ORIGINAL ARTICLE

Prospective Randomized Double-Blind Study of Effectiveness of Dexmedetomidine on Pressor Response during Laryngoscopy and Tracheal Intubation

Surekha S. Chavan[1], Madhu Chavan[1], Ilavarasan Kunasekaran[2]

[1]Department of Anesthesiology, BJGMC, Pune, Maharashtra, India, [2]Department of Anesthesia, Institute of Transplant, Madras Medical college, Chennai

ABSTRACT

Introduction: Laryngoscopy and endotracheal intubation is associated with transient increase in heart rate (HR) and arterial blood pressure due to the sympathoadrenal stimulation. It can produce deleterious effects in patients with cardiovascular and cerebrovascular disease, in the form of myocardial ischemia, pulmonary edema, and cerebral hemorrhage. Dexmedetomidine has been effective in blunting the hemodynamic response to laryngoscopy and tracheal intubation. In this study, we used dexmedetomidine in pre-operative intravenous infusion dose of 1 mcg/kg over 20 min before induction. **Aims and Objectives:** The aim of the study was to study the efficacy and safety of dexmedetomidine on attenuation of pressor response during laryngoscopy and tracheal intubation, w.r.t. (1) pressor response during laryngoscopy and tracheal intubation, (2) hemodynamic stability, and (3) any adverse effects. **Materials and Methods:** After obtaining Institutional Ethical Committee approval and written informed consent, double-blinded randomized prospective study, 100 patients requiring general anesthesia for surgery duration of 2–3 h were included. Patients were divided into two groups: Group-C (control group) normal saline 0.9%–20cc and Group-D (study group) dexmedetomidine (infusion 1 mcg l kg diluted in 20cc normal saline. All patients were premedicated with injection glycopyrrolate 0.2 mg, injection ondansetron 4 mg given intravenously before induction. Anesthesia was induced 20 min after the study drug with injection Thiopentone sodium (2.5%). Vecuronium 0.1 mg/kg was given to facilitate laryngoscopy and intubation. HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded at 1, 3, 5, and 10 min after intubation, respectively. **Results:** Basal mean HR, SBP, DBP, and MAP between Group I and group II should be written as Group C and Group D were statistically not significant ($P = 0.816$). At pre-induction, induction, 1, 3, 5, and 10 min after intubation, the HR changes, SBP, DBP, and MAP were statistically highly significant ($P < 0.01$). Maximum HR changes, SBP, DBP, and MAP were observed at 1 min after intubation in both the Groups 2. No occurrence of adverse effects in any group. **Conclusion:** From the present study, it can be concluded that, in the dexmedetomidine group, showed a significant decrease in HR, SBP, DBP, and MAP throughout the study period. In the control group, patients had significant rise in HR, SBP, DBP, and MAP throughout the study period with maximum changes observed at 1 min after intubation.

Key words: Dexmeditomidine, pressor response, general anesthesia, laryngoscopy and intubation

INTRODUCTION

Laryngoscopy and endotracheal intubation is often associated with an increased heart rate (HR) and arterial blood pressure due to the sympathoadrenal stimulation which is usually transient and lasts for 5–10 min.[1,2] Patients with cardiovascular and cerebrovascular disease, this sudden rise in HR and blood pressure can produce deleterious effects in the form of myocardial ischemia, pulmonary edema, and cerebral hemorrhage.[3-6] Dexmedetomidine has been

Address for correspondence:
Dr. Surekha S. Chavan, Department of Anesthesiology, BJGMC and SGH, Pune, Maharashtra, India.
E-mail: surekhachavan659@gmail.com

particularly effective in blunting the hemodynamic response to laryngoscopy and tracheal intubation. Dexmedetomidine is selective alpha-2 agonists (eight-fold greater selectivity than clonidine) with sedative effect without respiratory depression.

We used dexmedetomidine in pre-operative intravenous (IV) infusion dose of 1 mcg/kg over 15 min before induction. The purpose of this research was to study the dexmedetomidine as an effective agent in attenuating the pressor response during laryngoscopy and intubation.

Aims and Objectives

The aim of the study was **t**o study the efficacy and safety of dexmedetomidine on attenuation of pressor response during laryngoscopy and tracheal intubation w.r.t. (1) pressor response during laryngoscopy and tracheal intubation, (2) hemodynamic stability, and (3) any adverse effects.

MATERIALS AND METHODS

This was a double-blinded randomized prospective study. Institutional Ethical Committee approval and written informed consent were taken.

Selection of cases

Pre-anesthetic evaluation was done. Patients were divided into two groups of 50 each by computer-generated random numbers: Group-C (control group) normal saline 0.9% −20cc and Group-D (study group) dexmedetomidine (dexmedetomidine infusion in a dose of 1 mcg/kg diluted in 20 cc normal saline was given over 20 min before induction of GA).

