Original Research Article

Study between clonidine and dexmedetomidine in attenuation of pressor response during endotracheal intubation

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Abstract

Background: Laryngoscopy and endotracheal intubation, which are a basic and integral part of general anesthesia (GA), are associated with reflex sympathetic stimulation, manifested by tachycardia and hypertension.

Aim: The aim was to compare the effect of dexmedetomidine and clonidine on the pressor response among patients undergoing tracheal intubation in elective surgeries under general anesthesia.

Materials and methods: A prospective and randomized control study conducted in 80 adult patients of age 18-55 years in ASA I and II were included in this study. Patients were divided into Group D and Group C of 40 patients each.

Results: Mean SBP, DBP and MAP in the dexmedetomidine group remained close to the baseline throughout the study period showing a significant difference from clonidine groups following the induction interval. In present study after intubation heart rate, SBP, and DBP was increased in all patients but the increase was more in patients of clonidine group when compared to dexmedetomidine group. There was statistically significant difference in heart rate between the two groups at 1, 3 and 4 min interval after intubation (p value<0.05). No significant changes in peripheral oxygen saturation

(SpO2) and cardiac rhythm (ECG) were observed in any patients of both groups. Bradycardia (HR<50/min) was observed in one patient of dexmedetomidine group and two patients in clonidine group, five minutes after intubation. Intraoperative hypotension was observed in one patient of dexmedetomidine group and in two patients of clonidine group.

Conclusion: Premedication with dexmedetomidine can safely be recommended for attenuation of provided more stable hemodynamics response to endotracheal intubation.

Key words

Clonidine, Dexmedetomidine, Pressor response, Endotracheal intubation.

Introduction

Laryngoscopy and endotracheal intubation, which are a basic and integral part of general anesthesia (GA), are associated with reflex sympathetic stimulation, manifested by tachycardia and hypertension [1]. This is known as pressor response and has the potential to cause major complications such as myocardial ischemia, ventricular arrhythmia, left ventricular failure, and cerebral haemorrhage [1, 2]. Usually these changes are well tolerated by healthy individuals, but may prove to fatal in patients with untreated severe hypertension, coronary artery disease or intracranial aneurysm. The cardiovascular response is a reflex phenomenon and is mediated by vagus and glossopharyngeal nerve which activate the vasomotor centre to lead a peripheral sympathetic adrenal response. The appropriate premedication, smooth induction and rapid intubation would prevent these associated risks of hemodynamic pressor response. This response is harmful in neurosurgical cases as it may cause an increase in intracranial pressure, intracranial bleed, adverse hemodynamic effects, increasing the morbidity, and prolonged hospital stay [3, 4] and therefore has to be attenuated.

Various pharmacological methods are evaluated either in the premedication or during induction to attenuate these adverse hemodynamic responses of laryngoscopy and intubation, such as inhalational anesthetics, lidocaine, narcotic analgesics, topical anaesthetic, beta blockers, calcium channel blockers, ACE inhibitors and vasodilators but with variable results. As none of the above methods were proved to be ideal, the search of an ideal agent to attenuate the hemodynamic responses is still continuing.

Dexmedetomidine and clonidine, an α2 adrenergic agonist, have been used to induce preoperative sedation, intraoperative reduction of anaesthetic and analgesic requirements and hemodynamic stability along with postoperative analgesia. These pharmacological effects made them suitable for premedication for general anesthesia. We are comparing attenuating effect of dexmedetomidine versus clonidine on the pressor response to laryngoscopy and endotracheal intubation in neurosurgical cases.

Materials and methods

This was a prospective, randomized, controlled study on 80 adult patients aged between 18 and 55 years in American Society of Anesthesiologists (ASA) physical status I and II undergoing elective surgeries under general anesthesia after obtaining written informed consent from patients.

Inclusion criteria: Adult patients aged between 18 and 55 years of ASA-I and II physical status Scheduled for elective surgery under GA.

Exclusion criteria: Patients with significant coronary artery disease or ischemic heart disease, chronic obstructive pulmonary disease, renal failure, hepatic dysfunction, morbid obesity, moderate or severe anemia, hypertension.

The patients were allocated randomly into Group D and Group C of 40 patients each group received as

Group-D: dexmedetomidine (D, 0.5 μg/kg)

Group-C: clonidine (C, 3 μg/kg) diluted in 100 ml NaCl 0.9% were infused over a 10 min period.

