Original research article

To Compare the Efficacy of Bolus Administration of Intravenous Dexmedetomidine 1 Microgram/Kg with Intravenous Esmolol 1.5 Mg/Kg in Attenuating the Cardiovascular Stress Response Accompanying Laryngoscopy and Endotracheal Intubation.

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Abstract

Background: Laryngoscopy and intubation induce huge spectrum of stress responses such as tachycardia and hypertension. Those are in association with the surge of plasma adrenaline concentration following intubation. This study was performed to compare the efficacy of an accurate bolus dose of esmolol and bolus dose of dexmedetomidine in attenuating the pressor response to laryngoscopy and endotracheal intubation in general anaesthesia.

Materials and Methods*:* Randomised, comparative and double blinded study in which 30 patients were recruited in both the groups**,** Group D received injection Dexmedetomidine and Group E received injection Esmolol assesment done for change in Heart rate, Systolic, Diastolic and mean blood pressure with any adverse effects.

Results and Observations*:* Heart rate, SBP, DBP and MAP was lower in Group D as compared to Group E. No patients in either group required treatment for bradycardia and hypotension. No other adverse effects were noted in any patient.

Conclusion: Dexmedetomidine is effective in attenuating hemodynamic response to laryngoscopy and tracheal intubation without any side effect.

key words: Larngoscopy, Intubation, Dexmedetomidine, Esmolol

INTRODUCTION

Laryngoscopy and intubation induce huge spectrum of stress responses such as tachycardia and hypertension. Those are in association with the surge of plasma adrenaline concentration following intubation.[1] A sudden change in haemodynamic status may precipitate myocardial ischemia, especially in high-risk patients.[2] Dexmedetomidine (DEX), a highly selective, short-acting, alpha2-adrenoreceptor agonist, has sedative, analgesic and anxiolytic property without any respiratory depressive action but adverse haemodynamic complications like hypotension, bradycardia and delayed postoperative recovery. Esmolol cardioselective β-adrenergic antagonist reduces the force of contraction and heart rate. Esmolol 2 mg/kg is effective in suppressing the pressor response without any deleterious effects. This study was

performed to compare the efficacy of bolus dose of esmolol and bolus dose of dexmedetomidine in attenuating the pressor response to laryngoscopy and endotracheal intubation.

MATERIALS AND METHODS:

A Randomised, comparative and double blinded study was conducted after obtaining ethical clearance from the Institute Ethics Committee, IGIMS, Patna. The CTRI NO. REF/2021/01/039855, Written informed consent was obtained from all the patients before enrolling them for the study.

Inclusion Criteria:

- Patients of ASA physical status 1 and 2
- Patients between 18-50 years of age of either sex
- Patients with airway of mallampati Grade I and II
- Patients willing to participate

Exclusion Criteria:

- Patient's refusal to participate
- Patients with pregnancy, morbid obesity, full stomach and emergency surgery.
- Patients with ASA physical status III and above.
- Patient with suspected difficult airway and mallampatti Grade III and IV.
- Patient in which duration of laryngoscopy is expected to last more than 25 seconds

Sample size: 30 patients were recruited in both the group. Keeping alpha error <0.05,beta error <0.2 and power of study 80% . Patient were randomly divided into two groups Group D and Group E

A preoperative evaluation was carried out in all patients for demographic data like age, gender, weight and detailed clinical history, physical examination, routine laboratory investigations were done. The factors indicating difficult intubation on clinical examination were ruled out.

All patients received tablet Ranitidine 150 mg at night before surgery and 3 hours before surgery and tablet alprazolam 0.5 mg was given night before surgery. Intravenous(i.v)line was secured and i.v fluid ringer lactate 500 ml as maintenance was started about 3 hours prior to surgery. About one hour prior to surgery, baseline readings were taken for heart rate(H.R) and systolic blood pressures(SBP), diastolic blood pressures(DBP) and mean arterial pressures(MAP)) and were considered as preoperative baseline reading.