Inclusion criteria

Age: 18–50 years, ASA: Grade I and II, Sex: Male and female, posted for elective surgery under GA, and duration of 2–3 h were included in this study.

Exclusion criteria

Known allergy to dexmedetomidine, severe bradycardia or heart block, cardiac or other systemic disease, pregnancy, patient taking any drugs (antihypertensive, oral hypoglycemic, and cardic drugs), intubation attempts lasting longer than 25 s were excluded from the study.

INVESTIGATIONS

Hemoglobin, bleeding time/clotting time/prothrombin time, urine, blood sugar level, serum electrolytes, liver function test, electrocardiogram, chest X-ray were normal at the end of all investigations list. Thorough pre-anesthetic evaluation was done patients were kept Nothing per oral (NPO) for 6 h before surgery.

Technique of anesthesia/procedure

In the operation room multipara monitors (ECG, NIBP, SPO2) were connected to patient. Basal systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, and SpO2 were recorded (To). An IV line was secured with 18G cannula and preloading with 500ml of ringer lactate done over 30 min for all patients. Following this, Group C patients received 20 ml normal saline infused over 15 min. Group D patients received IV dexmedetomidine 1 μg/kg in 20 ml normal saline infused over 20 min. SBP, DBP, MAP, HR, and SpO2 (T1) were recorded. Before induction, injection glycopyrrolate 0.2 mg and injection ondansetron 4 mg administered IV. All patients were pre-oxygenated for 3 min and anesthesia induced with 5 mg/kg. Thiopentone sodium (2.5%). After successful trial ventilation with 100% oxygen, vecuronium 0.1 mg/kg given to facilitate laryngoscopy and intubation. Oxygenation continued by positive pressure mask ventilation using Bains circuit. Maintained with 50% O_2 and 50% N_2O. At 2 min after induction, SBP, DBP, MAP, HR, and SpO2 were recorded (T2). At 3 min after induction, using laryngoscope with a Macintosh blade, intubation was done with well lubricated, appropriate sized cuffed, and disposable oral endotracheal tube by an experienced anesthesiologist within 20 s. SBP, DBP, MAP, HR, and SpO2 were recorded. After confirmation of the tube position by bilateral auscultation for air entry, cuff inflated, and tube fixed, connected to Boyle's machine through Bains circuit. Anesthesia maintained with N_2O, O_2, isoflurane, controlled ventilation with the appropriate fresh gas flow. Isoflurane was used in the lower possible concentration necessary to keep the BP and HR within 20% of the patients pre-operative baseline values. SBP, DBP, MAP, HR, and SpO2 were recorded during intubation (T3), at 1 min (T4), 3 min (T5), 5 min (T6), and 10 min (T7) after laryngoscopy and intubation and during skin incision (T8). Duration of surgery, time for intubation, and sedation score were noted. After extubation, patients were shifted to the postanaesthesia care unit, observed for 2 h for nausea, vomiting, bradycardia, and hypotension. After assessing the Steward awakening score (maximum 6), patients shifted to the ward. Post-operative follow-up for 24 h was done; side effects if any were treated and recorded.

Statistical method employed

All data presented as mean ± standard deviation. Demographic data were analyzed by "t" test. Analysis of variance for repeated measures (RMANOVA) was used to analyze changes over time. $P < 0.01$ which is statistically highly significant (HS), $P < 0.05$ which is statistically significant (S), and $P > 0.05$ which is statistically not significant (NS).

Statistical software

The statistical software SPSS version 16.0 was used for the analysis of the data, and Microsoft Word and Excel have been used to generate graphs, tables, etc.

OBSERVATION AND RESULTS

Statistical evaluation between the groups showed that the basal mean HR between Group C and Group D was statistically NS ($P = 0.816$), and at pre-induction, induction, 1, 3, 5, and 10 min after intubation, the HR changes were statistically highly significant ($P < 0.01$). Maximum HR changes were observed at 1 min after intubation in both the Groups. In Group D, there was 8.75% decrease in HR compared to basal. In Group C, there was 10.1% increase in mean HR compared to basal. In Group D, there was a constant decrease in HR from the time of pre induction until 5th min of intubation which when compared to that of Group C was statistically highly significant ($P = 0.000$).