Thereafter the patients received injection glycopyrrolate 0.2 mg IV. After preoxygenation with 100% oxygen for 3 min patients were induced with injection propofol (2 mg/kg). Endotracheal intubation was facilitated following a paralyzing dose of injection succinylcholine (2 mg/kg) IV maintenance of anesthesia was carried out with inhalation anesthetics (sevofluran) and nitrous oxide: Oxygen (60:40). Intraoperative relaxation was maintained with injection atracurium 0.5 mg/kg (bolus dose) followed by 0.1 mg/kg incremental doses on return of respiration. On the conclusion of surgery, patients were reversed with an injection neostigmine (50 μg/kg) and injection glycopyrrolate (10 μg/kg) and extubated. The blood pressure, heart rate, ECG and SpO2 were recorded at baseline, after study drug infusion, after induction, then immediately after intubation at 1 min interval till 10 min, then at 15 min after intubation. Routine monitoring was continued at 5 min interval till the end of surgery and after extubation.

At the end of the surgery residual neuromuscular blockade was antagonized with appropriate doses of neostigmine (0.05mg / kg) and glycopyrrolate (0.01mg / kg). Extubation was performed when respiration became adequate in tidal volume and the patient was able to obey simple verbal commands. Patients were transferred to post anesthesia care unit for monitoring of sedation, hemodynamic abnormalities, postoperative shivering, respiratory depression, nausea and vomiting or any other drug related side effects and treated according to clinical protocol.

The statistical analysis was performed using Statistical Package for Social Sciences version 15.0 statistical analysis software. The values were represented in number (%) and mean ± standard deviation.

Results

Data of all patients were included for statistical analysis. The demographic profiles of the patients were comparable in respect of age, sex, weight and ASA physical status. None of the demographic data was significant compared in both groups (**Table – 1**).

Table - 1: Demographic details.

Parameters	Group-D	Group-C	P-Value
Age in years	38.4+9.32	37.8+10.1	>0.05
weight in Kgs	57.1+9.9	58.3+10.56	>0.05
Gender(M/ F)	19/21	17/23	>0.05
ASA(I/II)	22/18	19/21	>0.05

No significance was observed in baseline and after induction in both groups. After intubation, heart rate increased in all patients but the increase was more in patients of clonidine group when compared to dexmedetomidine group. There was statistically significant difference in heart rate between the two groups at 1, 3 and 4 min interval after intubation (p value<0.05). Thereafter the difference of mean heart rate did not show statistically significant inter group difference till 15 minute in subsequent time interval (p value>0.05) as per **Figure – 1**.

Preoperatively, there was no significant difference in mean SBP between groups. After induction, there was fall in systolic blood pressure in both groups but it was not statistically significant (p value>0.05). After intubation, SBP increased in all patients but the increase was more in patients of clonidine group as compared to dexmedetomidine group. The difference was statistically significant after intubation at interval of 1and 3 min (p value<0.05). Further difference was not significant as the time advanced (**Figure – 2**).

Figure - 1: Heart rate in various intervals in both groups.

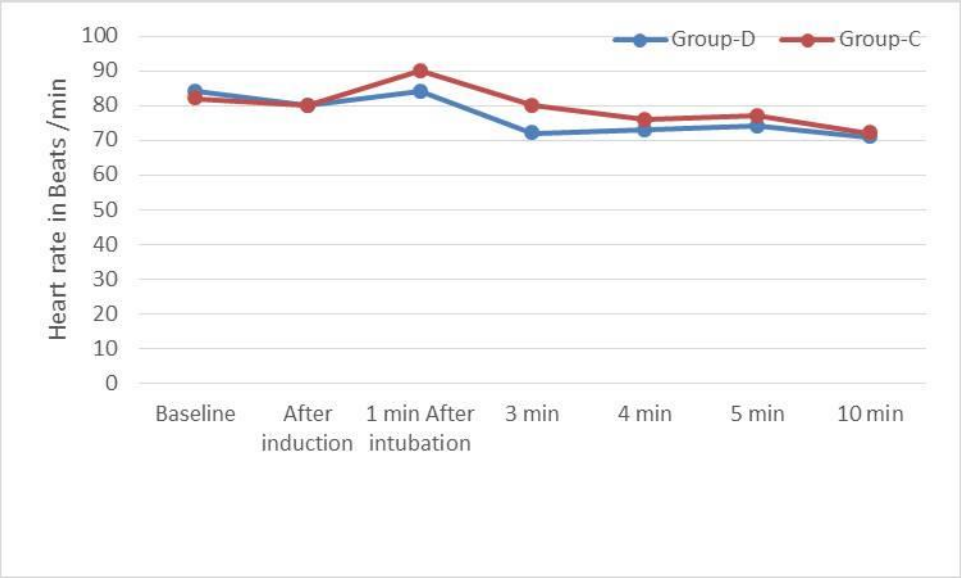

Figure - 2: Systolic blood pressure in various intervals in both groups.

