

Bon Sebastian et al[9], in 2017 conducted a study on Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. They concluded that dexmedetomidine in a dose of 0.75µg/kg intravenous is the optimal dose to attenuate stress response to laryngoscopy and endotracheal intubation.

Systolic blood pressure

From the results of our study, on comparison among the groups D, C, M and S, there was a statistically insignificant difference between the mean SBP values of the four groups at baseline. From baseline, after infusion of study medication, after induction, before intubation there was decrease in mean SBP values of the Group D and M but remains the same in group C and S. Whereas immediately after intubation, the mean SBP was increased in all the four groups but in this, group D shows least increase in mean SBP followed by group M, C and S which is statistically significant (p<0.05). From 1 minute to 10 minutes after intubation, the mean SBP starts decreasing in all the groups, but the considerable decrease is seen in group D, followed by group M, C and S. By ANOVA test and POST HOC test, the p-value is <0.05 (significant). This is in correlation to the study done by **Bidyut borah et al[13]**.

In the study done by **Bidyut borah et al[13]**, they found that the SBP values were below the baseline values in the Dexmedetomidine group compared to other groups at all measurement times which was in accordance with our results. In this study, there was a lesser rise in SBP in group D, immediately after intubation compared to other groups, and SBP is below baseline value in group D after 1,3,5, and 10 minutes after intubation, which could be due to dexmedetomidine-induced sedation, analgesia and decreased catecholamine levels, inhibition of central sympathetic outflow and enhanced vagal activity. In another study, **Hussain SY et al[16]**, compared the effects of dexmedetomidine (1 mcg/kg) and clonidine (2 mcg/kg) in patients posted for elective surgeries under General anaesthesia and concluded that dexmedetomidine was more effective in attenuating the rise in SBP to endotracheal intubation compared to clonidine.

In another study, **Lee CW et al[17]** studied the effect of dexmedetomidine (0.5 µg/kg) given intravenously over 10 minutes in hypertensive patients undergoing elective noncardiac surgery and concluded that a single preanesthetic dose of dexmedetomidine (0.5 µg/kg) effectively suppressed the rise in SBP to laryngoscopy and intubation. All the above-mentioned studies are consistent with our study showing that dexmedetomidine is superior to Clonidine and Magnesium sulfate in attenuating the intubation responses.

Diastolic blood pressure

From the results of our study, on comparison among the groups D, C, M and S, there was a statistically insignificant difference between the mean DBP values of the four groups at baseline. From baseline, after infusion of study medication, after induction, before intubation there was decrease in mean DBP values of the group D but remains the same in the groups M, C and S. Whereas immediately after

intubation, mean DBP was increased in all the four groups, but in this, group D shows least increase in mean DBP followed by group M, C and S which is statistically significant (p<0.05). From 1 minute to 10 minutes after intubation, the mean DBP starts decreasing in all the groups, but the considerable decrease is seen in group D, followed by group M, C and S. By ANOVA test and POST HOC test, the p-value is <0.05 (statistically significant). This is in correlation to the study done by **Bidyut borah et al[13]**. In the study done by **Bidyut borah et al[13]**, they found that the DBP values were above the baseline values but insignificant in the Dexmedetomidine group immediately after intubation. But, at 1,3,5, and 10 min after intubation DBP values are below baseline values compared with Clonidine and Magnesium sulphate groups, which was in accordance with our results. In this study, there was a lesser rise in DBP immediately after intubation in Group D compared to other groups which could be due to Dexmedetomidine-induced sedation, analgesia and decreased catecholamine levels, inhibition of central sympathetic outflow and enhanced vagal activity.

Our study results were also in accordance with the results of **Chhaya Joshi et al[14]**, who observed that Dexmedetomidine 1µg/kg given before induction was able to suppress the rise in DBP better compared with Mgso4 (30mg/kg).