In Group C (Control), the mean SBP 1 min after intubation was 138.68 ± 2.478 mmHg, an increase of 9.84 mmHg (7.63%) from the basal value. By 3 min mean SBP values were 133.38 ± 2.571 mmHg with a rise of 4.54 mmHg (3.52%) from the basal, and at 5 and 10 min mean SBP was 131.92 ± 3.076 mmHg and 128.92 ± 3.361 mmHg, respectively. The increase in SBP at 1 min after intubation compared to basal value was statistically significant ($P = 0.03$). In the Group D (dexmedetomidine), the basal value of mean SBP was 128.96 ± 3.386 mmHg, at pre-induction it was 127.16 ± 3.171 mmHg and 2 min after induction it was 124.88 ± 3.166 mmHg, a decrease in SBP. 1 min following intubation, the mean SBP was 127.60±2.020 mmHg representing a fall of 1.36 mmHg from the basal value (1.1%). By 3, 5, and 10 min, mean SBP values were 125.72 ± 1.666 mmHg, 119.96±15.910 mmHg, and 119.96±15.910 mmHg, respectively. The SBP continued to be below the basal value even after 10 min of intubation. The decrease in SBP at 1 min after intubation compared to basal value was statistically significant ($P = 0.01$). Statistical evaluation between the groups showed that the basal mean SBP between Group C and Group D was statistically NS (p = 0.8597), but the comparison of SBP changes between the two groups at all other levels was statistically highly significant. In Group D, SBP continued to remain below the basal value from the time of pre-induction until skin incision which was statistically significant.

Statistical evaluation between the groups showed that the basal mean DBP between Group C and Group D was statistically NS ($P = 0.9270$). The comparison between the two groups at pre-induction, induction, 1, 3, 5, and 10 min, after intubation was statistically highly significant ($P = 0.0001$). Maximum DBP changes were observed at 1 min after intubation in both the groups, compared to basal there was a 7.54% decrease in Group D in DBP and 3.22% increase in Group C. In Group D, there was a steady decrease in DBP from the time of pre-induction until 10th min of intubation which when compared to that of Group C was statistically highly significant.

Statistical evaluation between the groups showed that the basal mean MAP between Group C and Group D was statistically NS ($P = 0.9469$), but the changes observed at pre-induction, induction,1, 3, 5, and 10 min after intubation were statistically highly significant ($P = 0.0001$). Maximum MAP changes were observed at 1 min after intubation in both the Groups, compared to basal there was 14.92% decrease in MAP in Group D and 4.24% increase in MAP in Group C. In Group D, there was a constant decrease in MAP from the time of pre-induction until 10th min of intubation which when compared to that of Group C was statistically highly significant.

Table 6 show that at the end of 30 min, in Group C all patients (100%) had scores between 12 and 14 indicating excellent recovery. In Group D, 46 patients (93.33%) had a score between 12 and 14 indicating excellent recovery and 4 patients (6.66%) had scores between 9 and 11 indicating satisfactory recovery and were fit for discharge from the post-anesthesia care unit (PACU). Score <9, indicating poor recovery was not observed in any of the patients.

Side effects

Side effects attributed to the study drug (Dexmedetomidine) such as nausea, vomiting, dryness of mouth, and sedation were not observed.

DISCUSSION

Most of the general anesthetic procedures in the modern anesthetic practice are carried out with endotracheal intubation. Laryngoscopy and tracheal intubation are

Table 1: Comparison of demographic data

Variable	Group C	Group D	*P* value	Statistical significance
Age (years)	36.04+10.37	36.16+9.39	0.969	N.S.
Sex (M/F)	24/26	24/26	0.579	N.S.
ASA grade I/II	28/22	28/22	0.580	N.S.
Weight (Kg)	58.26+5.32	58.42+5.49	0.882	N.S.
Surgery Duration (min)	125.40+25.87	120.40+23.30	0.312	N.S.

Table 2: The intergroup comparison of mean HR (bpm) changes in response to laryngoscopy and intubation

Time	Group C	Group D	*P*-value	Statistical significance
T0 (Basal)	81.82±4.275	82.02±4.326	0.8166	NS
T1 (pre-induction)	82.02±4.326	79.58±3.812	0.0035	HS
T2 (2 min post-induction)	82.02±4.326	78.88±4.676	0.0007	HS
T3 (1 min post- intubation)	90.08±2.633	74.84±2.376	0.0001	HS
T4 (3 min post-intubation)	92.82±4.388	72.26±1.275	0.0001	HS
T5 (5 min post-intubation)	82.02±4.326	77.00±3.482	0.0001	HS
T6 (10 min post-intubation)	82.02±4.326	72.42±1.679	0.0001	HS
T7 (during skin incision)	91.76±3.027	72.26±1.275	0.0001	HS

HR: Heart rate

Table 3: Intergroup comparison of mean (SBP in mmHg) changes in response to laryngoscopy and intubation between saline group and dexmedetomidine group

Time	Saline	Dexmedetomidine	*P*-value	Remarks
T0 (basal)	128.84±3.33	128.96±3.386	0.8597	NS
T1 (Pre-induction)	131.90±3.02	127.16±3.171	0.0001	HS
T2 (2 min post-induction)	131.96±3.04	124.88±3.166	0.0001	HS
T3 (1 min post-intubation)	138.68±2.48	127.60±2.020	0.0001	HS
T3 (1 min post-intubation)	138.68±2.48	127.60±2.020	0.0001	HS
T4 (3 min post-intubation)	133.38±2.51	125.72±1.666	0.0001	HS
T5 (5 min post-intubation)	131.92±3.06	119.96±15.910	0.0001	HS
T6 (10 min post-intubation)	128.92±3.31	119.96±15.910	0.0001	HS
T7 (during skin incision)	135.74±2.31	119.96±15.910	0.0001	HS

(*P*<0.01) - Statistically highly significant, (*P*<0.05) - Statistically significant, (*P*>0.05) - Statistically not significant (NS)

Table 4: Intergroup comparison of mean DBP (in mmHg) changes in response to laryngoscopy and intubation between saline and dexmedetomidine group

Time	Saline	Dexmedetomidine	*P* value	Remarks
T0 (basal)	86.92±2.257	86.96±2.294	0.9270	NS
T1 (pre-induction)	87.52±2.341	85.82±2.097	0.0002	HS
T2 (2 min post-induction)	87.52±2.341	83.48±2.880	0.0001	HS
T3 (1 min post-intubation)	89.72±2.770	80.40±3.077	0.0001	HS
T4 (3 min post-intubation)	91.52±3.340	79.76±3.549	0.0001	HS
T5 (5 min post-intubation)	87.52±2.341	79.76±3.549	0.0001	HS
T6 (10 min post-intubation)	86.92±2.257	73.72±2.223	0.0001	HS
T7 (During skin incision)	89.70±2.476	79.96±3.833	0.0001	HS

(*P*<0.01) - Statistically highly significant, (*P*<0.05) statistically significant, (*P*>0.05) - statistically not Significant (NS). DBP: Diastolic blood pressure

considered as the most critical events during th administration of general anesthesia as they provoked transient but marked sympathoadrenal response manifesting as hypertension and tachycardia.[1] These responses are transitory, variable and may not be significant in otherwise normal individuals. However, in patients with a cardiovascular compromise such as hypertension, ischemic heart disease, and cerebrovascular disease and in patients with intracranial aneurysms even these transient changes in hemodynamics can result in potentially harmful effects such as left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias, and cerebral hemorrhage.[3] This is by far the most important indication for attenuation of the hemodynamic response to laryngoscopy and tracheal intubation.[6]

Table 5: Intergroup comparison of MAP (in mmHg) changes in response to laryngoscopy and intubation between the control group and dexmedetomidine group

Time	Saline	Dexmedetomidine	*P*-value	Remarks
T0 (Basal)	91.86±2.983	91.90±3.012	0.9469	NS
T1 (pre-Induction)	91.86±2.983	88.90±0.995	0.0001	HS
T2 (2 min post-Induction)	91.86±2.983	87.52±2.787	0.0001	HS
T3 (1 min post-Intubation)	87.96±1.358	78.18±2.753	0.0001	HS
T4 (3 min post-Intubation)	95.60±3.143	73.56±2.120	0.0001	HS
T5 (5 min post-Intubation)	91.76±3.027	73.56±2.120	0.0001	HS
T6 (10 min post-intubation)	91.86±2.983	72.34±1.379	0.0001	HS
T7 (during skin incision)	97.34±2.353	73.60±2.148	0.0001	HS

(*P*<0.01) - Statistically highly significant, (*P*<0.05) - Statistically significant, (*P*>0.05) - statistically not significant (NS). MAP: Mean arterial pressure

Table 6: Steward awakening score: At 30 min in PACU

Group	Number of patients	Steward awakening score (%)
Group C	50	12–14 (100)
	0	9–11
Group D	46	12–14 (93.33)
	4	9–11 (6.66)

PACU: Post-anesthesia care unit

Many methods such as use of inhalational anesthetic agents, lidocaine,[7-9] opioids,[10-12] direct acting vasodilators,[13,14] calcium channel blockers,[15-17] and β-blockers[18-20] have been tried by various authors for blunting hemodynamic responses to laryngoscopy and intubation. However, all such maneuvers had their limitations. For example, with opioids, respiratory depression and chest wall rigidity were potential problems, use of halothane was associated with dysrhythmias, calcium channel blockers produced reflex tachycardia, direct acting vasodilators needed invasive hemodynamic monitoring, and lidocaine showed inconsistent results in blunting the hemodynamic responses to laryngoscopy and intubation.

Beta-blockers are also one group of pharmacological agents employed for blunting hemodynamic response to laryngoscopy and intubation. However, they blunt the HR response better than blood pressure response.[18,19]

Hence, a drug which can blunt both the HR and blood pressure response to laryngoscopy and intubation, without having any adverse effects such as respiratory depression and post-operative nausea and vomiting (PONV), was required for the purpose.

Recently, α–2 agonists such as clonidine[21] and dexmedetomidine[22] have been tried for suppressing the response to intubation and have been found to have better effects compared to all the drugs mentioned above, without any of the side effects such as respiratory depression or increased incidence of PONV. Clonidine being less potent (α–1: α–2 = 1: 220) compared to dexmedetomidine (α–1: α–2 = 1: 1620) in its agonism to α–2 receptors.[22] Hence, dexmedetomidine may be a better drug among α–2 agonists for suppressing the hemodynamic responses to laryngoscopy and intubation.