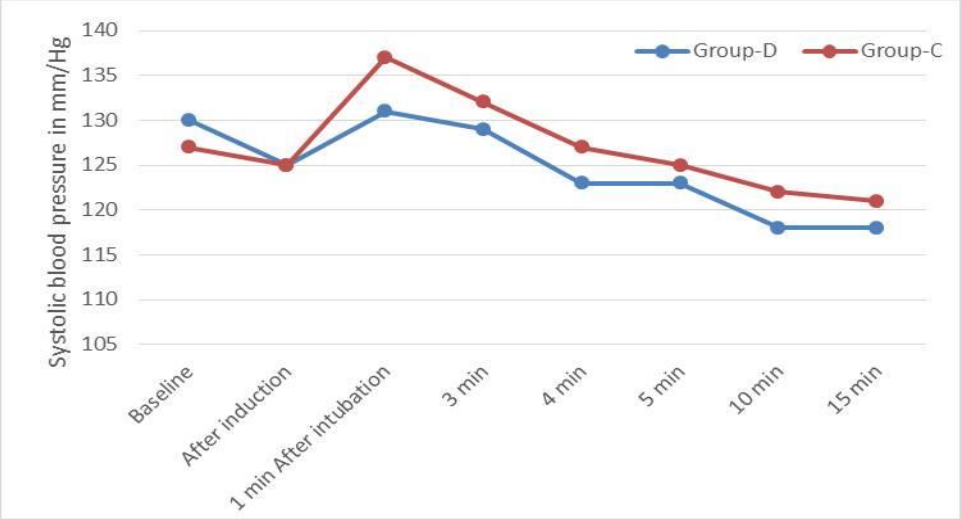

Figure - 3: Diastolic blood pressure in various intervals in both groups.

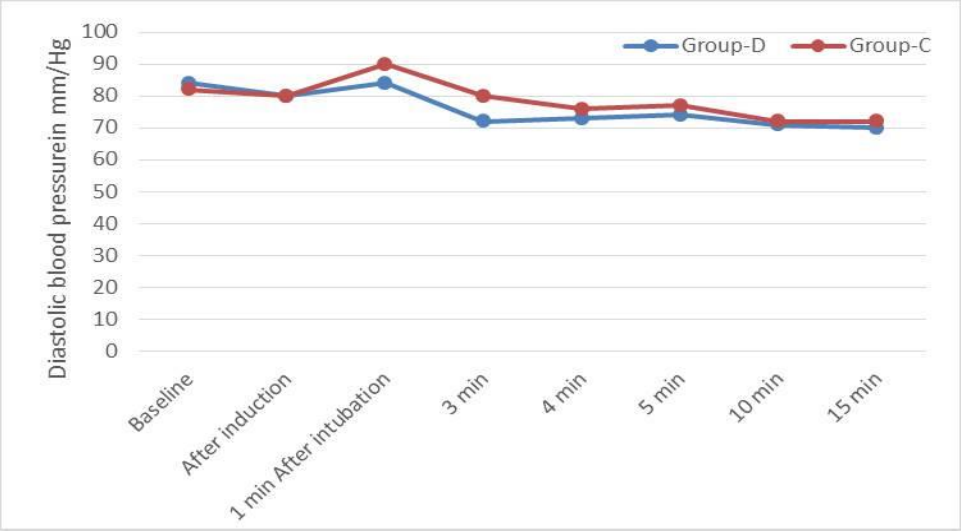

Table - 2: Adverse effects in study.

Adverse effects	Group-D	Group-C	P-Value
Hypotension	1/40(2.5%)	2/40(5%)	>0.05
Hypertension	0/40	0/40	A
Bradycardia	1/40(2.5%)	2/40(5%)	>0.05
Other side effects	0/40	2/40(5%)	>0.05

The baseline mean diastolic blood pressure was comparable between the two groups (p value>0.05). It decreased after induction in both group with no statistically significant intergroup difference (p value>0.05) but it increased after intubation. The patients of clonidine group showed marked increase in DBP in comparison to dexmedetomidine group. There was statistically significant difference (in diastolic blood pressure) between two groups at 1, 3 and 4 min interval after intubation (p value<0.05). Thereafter, there was no statistically significant changes occurred in diastolic blood pressure in patients of both groups (p value>0.05) as per **Figure - 3**.