In operation theatre(O.T) standard monitors were attached and parameters were recorded. All patients received sedation with i.v midazolam 0.02 mg/kg and fentanyl 2 mcg/kg about 15 minutes before induction. Preoxygenation with 100% oxygen by using facemask in closed circuit to achieve oxygen saturation (SpO2) of 98-99% was done.

Group D: Received injection dexmedetomidine 1 microgram/kg diluted up to 10 ml by adding normal saline over 10 minutes before induction and 10 ml normal saline 60 second before induction.

Group E: Received 10 ml normal saline over 10 minute before induction and 1.5 mg/kg esmolol diluted up to 10 ml by adding normal saline, 60 second before induction.

Two sets of 10 ml syringes was prepared coded by other anaesthetist as per randomization , who was not involved in observation,data collection or analysis A & B. Set "A" was randomly contain either dexmedetomidine whereas set "B" contain esmolol.
Induction of anesthesia was done with i.v Propofol 2 mg/kg body weight given slowly till loss of verbal communication. Then facemask ventilation was done and direct laryngoscopy was conducted by the trained anesthetics with standard size Mcintosh blade and an appropriate sized cuffed endotracheal tube was inserted in single attempt and cuff was immediately inflated with air to a pressure of 25 cm of water. Patients requiring more than one attempt were decided not include in this study.
After confirming bilateral equal air entry by auscultation, the endotracheal tube was secured with the adhesive tape. Ventilation was done by Intermittent positive-pressure ventilation (IPPV) on ventilator. Ventilatory setting was set to provide tidal volume of 8-10 mg/kg and respiratory rate 14/minute for 10 minutes. No noxious stimulus or surgical incision was applied over 10 minutes after intubation. Supine position was maintained. Anesthesia was maintained using 50% nitrous oxide and 50% oxygen with Isoflurane (MAC-1.0). Hemodynamic parameters monitored were as follows: HR, SBP, DBP, MAP by non-invasive technique.
Parameters were observed at an interval of 2 minutes before tracheal intubation and at an interval of 1 minute, and 5 minutes after tracheal intubation and cuff inflation. We have decided to administer i.v Atropine (0.6 mg) and Mephentramine (6 mg) as rescue medication if HR will drop down to 50 beats per minute and MAP will fall more than 20% of baseline respectively.

Statistical Analysis: Statistical analysis was carried out with the help of Statistical package for the social sciences (SPSS) version 20 for windows package (Chicago, IL, USA). The description of the data was done in form of mean±standard deviation (SD) for quantitative data while in the form of % proportion for qualitative (categorical) data. $p<0.05$ was considered significant. For quantitative data, unpaired student's t-test was used to test statistical significance of difference between two independent group means. For comparison of categorical variables chi-square test was used.

RESULTS:
Patients of both the groups was demographically comparable for age, sex, height, weight and body mass index **[Table1**]. Distribution of study participants according to ASA status, Both the groups were comparable (p value = 0.781). Majority of the patients i.e. 60% of Group D and 63.3% of Group E belonged to MPG class II. We found there was no statistically significant difference regarding mallampati grading between two groups **[Table 2]**. There was no statistically significant difference in mean HR at baseline, before sedation, after induction or immediately after intubation. After that the HR at 2 minutes, 5minutes and 10 minutes after intubation was significantly lesser in the group D as compared to the group E and difference was statistically significant **[Table 3].** There was no statistically significant difference at baseline, before sedation, after induction or immediately after intubation. After that the SBP at 2 minutes, 5minutes and 10 minutes after intubation was significantly lesser in the group D as compared to the group E and difference was statistically significant [**Table 4]**. After

induction and immediately after intubation we observed DBP was statistically significant lower in group D. After that the DBP at 2 minutes, 5minutes and 10 minutes after intubation was significantly lesser in the dexmedetomidine group as compared to the esmolol group and difference was statistically significant **[Table 5].** There was no statistically significant difference at baseline, before sedation or after induction, Thereafter mean MAP was statistically significant lower in Group D except at 10 minutes after intubation, where difference was not statistically significant **[Table 6].** No patients in either group required treatment for bradycardia and hypotension. No other adverse effects were noted in any patient.