The present study was undertaken to evaluate the effects of single premedication dose of IV dexmedetomidine in attenuating the pressor response to laryngoscopy and endotracheal intubation.

The study population consisted of 100 patients in the age group of 20–50 belonging to ASA Grade I and II which were randomly divided into two groups. Each group consists of 50 patients. Group C (control) patients received 20 ml normal saline infused over 20 min before induction. Group D (dexmedetomidine) patients received IV dexmedetomidine 1 μg/kg in 20 ml normal saline infused over 20 min before induction. Both the groups received injection glycopyrrolate 0.2 mg and injection ondansetron 4mg as premedication before induction.

Demographic criteria

Both the groups were comparable, and there was no statistically significant difference with regard to mean age, weight, gender distribution, and duration of surgery.

Dose of dexmedetomidine employed and administration

Various authors have employed IV dexmedetomidine for blunting hemodynamic responses to laryngoscopy and intubation in different doses as shown in Table 7. Tables 7-10 show that various authors have used different doses of dexmedetomidine for attenuation of the sympathetic response to intubation. Since most of the authors found dexmedetomidine effective at the dose of

Table 7: Mean changes in HR

Group	Mean changes in HR following intubation (bpm)				
	1 min	3 min	5 min	10 min	During skin Incision
Saline	+8.26	+11	+5.26	+3.64	+9.96
Dexmedetomidine	−7.97	−10.3	−12.4	−12.9	−9.26

The sign (-) denotes decrease and (+) denotes increase in HR compared to basal. HR: Heart rate

Table 8: Mean changes in SBP

Group	Mean changes in SBP following intubation (mmHg)				
	1 min	3 min	5 min	10 min	During skin incision
Saline	+9.84	+4.54	+3.08	+2.94	+6.90
Dexmedetomidine	−1.36	−3.24	−9.00	−9.00	−7.6

The sign (-) denotes decrease and (+) denotes increase in SBP compared to basal. SBP: Systolic blood pressure

Table 9: Mean changes in DBP

Group	Mean changes in DBP following intubation (mmHg)				
	1 min	3 min	5 min	10 min	During skin incision
Saline	+2.8	+4.6	+2.4	+1.2	+3.34
Dexmedetomidine	−6.56	−7.20	−7.20	−10.22	−7.2

The sign (-) denotes decrease and (+) denotes increase in DBP. DBP: Diastolic blood pressure

Table 10: Mean changes in MAP

Group	Mean changes in MAP following intubation (mmHg)				
	1 min	3 min	5 min	10 min	During skin incision
Saline	+6.9	+3.6	+1.84	+1.64	+5.84
Dexmedetomidine	−6.42	−8.14	−8.64	−9.20	−5.82

The sign (-) denotes decrease and (+) denotes increase in MAP compared to basal. MAP: Mean arterial pressure

1 µg/kg body weight in attenuating pressor response to intubation, 1 µg/kg body weight dose was chosen in this study. The dose selected in our study is similar as in the studies conducted by Yildize *et al.*,[23] Kunisawa *et al.*,[24] Ferdi *et al.*,[25] and Keniya *et al.*[26]

Method of administration

In the present study, dexmedetomidine was given IV (infusion) 1 mcg/kg in 20 ml normal saline infused over 20 min. Administration of bolus dose of dexmedetomidine rapidly, initially results in a transient increase in blood pressure and a reflex decrease in HR. The initial reaction is due to peripheral α–2 adrenoceptors stimulation of vascular smooth muscle and can be attenuated by a slow infusion over 20 min.[22] Hence, in the present study, dexmedetomidine was administered over 20 min. Kunisawa *et al.*[24] and Ferdi *et al.*[25] have employed dexmedetomidine in 20 ml NS over 20 min before induction.

Timing of administration of dexmedetomidine

From the pharmacokinetic profile, it is seen that the distribution half-life of IV dexmedetomidine is approximately 6 min.[22] Various authors Kunisawa *et al.*[24] and Ferdi *et al.*[25] have administered dexmedetomidine 20 min before induction and found better hemodynamic stability.

Hence, in the present study, dexmedetomidine was administered 20 min before induction to blunt the hemodynamic response to laryngoscopy and intubation.

Hemodynamic changes: HR

The basal mean HR in the present study in Group C and Group D was 81.82 bpm and 82.02 bpm, respectively. 1 min after intubation in Group C there was 8.80 bpm increase in mean HR compared to basal, whereas in Group D there was 7.18 bpm decrease in mean HR which was statistically significant.

Aho *et al.*[27] studied the effect of 0.3 and 0.6 µg/kg body weight of dexmedetomidine on perioperative hemodynamics and concluded that dexmedetomidine at a dose of 0.6 µg/kg body weight had effectively blunted hemodynamic response to laryngoscopy and intubation than 0.3 µg/kg body weight dose. They noted that following laryngoscopy and intubation HR at 1 min increased by

15 bpm in dexmedetomidine group and by 35 bpm in the control group. The increase in HR observed by Aho *et al.*[27] is probably due to peripheral alpha-2B adrenoceptors stimulation of vascular smooth muscles. In the present study, dose of 1 μg/kg was used and an increase was not observed. Basar *et al.*[28] used 0.5 μg/kg body weight of dexmedetomidine in 10 ml saline over 60 s and noted that the following laryngoscopy and intubation HR decreased by 8 bpm in dexmedetomidine group and increased by 10 bpm in control group which was statistically highly significant. Kunisawa *et al.*[24] used 1 μg/kg body weight of dexmedetomidine with fentanyl and found that, though there was a decrease in HR, the decrease in blood pressure was suppressed. The authors opined that vasoconstrictive effects of dexmedetomidine through α-2 adrenoceptors which are located in vascular smooth muscle might be responsible for this suppression. They noted that following laryngoscopy and intubation, HR at 1 min decreased by 7 bpm in the dexmedetomidine group and increased by 12 bpm in the control group which was statistically significant. Basar *et al.*[28] and Kunisawa *et al.*[24] have found a statistically significant ($P < 0.05$) obtundation of HR response to intubation at 1 min which is similar to our study. At 3 min after intubation decrease in mean HR in dexmedetomidine group was 10.3 bpm whereas in control group mean HR increased by 11 bpm compared to basal which was statistically highly significant ($P = 0.000$) and is in concurrence with Ferdi *et al.*[25] who also observed a decrease of 5 bpm in the dexmedetomidine group and an increase of 14 bpm in the control group.

At 5 min, there was further decrease in mean HR by 12.4 bpm in the dexmedetomidine group but the mean HR in the control group increased by 5.26 bpm compared to basal which was statistically highly significant ($P = 0.000$) and is similar to Ferdi *et al.*,[25] Keniya *et al.*,[26] and Scheinin *et al.*[29]

At 10 min, there was decrease in mean HR by 9.26 bpm in the dexmedetomidine group compared to basal value whereas in control group the HR increased by 9.96 bpm which was statistically highly significant ($P = 0.000$). Although majority of studies are done only for 5 min, Basar *et al.*[28] observed a decrease in HR by 5 bpm in the dexmedetomidine group and an increase in HR by 5 bpm in control group at 10 min after intubation. The results of our study correlate with the study of Basar *et al.*[28]

The decrease in HR is due to the inhibition of the central sympathetic outflow overriding the direct stimulant effects and stimulation of presynaptic alpha-2 adrenoceptors, leading to a decrease in norepinephrine release.[30]

SBP

In the present study, the basal mean SBP in Group C and Group D was 128.84 mmHg and 128.96 mmHg, respectively. 1 min after intubation in Group C there was 9.16 mmHg increase in SBP compared to basal whereas in Group D there was 1.36 mmHg decrease in SBP which was statistically significant. At 3, 5, and 10 min, after intubation in Group D the decrease in SBP when compared to basal was 3.24 mmHg, 9 mmHg, and 9mmHg, respectively. In Group C, there was an increase in SBP at 1 and 3 min but returned to basal at 5 min after intubation.

Scheinin *et al.*,[29] with a dose of 0.6 μg/kg, observed an increase in SBP by 18 mmHg immediately after intubation compared to the values after induction in dexmedetomidine group, but the SBP was less than the basal values.

They also observed an increase in SBP by 25 mmHg in the control group compared to basal value which returned to below the basal value by 10th min and is in concurrence with our study. Jaakola *et al.*[31] have observed a fall of 17 mmHg in SBP 5 min after intubation in dexmedetomidine group and control group an increase of SBP by 10 mmHg, compared to the basal values and is similar to our study.

Aho *et al.*[27] noted an increase in SBP by 18 mmHg and 48 mmHg in dexmedetomidine group and control group, respectively, at 1 min after intubation which was statistically significant. In this study, in dexmedetomidine group a dose of 1 μg/kg was administered in the form of infusion over 15 min with adequate preloading, and a decrease in SBP of 8 mmHg was observed whereas Aho *et al.*[27] observed an increase in SBP with a dose of 0.3 μg/kg and 0.6 μg/kg administered IV over 1 min. The difference between in SBP observed may be attributed to the difference in dosage and mode of administration. In our study, SBP decreased from pre-induction and continued to remain below basal value until 10 min after intubation which was statistically significant.

Many authors have observed a transient increase of the blood pressure and a reflex decrease in HR, especially in young healthy patients following dexmedetomidine bolus doses. The initial reaction can be explained by the peripheral alpha-2 adrenoceptors stimulation of vascular smooth muscles and can be attenuated by a slow infusion. We have not observed this transient increase in blood pressure probably due to slow infusion over 20 min and adequate preloading.