Our study results were also in accordance with the results of **Arindam Sarkar et al[15]**, who observed that the effect of intravenous Dexmedetomidine infusion 0.5 mcg/kg given 10 min prior to induction stabilizes hemodynamic parameters better compared with Clonidine 3mcg/kg. In another study, **Hussain SY et al[16]**, compared the effects of Dexmedetomidine (1 mcg/kg) and Clonidine (2 mcg/kg) in patients posted for elective surgeries under General anaesthesia and concluded that dexmedetomidine was more effective in attenuating the rise in DBP to endotracheal intubation compared to clonidine. All the above-mentioned studies are consistent with our study showing that Dexmedetomidine is superior to Clonidine and Magnesium sulfate in attenuating the intubation responses.

Mean arterial pressure

From the results of our study, on comparison among the groups D, C, M and S, there was a statistically insignificant difference between the mean MAP values of the four groups at baseline. From baseline, after infusion of study medication, after induction, before intubation there was decrease in mean MAP values of the group D but almost remains the same in group C, M and S. Whereas immediately after intubation, the mean MAP was increased in all the four groups but in this, group D shows least increase in mean MAP followed by group M, C and S which is statistically significant (p<0.05). From 1 minute to 10 minutes after intubation, the mean MAP starts decreasing in all the groups, but the considerable decrease is seen in group D, followed by group M, C and S. By ANOVA test and POST HOC test, the p-value is <0.05 (significant). This is in correlation to the study done by **Bidyut borah et al[13]**.

In the study done by **Bidyut borah et al[13]**, they found that the MAP values were below the baseline values in group D throughout the study period, but significant raise is seen compared to their baseline values in group C, M, and S immediately after intubation, 1,3,5, and 10 min after intubation which was in accordance with our results. In this study, there was no raise in MAP immediately after intubation in Group D compared to other groups which could be due to dexmedetomidine-induced sedation, analgesia and decreased catecholamine levels, inhibition of central sympathetic outflow and enhanced vagal activity. Our study results were also in accordance with the results of **Chhaya Joshi et al[14]**, who observed that Dexmedetomidine 1µg/kg given before induction was able to suppress the rise in MAP better compared with Mgso4 (30mg/kg). In another study, **Hussain SY et al[16]**, compared the effects of Dexmedetomidine (1 mcg/kg) and Clonidine (2 mcg/kg) in patients posted for elective surgeries under General anaesthesia and concluded that Dexmedetomidine was more effective

in attenuating the rise in MAP to endotracheal intubation compared to Clonidine.

In another study, Lee CW, Kim M et al[17], studied the effect of Dexmedetomidine (0.5 µg/kg) given intravenously over 10 minutes in hypertensive patients undergoing elective noncardiac surgery and concluded that, a single preanesthetic dose of Dexmedetomidine (0.5 µg/kg) effectively suppressed the rise in MAP response to intubation.

Limitations

- In this study, hemodynamic changes were recorded only during induction and intubation and up to 10 mins thereafter. But the effect of Dexmedetomidine, Clonidine and Magnesium sulfate on hemodynamic parameters during the intraoperative and postoperative period were not included in the present study.
- Effect of the study drugs is not studied in hypertensives, coronary artery disease and ASA 3 and 4 patients.
- The study should be tested in a larger sample size.
- The study was not blinded so, there can be bias from the observer.

Conclusion

1. Dexmedetomidine (1mcg/kg), Clonidine (1mcg/kg) and Magnesium sulfate (30mg/kg) were effective in blunting the hemodynamic response to laryngoscopy in patients undergoing surgical procedures under general anaesthesia.
2. Dexmedetomidine in comparison to clonidine and magnesium sulfate was more effective in blunting the hemodynamic response to laryngoscopy and endotracheal intubation.
3. Magnesium sulfate was also effective in attenuating the stress response to laryngoscopy and intubation compared to Clonidine, but not effective when compared to Dexmedetomidine.

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