No significant changes in peripheral oxygen saturation (SpO2) and cardiac rhythm (ECG) were observed in any patients of both groups. Hypotension occurred in three patients of no clinical significance. Bradycardia occurred in three patients and was treated with bolus of 0.6 mg atropine (**Table – 2**).

Discussion

A total of 80 patients were recruited in three groups of 40 each. The baseline parameters for demography and hemodynamic variables were matched in the two groups.

It was observed that mean SBP, DBP and MAP in the dexmedetomidine group remained close to the baseline throughout the study period showing a significant difference from clonidine groups following the induction interval. In present study after intubation heart rate, SBP, and DBP is increased in all patients but the increase was more in patients of clonidine group when compared to dexmedetomidine group. There was statistically significant difference in heart rate between the two groups at 1, 3 and 4 min interval after intubation (p value<0.05). No significant changes in peripheral oxygen saturation (SpO2) and cardiac rhythm (ECG) were observed in any patients of both groups. Hypotension occurred in three patients of no clinical significance. Bradycardia occurred in three patients. Oxygen saturation was maintained between 98% and 100% in all the cases throughout. Study of pattern of these relative changes gives the idea of the hemodynamic stability brought in by dexmedetomidine as compared to placebo and clonidine group. Similar trends were obtained for DBP, MAP and HR too.

A similar observation was made by Yildiz, et al. (2006) [5]. In some studies, it is observed that MAP was decreased by low dosage of dexmedetomidine (0.25 μg/kg) and MAP was increased transiently, and HR was decreased significantly by high dosage of (1–4 μg/kg) dexmedetomidine. Scheinin, et al. [6] reported that the use of α_2-agonist leads to bradycardia. Belleville, et al. [7] found that the dexmedetomidine given in 2 min in the doses of 1–2 μg/kg causes irregular ventilation and apnea episodes. Ebert, et al. [8] did not observe any episode of apnea, airway obstruction and hypoxemia with bolus doses of dexmedetomidine in their study, and they reported that the depression of respiration may be seen due to deep sedation, for the reason that the α_2 adrenergic agonists don't have an active role on the respiration center. However, in the present study a transient rise of MAP and HR was observed immediately following dexmedetomidine infusion. In another study in which the infusion of opioid and α_2 adrenergic agonists was compared, it was concluded that dexmedetomidine doesn't cause significant

respiratory depression, and it decreases the risk of apnea.

Saoyroolu AE, et al. [9] compared the clinical effects of two different doses of Dexmedetomidine (1 μg/kg and 0.5μg/kg) on hemodynamic responses of tracheal intubation and concluded that Dexmedetomidine in dose of 1 μg/kg was more effective than dexmedetomidine 0.5μg/kg [8]. In the present study, the dose of Dexmedetomidine 1 μg/kg diluted to 10ml in normal saline was infused over in 10 minutes. The selection of doses of Dexmedetomidine was also in accordance with studies done by Varshali MK, et al. [10].

Scheinin B, et al. [6] concluded in this study that dexmedetomidine causes significant reduction in circulating catecholamine with a decrease in blood pressure and heart rate [11]. In the present study, a decrease in heart rate, systolic blood pressure, diastolic blood and mean blood pressure was observed after induction in both groups but the decrease was more in patients who received dexmedetomidine as premedication.

Yildiz M, et al. [11] and Varshali M K, et al. [10] studied the effect of dexmedetomidine on hemodynamic response to laryngoscopy and intubation and intraoperative anesthetic requirement [9, 13]. They concluded that increase in blood pressure and heart rate were significantly less in dexmedetomidine group.

When dexmedetomidine premedication was compared to clonidine, a significant control of blood pressure and heart rate within a normal range was observed in the present study. Various other studies have also concluded that dexmedetomidine is effective in keeping the patient hemodynamically stable during laryngoscopy and intubation as well as throughout the intraoperative period [12-14]. Their observations were in consistence with present study.

Conclusion

Present study concluded that preremedication with dexmedetomidine in dose has significantly attenuated the hemodynamic pressor responses to laryngoscopy and intubation when compared to clonidine. Dexmedetomidine provided more stable hemodynamics during induction, laryngoscopy and intubation and is proved to be a better drug for premedication during general anesthesia.

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