DBP

The basal mean DBP in the present study in Group C and Group D was 86.92 mmHg and 86.96 mmHg, respectively. There was a steady decrease in DBP from pre-induction in Group D. At 1 min after intubation, the DBP was 6.56mmHg less compared to that of the basal value whereas in Group C there was 3.2 mmHg increase in DBP which was statistically significant. At 3, 5, and 10 min, after intubation the fall in DBP in Group D compared to basal value was 7.20 mmHg, 7.20 mmHg, and 10.22 mmHg, respectively.

Jaakola *et al.*[31] observed a fall of DBP by 10 mmHg in dexmedetomidine group and an increase of 16 mmHg in the control group compared to basal values which are similar to our study. They noted an increase of 5 mmHg post-induction in dexmedetomidine group compared with 17 mmHg of increase in the control group. This correlates with our study.

Ferdi *et al.*[25] also noticed a fall in DBP by 10 mmHg at 1st min and 13 mmHg at 5th min and is similar with our study.

In the study done by Kunisawa *et al.*,[24] there was a fall of DBP by 5 mmHg after intubation compared to the basal value in dexmedetomidine group. The study done by Kunisawa *et al.*[24] concurred with our study.

MAP

In the present study, basal mean MAP in Group C and Group D was 91.86 mmHg and 91.90 mmHg, respectively. There was a steady decrease in MAP from pre-induction in Group D. At 1 min after intubation the MAP was 13.72 mmHg less compared to basal value whereas in Group C there was 5 mmHg increase in MAP which was statistically significant. At 3, 5, and 10 min, the fall in MAP in Group D was 6.42 mmHg, 8.14 mmHg, and 9.20 mmHg, respectively.

Mowafi *et al.*[32] observed an increase in MAP by 5 mmHg immediately after intubation in dexmedetomidine group compared to an increase of 12 mmHg in the control group in comparison with values after induction. Basar *et al.*[28] found a decrease in MAP by 10 mmHg in dexmedetomidine group at 10th min compared to basal value which is almost similar to our study. in the present study, the decrease observed in MAP is due to the inhibition of central sympathetic outflow overriding the direct stimulant effects.

Recovery score

In PACU, steward awakening score was monitored once in 15 min for 1 h. 46 patients (93.33%) in Group D had a steward awakening score between 12 and 14 indicating excellent recovery and 4 patients (6.66%) had scores between 9 and 11 indicating satisfactory recovery and were fit for discharge from the PACU. Scores <9, indicating poor recovery was not observed in any of the patients. Yildiz *et al.*[23] applied steward awakening score at 5 and 10 min after extubation and observed that at 10 min all patients had excellent recovery.

Side effects

No side effects were observed.

CONCLUSION

From the present study, it can be concluded that, in dexmedetomidine group, showed significant decrease in HR, SBP, DBP, and MAP throughout the study period. In the control group, patients had significant rise in HR, SBP, DBP, and MAP throughout the study period with maximum changes observed at 1 min after intubation. Side effects were not observed in any patients and recovery was satisfactory.

Hence, dexmedetomidine in the dose of 1 μg/kg as IV infusion, given 20 min before induction can be used safely to attenuate the pressor response to laryngoscopy and intubation without significant side effects.

However, the study has to be done on a larger population and in other associated comorbid risks for further evaluation.

REFERENCES

1. Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect on heart-surgery. Gynaecol Obstet 1940;70:157.
2. Derbyshire DR, Chmielewski A, Fell D, Vater M, Achola K, Smith G, *et al*. Plasma catecholamine responses to tracheal intubation. Br J Anaesth 1983;55:855-60.
3. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anesthesiology 1977;47:524-5.
4. Karl. Insertion of LMA in place of endotracheal intubation to attenuate the cardiovascular response. Indian J Anaesth 1999;43:30-5.
5. Kumar. Blocking glossopharyngeal and superior laryngeal nerves to attenuate the cardiovascular response to laryngoscopy and endotracheal intubation. Indian J Anaesth 1993;41:20-5.
6. King BD, Harris LC Jr., Greifenstein FE, Elder JD Jr., Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology 1951;12:556-66.
7. Denlinger JK, Ellison N, Ominsky AJ. Effects of intratracheal lidocaine on circulatory responses to tracheal intubation. Anesthesiology 1974;41:409-12.
8. Stoelting RK. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation: Influence of viscous or intravenous lidocaine. Anesth Analg 1978;57:197-9.
9. Stoelting RK. Circulatory changes during direct laryngoscopy and tracheal intubation: Influence of duration of laryngoscopy with or without prior lidocaine. Anesthesiology 1977;47:381-4.
10. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (Bayl Univ Med Cent) 2001;14:13-21.
11. Scheinin B, Lindgren L, Randell T, Scheinin H, Scheinin M. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. Br J Anaesth 1992;68:126-31.
12. Jaakola ML, Ali-Melkkilä T, Kanto J, Kallio A, Scheinin H, Scheinin M, *et al*. Dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in patients undergoing ophthalmic surgery. Br J Anaesth 1992;68:570-5. Burstein CL, Lopinto FJ, Newman W. Electrocardiographic studies during endotracheal intubation. I. Effects during usual routine technics. Anesthesiology 1950;11:224-37.
13. Burstein CL, Lopinto FJ, Newman W. Electrocardiographic studies during endotracheal intubation. I. Effects during usual routine technics. Anesthesiology 1950;11:224-37.

14. Russell WJ, Morris RG, Frewin DB, Drew SE. Changes in plasma catecholamine concentrations during endotracheal intubation. Br J Anaesth 1981;53:837-9.
15. Yazbek-Karam VG, Aouad MM. Perioperative uses of dexmedetomidine. Middle East J Anaesthesiol 2006;18:1043-58.
16. Drew GM, Whiting SB. Evidence for two distinct types of postsynaptic alpha-adrenoceptor in vascular smooth muscle *in vivo*. Br J Pharmacol 1979;67:207-15.
17. Hunter JC, Fontana DJ, Hedley LR, Jasper JR, Lewis R, Link RE, *et al*. Assessment of the role of alpha2-adrenoceptor subtypes in the antinociceptive, sedative and hypothermic action of dexmedetomidine in transgenic mice. Br J Pharmacol 1997;122:1339-44.
18. Aho M, Lehtinen AM, Erkola O, Kallio A, Korttila K. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. Anesthesiology 1991;74:997-1002.
19. Basar H, Akpinar S, Doganci N, Buyukkocak U, Kaymak C, Sert O, *et al*. The effects of preanesthetic, single-dose dexmedetomidine on induction, hemodynamic, and cardiovascular parameters. J Clin Anesth 2008;20:431-6.
20. Maze M, Tranquilli W. Alpha-2 adrenoceptor agonists: Defining the role in clinical anesthesia. Anesthesiology 1991;74:581-605.
21. Shribman AJ, Smith G, Achola KJ. Cardiovascular and catecholamine responses to laryngoscopy with and without tracheal intubation. Br J Anaesth 1987;59:295-9.
22. Abramov D, Nogid B, Nogid A. Drug forecast. P and T 2005;30:158.
23. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S, *et al*. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: Perioperative haemodynamics and anaesthetic requirements. Drugs R D 2006;7:43-52.
24. Kunisawa T, Suzuki A, Takahata O, Iwasaki H. High dose of dexmedetomidine was useful for general anesthesia and post-operative analgesia in a patient with postpolio syndrome. Acta Anaesthesiol Scand 2008;52:864-5.
25. Menda F, Köner O, Sayin M, Türe H, Imer P, Aykaç B, *et al*. Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response to endotracheal intubation in patients undergoing fast-track CABG. Ann Card Anaesth 2010;13:16-21.
26. Keniya VM, Ladi S, Naphade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth 2011;55:352-7.
27. Aho M, Lehtinen AM, Erkola O, Kallio A, Korttila K. The effect of intravenously administered dexmedetomidine on perioperative hemodynamics and isoflurane requirements in patients undergoing abdominal hysterectomy. Anesthesiology 1991;74:997-1002.
28. Al-Metwalli RR, Mowafi HA, Ismail SA, Siddiqui AK, Al-Ghamdi AM, Shafi MA, *et al*. Effect of intra-articular dexmedetomidine on postoperative analgesia after arthroscopic knee surgery. Br J Anaesth 2008;101:395-9.
29. Scheinin H, Aantaa R, Anttila M, Hakola P, Helminen A, Karhuvaara S, *et al*. Reversal of the sedative and sympatholytic effects of dexmedetomidine with a specific alpha2-adrenoceptor antagonist atipamezole: A pharmacodynamic and kinetic study in healthy volunteers. Anesthesiology 1998;89:574-84.
30. Bührer M, Mappes A, Lauber R, Stanski DR, Maitre PO. Dexmedetomidine decreases thiopental dose requirement and alters distribution pharmacokinetics. Anesthesiology 1994;80:1216-27.
31. Jaakola ML, Ali-Melkkilä T, Kanto J, Kallio A, Scheinin H, Scheinin M, *et al*. Dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in patients undergoing ophthalmic surgery. Br J Anaesth 1992;68:570-5.
32. Mowafi HA, Aldossary N, Ismail SA, Alqahtani J. Effect of dexmedetomidine premedication on the intraocular pressure changes after succinylcholine and intubation. Br J Anaesth 2008;100:485-9.

How to cite this article: Chavan SS, Chavan M, Illavarasan. Prospective Randomized Double-Blind Study of Effectiveness of Dexmedetomidine on Pressor Response during Laryngoscopy and Tracheal Intubation. J Clin Res Anesthesiol 2018;1(2):1-9.