Table 1: **Distribution according to Age, Sex, Height, Weight and Body mass index**

S.N	Parameters	Group D (Mean ± SD)	Group E (Mean ± SD)	P value
1.	Age	36.833±7.77	37.600±5.61	0.158
2.	Sex	1.14:1	1.30:1	0.795
3.	Height (cms)	162.5±10.61	164.2±10.10	0.158
4.	Weight (kg)	65.63±7.07	65.26±4.81	0.029
5.	B.M.I (Kg/m^2)	24.84±1.97	24.07±2.55	0.431

Table 2: Distribution according to Mallampati Grading (MPG)

Mallampati Grading	Group D (Intravenous Dexmedetomidine) (n=30)		Group E (Intravenous Esmolol) (n=30)		p value
	Frequency	Percentage	Frequency	Percentage	
Class I	12	40.0	11	36.7	0.790
Class II	18	60.0	19	63.3	
Total	30	100.0	30	100.0	

Table 3: Comparison of Mean Heart Rate (bpm) at different time intervals

Time Intervals	Group D (Intravenous Dexmedetomidine) (n=30)		Group E (Intravenous Esmolol) (n=30)		p value
	Mean	±SD	Mean	±SD	
Baseline	84.33	±5.30	84.46	±5.22	0.924
Before Sedation	83.80	±5.15	83.00	±5.05	0.546
After Induction	80.20	±5.15	80.46	±5.05	0.840
Immediately after Intubation	84.93	±4.57	87.33	±5.07	0.059
2 minutes	80.20	±4.40	85.13	±4.89	0.0001
5 minutes	74.73	±4.34	81.46	±5.19	0.0001
10 minutes	72.26	±3.99	80.53	±4.63	0.0001

Table 4: Comparison of Mean Systolic Blood Pressure (mmHg) at different time intervals

Time Intervals	Group D (Intravenous Dexmedetomidine) (n=30)		Group E (Intravenous Esmolol) (n=30)		p value
	Mean	±SD	Mean	±SD	
Baseline	125.33	±5.15	126.5	±4.85	0.863
Before Sedation	123.0	±3.78	127.0	±4.0	0.897
After Induction	126.67	±3.49	124.5	±3.5	0.733
Immediately after Intubation	132.0	±3.55	153.0	±7.25	0.0001
2 minutes	126.0	±3.51	143.0	±7.02	0.0001
5 minutes	118.16	±2.73	132.16	±7.03	0.0001
10 minutes	116.33	±2.56	125.16	±5.84	0.011

Table 5: Comparison of Mean Diastolic Blood Pressure (mmHg) at different time intervals

Time Intervals	Group D (Intravenous Dexmedetomidine) (n=30)		Group E (Intravenous Esmolol) (n=30)		p value
	Mean	±SD	Mean	±SD	
Baseline	79.83	±4.17	80.16	±4.17	0.762
Before Sedation	81.67	±4.71	80.83	±4.09	0.475
After Induction	84.0	±3.26	81.33	±4.64	0.014
Immediately after Intubation	85.83	±3.67	96.67	±4.71	0.0001
2 minutes	80.5	±3.73	90.0	±5.16	0.0001
5 minutes	75.33	±3.39	85.0	±4.65	0.0001
10 minutes	70.33	±3.39	79.33	±4.22	0.001

Table 6: Comparison of Mean MAP (mmHg) at different time intervals

Time Intervals	Group D (Intravenous Dexmedetomidine) (n=30)		Group E (Intravenous Esmolol) (n=30)		p value
	Mean	±SD	Mean	±SD	
Baseline	91.56	±15.65	95.3	±2.97	0.592
Before Sedation	95.56	±2.43	95.83	±3.04	0.120
After Induction	98.06	±2.04	95.36	±3.01	0.094
Immediately after Intubation	100.9	±2.61	115.23	±4.46	0.037
2 minutes	95.43	±2.76	107.33	±4.49	0.006
5 minutes	89.33	±2.53	100.4	±4.00	0.028
10 minutes	85.36	±2.75	94.7	±3.32	0.152

DISCUSSION:

