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Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation with single dose dexmedetomidine in controlled hypertensive patients: prospective randomized double-blind study

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Abstract

Background: Laryngoscopy and endotracheal intubation may be associated with adverse events as hypertension, tachycardia, and increased serum concentrations of catecholamines. These events are serious in patients with cardiac diseases or hypertension. This work was designed to assess the effects of single dose dexmedetomidine on hemodynamic response to endotracheal intubation in controlled hypertensive patients.

Methods: Seventy patients were randomly assigned into two equal groups; dexmed group received intravenous dexmedetomidine 0.5 mcg/kg diluted to 20 ml with 0.9% sodium chloride and control group received 20 ml of 0.9% sodium chloride. Changes in heart rate, systolic, diastolic, and mean blood pressures were recorded in both groups at baseline, after 5 min of study drug infusion, 3 min after induction and prior to intubation, 1 min after intubation, 3 min after intubation, and 5 min after intubation.

Results: Dexmed group had a significantly lower heart rate, systolic blood pressure, diastolic blood pressure, and mean blood pressure at 1 min, 3 min, and 5 min after intubation.

Conclusions: Single dose dexmedetomidine attenuated the hemodynamic response to laryngoscopy and intubation in controlled hypertensive patients.

Trial registration: ClinicalTrial.Gov (NCT03204006) (March2018).

Keywords: Controlled, Dexmedetomidine, Direct laryngoscope, Hemodynamic response, Hypertension

Background

Instrumentation of the upper airway for intubation is known to cause the hemodynamic pressor response. This stress response may be associated with an increase in blood pressure, heart rate, and serum catecholamines (Vucevic et al. 1992). These adverse effects lead to an increase in heart workload which, in turn, may cause, in susceptible persons, perioperative myocardial ischemia and cardiac failure. Furthermore, these events are undesirable in cardiac patients undergoing any type of surgical intervention (Slogoff and Keats 1985).

The hemodynamic response that occurred during endotracheal intubation is centrally mediated sympathetic reflex secondary to stretching of the laryngeal and pharyngeal tissue. This hemodynamic response is characterized by a short-term stress response. However, it has serious effects on cerebral and coronary circulation,

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especially in patients with systemic hypertension (Barak et al. 2003).

Previous investigators revealed that hypertensive patients would experience periods of circulatory instability during general anesthesia either during endotracheal intubation or following emergence from anesthesia. These effects are attributed to the release of endogenous catecholamines (Hayashi and Maze 1993). Fentanyl (Gurulingappa et al. 2012) and esmolol (Sintetos et al. 1987) have been used to attenuate the stress response associated with endotracheal intubation and surgery.

Dexmedetomidine is an imidazole-derivative adrenoceptor agonist selective to alpha-2 receptors. It causes a reduction in the central noradrenergic activity of locus ceruleus and decreases in the production of catecholamines (Fox et al. 1977). This study was designed to assess the effects of single dose of dexmedetomidine on hemodynamic response to tracheal intubation in controlled hypertensive patients. We hypothesized that the use of dexmedetomidine would attenuate the hemodynamic response caused by endotracheal intubation.

Methods

After obtaining approval from our Ethical Committee (no: 17100267), we conducted this prospective, randomized, double-blind placebo controlled clinical study at the Department of Anesthesia and Intensive Care Unit during the period between April 2018 and March 2020. A written informed consent from all participants was obtained. The study was registered at ClinicalTrial.gov and the number is NCT03204006. The study was conducted and adherent to the CONSORT guidelines and to the regulations and amendments of Helsinki Declaration.

Seventy patients with controlled hypertension undergoing general anesthesia were enrolled in the study with the ages ranging from 20 to 60 years old with American Society of Anesthesiologists (ASA) class II. Based on join national committee on hypertension (JNC-8), hypertension was defined as systolic blood pressure >140 mmHg and or diastolic blood pressure > 90 mmHg.

The exclusion criteria included (1) failure to obtain patient's consent or patient's refusal; (2) history of myocardial infarction or abnormal electrocardiogram at the time of anesthesia; (3) cardiovascular, pulmonary, renal, or hepatic diseases; (4) patients on beta blockers; and (5) patient with difficult airway; laryngoscopy and intubation exceeded 20 s or requiring > 2 attempts.

Enrolled patients were randomly assigned into two equal groups: control which received 20 ml sodium chloride 0.9% and dexmed group which received intravenous dexmedetomidine 0.5 mcg/kg diluted to 20 ml with sodium chloride 0.9% as infusion over 10 min (Basar et al. 2008). Each group had 35 patients. Randomization was based on computer-generated codes maintained in sequentially numbered opaque envelopes. The infusions were prepared by an independent anesthesiologist not involved in this study.

Preoperative assessment, including history taking, physical examination, and review of the results of routine investigations, was done for all patients. