Original Research Article

A comparative study of clonidine versus dexmedetomidine in attenuation of stress response to laryngoscopy and intubation

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Abstract

Background: Endotracheal intubation produces various cardio vascular complications. Sometimes these complications lead to mortality. Various anaesthetic drugs are tried before intubation to reduce the haemodynamic changes. The present study aimed to evaluate the clonidine versus dexmedetomidine in attenuation of stress response to laryngoscopy and intubation. **Materials and Methods:** The study was done in Department of Anaesthesia , Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala. A total of 50 patients included in the study based on the inclusion and exclusion criteria and divided into two group each of 25. G-I received Clonidine (2mcg/kg) and G-II Dexmedetomidine (0.5mcg/kg). Drugs are given to respective groups 10 min before induction. Demographic data (age and gender) and clinical data (heart rate, SBP, DBP and MAP) was recorded. SPSS (20.0) version was used for analysis. **Results:** Group-I and II not showed any significant difference on comparison of demographic data. Comparison of mean heart rate between the group-I and II not showed any significant difference. SBP (PI, AL), DBP (PI) and MAP (PI) showed significant difference when compared between the group-I and II. **Conclusion:** Dexmedetomidine in the dose of 0.5µg/kg, given 10 minutes before laryngoscopy and intubation is better choice than clonidine in attenuating the haemodynamic responses to laryngoscopy and intubation.

Keywords: Clonidine, Dexmedetomidine, Intubation, Hemodynamic response, Laryngoscopy, Heart rate

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INTRODUCTION

The procedure of endotracheal intubation produces reflex cardiovascular responses, particularly tachycardia and hypertension, in man. This produces increased cardiac output and a transient rise in central venous pressure. These reflex responses are mediated by increased sympathetic nervous system activity[1]. Though these transient haemodynamic responses were of little significance to normal healthy patients, this could be life threatening to certain patients, especially hypertensive patients with ischaemic heart disease or raised intracranial pressures. In view of these complications and in an attempt to maintain normal physiology during anaesthesia and surgery, various attempts were made to attenuate these haemodynamic responses to intubation[2]. Numerous agents like opioids, calcium channel blockers, beta blockers, magnesium sulphate, local anaesthetics etc. have been used to blunt the haemodynamic responses to laryngoscopy and intubation. Clonidine is an α2-adrenoceptor agonist with sedative and analgesic effects, also has the beneficial effect

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of blunting haemodynamic responses due to laryngoscopy and tracheal intubation. Dexmedetomidine is a novel α2-adrenoceptor agonist that has been recently introduced in India. It is known to produce sedation, anxiolysis, hypnosis, analgesia, and sympatholysis. Dexmedetomidine is currently used in the ICU for mechanically ventilated patients for sedation and analgesia and rapid recovery after discontinuation[3]. Based on the available review of literature the present study is aimed to compare the effectiveness of intravenous clonidine and dexmedetomidine in attenuating the stress response to laryngoscopy and intubation**.**

MATERIALS AND METHODS

Study design and settings: It is a comparative study done in Department of Anaesthesia, Sree Gokulam Medical College and Research Foundation, Trivandrum, Kerala.

Inclusion criteria: Male and Females. Age between 18-60 years. ASA grade I, II. Undergoing elective non-cardiac surgery

Exclusion criteria: Heart rate <70/min. Basal systolic blood pressure <100 mmHg. Asthma. Cardiac diseases. Presence of heart block. ASA PS>II. Anticipated difficult intubation. Anxious or apprehensive patients. Intubation time more than 15sec.

Groups

Group-I: Clonidine (2mcg/kg)

Group-II: Dexmedetomidine (0.5mcg/kg)

Procedure

50 patients were randomly divided into 2 groups of 25 patients each, based on simple randomisation by lottery method. Group-I patients received i.v Clonidine preservative free 2 mcg/kg 10 mins before induction. Group-II patients given i.v Dexmedetomidine diluted in 10 cc of normal saline, 0.5 mcg/kg, as intravenous infusion 10 min before induction. In preanaesthetic preparation Pantoprazole (40 mg) given 1 hour before procedure.

Anaesthetic technique

Patients are taken to the operating room. Pre-induction monitors are attached- ECG, Non-invasive Blood Pressure (BP), Pulse Oximetry. Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP) are recorded from the monitor. These variables are noted at time points by my colleague as (time BL). Intravenous line is established on the forearm after local anaesthesia with 2% Lignocaine (1 ml) (without adrenaline) using intradermal needle. Group-I patients received i.v Clonidine (2 mcg/kg) 10 mins before induction. Group-II patients receive i.v Dexmedetomidine (0.5 mcg/kg) over 10 minutes as i.v infusion 10 min before induction. 0.9% normal saline solution started at 80-100 ml/hr. Priming dose of Vecuronium (0.01 mg/kg) is given i.v. HR, SBP, DBP and MAP are noted (time PI - prior to induction). Patient is induced with i.v Propofol (2 mg/kg). As soon as the patient loses consciousness, mask ventilation is checked and i.v Vecuronium bromide (0.1 mg/kg) is given. Meanwhile the patient is ventilated with 100% oxygen for 3 minutes after induction. Then laryngoscopy is performed with a Macintosh curved blade laryngoscope. HR, SBP, DBP and MAP noted during laryngoscopy (Time of AL). The patients are intubated with appropriate sized endotracheal tubes within 15 seconds of laryngoscopy. All the intubations were done by the same person. Patients are then ventilated with 60% nitrous oxide in oxygen. HR, SBP, DBP and MAP are noted at 1, 3 and 5 min after laryngoscopy. During these 8 min of monitoring, patients are not manipulated or subjected to any surgical stimulation. IPPV is continued throughout the surgery. Anaesthesia is maintained with maintenance doses of Vecuronium bromide, Sevoflurane and analgesics as needed. HR, SBP, DBP and MAP are recorded every 10 minutes. At the end of surgery patients are reversed with Neostigmine (0.05 mg/kg) and Glycopyrrolate (10 mcg/kg). Patients are extubated, adequate recovery is ensured and patients are transferred to the recovery room.

Statistical analysis

The data was expressed in number, mean and standard deviation. Statistical Package for Social Sciences (SPSS 20.0) version used for analysis. Un paired test and Chi square test applied to find the statistical significance between the groups. p value less than 0.05 considered statistically significant at 95% confidence interval.

RESULTS

Total 50 patients were divided into two groups each of 25. Comparison of age and gender between the groups not showed any significant difference (Table-1). Comparison of heart rate between the groups not showed any significant difference (Table-2). Systolic Blood Pressure in the two groups, there was significant difference between the groups ($p < 0.05$). After giving the loading dose of dexmedetomidine there was more fall in SBP.Also at the time of laryngoscopy the rise in SBP was lesser in dexmedetomidine group keeping parameters closer to baseline values. It is also observed that the return to baseline values was faster in dexmedetomidine group than in clonidine group (Graph-1). Diastolic Blood Pressure in the two groups, there was significant difference between the groups ($p < 0.05$). After giving the loading dose of dexmedetomidine there was more decrease in diastolic blood pressure than the clonidine group. Also at the time of laryngoscopy the rise in DBP was lesser in dexmedetomidine group keeping parameters closer to baseline values. After laryngoscopy the rise of values in dexmedetomidine group was less and returned to baseline

faster than the clonidine group (Graph-2). Mean Blood Pressure in the two groups, there was significant difference between the groups ($p < 0.05$). After giving the loading dose of dexmedetomidine there was a greater decrease in Mean blood pressure than the clonidine group. Also at the time of laryngoscopy the rise in MAP was lesser in dexmedetomidine group keeping parameters closer to baseline values (Graph-3).

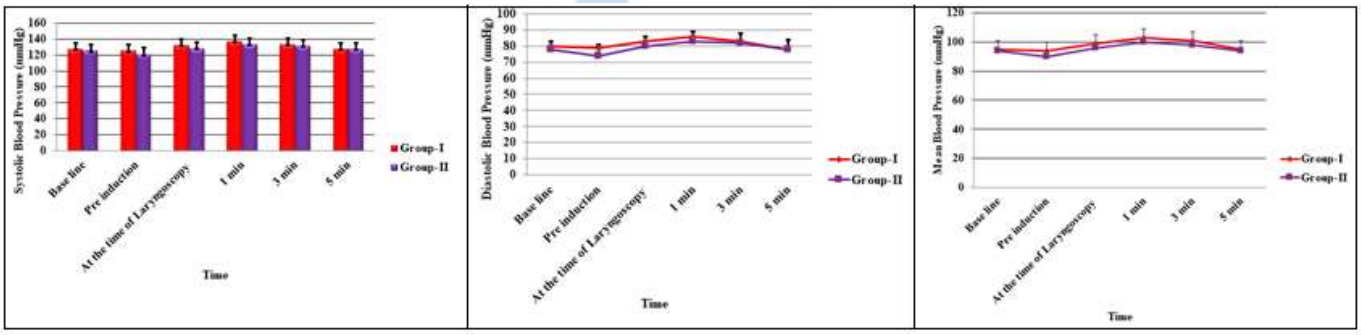
Table 1: Comparison of demographic data between the groups

Demographic data	Group-I	Group-II
Age (Years) (MEAN±SD)	28.28±9.52	34.12±11.27
Male (n)	8	8
Female (n)	17	17

Table-2: Comparison of mean heart rate between the groups

Heart rate	Group-I (MEAN±SD)	Group-II (MEAN±SD)	p value
Base line	83.48±11.16	83.24±10.76	0.93
Pre induction	82.84±11.81	82.72±11.40	0.97
At the time of Laryngoscopy	88.56±11.27	88.36±10.90	0.94
I min	92.36±10.26	92.12±10.62	0.93
3 min	89.84±10.14	90.20±10.45	0.90
5 min	87.40±10.56	87.84±10.33	0.88

(p>0.05 no significant difference between group-I and II)



Graph 1 **Graph 2** **Graph 3**

Graph 1: Comparison of mean systolic blood pressure between the groups. **Graph 2:** Comparison of mean diastolic blood pressure between the groups. **Graph 3:** Comparison of mean Blood pressure between the groups

DISCUSSION

The sequence of induction of anaesthesia, laryngoscopy and tracheal intubation are associated with marked haemodynamic changes and autonomic reflex activity which may be a cause of concern in many high risk patients[4]. Laryngoscopy and intubation is associated with rise in heart rate, blood pressure and incidence of cardiac arrhythmias. These potentially dangerous changes disappear within 5 min of onset of laryngoscopy. Although these responses of BP and HR are transient and short lived they may prove to be detrimental in high risk patients especially in those with cardiovascular disease, increased intracranial pressure or anomalies of the cerebral blood vessels. An average rise in MAP of 25mm Hg and 47.7 mmHg have been documented after laryngoscopy and intubation. A rise in mean heart rate of 29.9 beats/min has also been noted[5]. Many factors influence the cardiovascular changes associated with laryngoscopy and intubation. Age, drugs, type and duration of procedures, depth of anaesthesia, hypoxia, hypercarbia etc., influence the presser response. Variations of heart rate changes decrease with increasing age. Young patients show more extreme changes. Marked fluctuations in haemodynamic responses are often seen in geriatric patients. In our study we selected the optimal age range of 18 to 60 years. Patients on antihypertensive drugs may exhibit a decrease in pressor response[6]. A variable combination of drugs used for premedication, induction, and maintenance of anaesthesia can influence the sympathetic response to laryngoscopy and intubation. Midazolam at a dose of 0.2 mg/kg i.v decreases the blood pressure and increases the heart rate similar to thiopentone[7]. However premedication with 0.05 mg/kg im of midazolam has no effect on sympathetic response to laryngoscopy and intubation. Pentazocine an opioid agonist antagonist may increase the BP, HR and catecholamine levels. Glycopyrrolate premedication can moderately increase the HR. Propofol was selected for induction since it still continues to be the

most popular agent for induction. In normovolemic patients propofol 2mg/kg iv can transiently decrease 15-20 mm Hg of BP. Nasopharyngeal intubation causes significant pressor response. This response in heightened by the passage of tracheal tube in the larynx and trachea. In our study we included only direct laryngoscopy and orotracheal intubation. The most significant factor influencing cardiovascular responses is found to be the duration of laryngoscopy[8]. A linear increase in HR and MAP during the first 45 sec has been observed. Further prolongation has little effect. As the duration of laryngoscopy is normally less than 30 sec the results of studies in which it takes longer than this have less clinical relevance. The force applied during laryngoscopy has only minor effect. In our study the duration of laryngoscopy and intubation was limited to 15 sec. Adequate care was taken to achieve the required depth of anaesthesia avoiding hypoxia and hypercarbia which can influence the haemodynamic variations. Other contributory causes of hypertension and tachycardia could be manifestation of anxiety concerning anaesthesia and surgery, glycopyrrolate premedication and possible effect of suxamethonium. But they seem to be less important than laryngotracheal stimulation during laryngoscopy and intubation. Attenuation of sympathetic responses during laryngoscopy and intubation is of prime concern to the anaesthetist more so in high risk subjects as mentioned earlier. Many strategies have been recommended which include minimising the duration of laryngoscopy to less than 15 sec, topical application of local anaesthetics, IV β-blockers, calcium channel blockers, clonidine, sodium nitroprusside, lignocaine. No single drug or technique is satisfactory. Each technique has advantages and disadvantages, the most obvious being that the prevention often outlasts the stimulus. Bachofen M stated the criteria for selection of appropriate drug to prevent sympathetic response. The drug must be applicable regardless of patient collaboration, prevent impairment of cerebral blood flow and avoid arousal of the patients. It should neither be time consuming nor affect the modality of ensuing anaesthesia[9]. Clonidine and dexmedetomidine seem to be fulfilling the above criteria. Various studies have evaluated the efficacy of dexmedetomidine in attenuating the sympathoadrenal response to laryngoscopy and intubation. Menda F et.al., had shown that dexmedetomidine effectively blunted the haemodynamic responses to laryngoscopy and tracheal intubation compared to placebo. They also noted that the haemodynamic parameters were lower at all times compared to baseline values[10]. Sulaiman S et.al., have similarly shown that dexmedetomidine effectively blunts the haemodynamic response to laryngoscopy and intubation compared to saline placebo. In their study the mean HR was 69.10+ 10.7 in the dexmedetomidine group compared to 84.67±11.3 in the placebo group at one minute of post intubation[11,12]. The MAP was 87.43± 9.9 in the dexmedetomidine group and 107.23±14.3 in the placebo group at one minute post intubation. In our present study at 1 min, 3 mins and 5 mins after induction, the mean blood pressures in clonidine group were 103 mm Hg, 101 mmHg, 95 mmHg respectively where as in dexmedetomidine group, the mean blood pressures were 100 mmHg, 98 mmHg, 94 mmHg respectively. Group-II showed better control of pressures as compared to group-I. This control of haemodynamic variables of group-II as compared to group-I were statistically highly significant. In all the hemodynamic changes group-II showed better effects than group-I.

CONCLUSION

Hence it is concluded that dexmedetomidine in the dose of 0.5µg/kg, given 10 minutes before laryngoscopy and intubation is better choice than clonidine in attenuating the haemodynamic responses to laryngoscopy and intubation.

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