Laryngoscopy and endotracheal intubation induced hemodynamic response like tachycardia and hypertension is due to stimulation of mechanoreceptors in the pharyngeal wall, epiglottis and vocal cords which may leads to myocardial ischemia or infarction especially in patients

with coronary artery disease. Various methods have been used to blunt these responses including inhalational anesthetic agents, lignocaine, opioids, calcium channel blockers, and direct acting vasodilators.[3,4] These methods have got side effects such as bradycardia, hypotension, sedation, and respiratory depression. Thus, there is ongoing search for an ideal agent. Dexmedetomidine, a selective α2 agonist with an onset of action at 5 min in a dosage of 1 μg/kg, has a peak effect within 15 min. Its elimination half life is about 2–3 hrs.[5] It provides neurovegetative protection and has predictable cardiovascular and respiratory effects in a dose dependent manner.[6] Higher doses of dexmedetomidine have been associated with a significant increase in the incidence of bradycardia and hypotension. Rapid administration of dexmedetomidine might produce tachycardia, bradycardia, and hypertension followed by hypotension.[7]

Beta adrenergic blockers, another group of pharmacological agents was used for blunting the hemodynamic responses to laryngoscopy and intubation.[8-9] Esmolol, a selective beta blocker was introduced in 1986, fascinated many investigators because of its short duration of action and no risk of developing perioperative bradycardia or hypotension.[10] In our study, we found that dexmedetomidine bolus infusion 1.0 μg/kg before induction of anesthesia was more effective than esmolol bolus infusion 1.5 mg/kg for attenuation in hemodynamic responses to laryngoscopy and tracheal intubation in normotensive patients.

This suppression in cardiovascular responses was found to be greater with dexmedetomidine infusion than with esmolol. We observed that both dexmedetomidine and esmolol significantly attenuated the rise in HR after intubation and dexmedetomidine suppressed the response to intubation more than esmolol. While comparing SBP, DBP, and MAP, we found that dexmedetomidine attenuated the rise in these parameters significantly up to 10 min after intubation, showing that dexmedetomidine showed greater hemodynamic stability than esmolol. Our findings were in accordance to the study by **Reddy et al**. who compared dexmedetomidine 1 μg/kg and esmolol 0.5 mg/kg to suppress the response to intubation.[11] **Srivastava et al**. conducted a similar study in neurosurgical patients and found dexmedetomidine better.[12] **Gupta and Vyas**[13] and **Selvaraj and Manoharan**[14] also observed similar results. **Keniya et al**[15] stated that the pretreatment with dexmedetomidine 1.0 μg/kg attenuated, but not totally obtunded the cardiovascular response to tracheal intubation after induction of anesthesia similar in our study the mean HR became significant low across the groups. **Srivastava et al**[16] also documented statistically significantly lower DBP in dexmedetomidine receiving patient after induction and at all time observation of intubation, when compared with the other two group. We also had similar observations that during laryngoscopy and intubation. Unlike to our study, **Bajwa SS et al** had recorded increase in HR and MAP for 3-5 min was observed after the start of dexmedetomidine infusion and was probably due to the vasoconstriction effect of dexmedetomidine appearing earlier than the central sympathetic action.[17]**Liu et al**[18] who used esmolol infusion to control hemodynamic responses associated with intubation, found significant decreases in SBP prior to induction and post-intubation, compared than to placebo group. This could be because in their study patients received infusion rather than bolus. **Miller et al**[19] observed adverse effects like hypotension with higher doses of esmolol during induction and claimed optimal results with lesser dose.Above studies interpretation helped us to decide the study dose of dexmedetomidine 1 mcg/kg because dose below 1mcg/kg was not effective in attenuating hemodynamic response to laryngoscopy and tracheal intubation and dose more than 1 mcg/kg lead to adverse effects like hypotension and bradycardia.

CONCLUSION:

Dexmedetomidine in dose of 1 microgram/kg diluted up to 10 ml by adding normal saline over 10 minutes before induction is effective in attenuating hemodynamic response to laryngoscopy and tracheal intubation without any side effect.

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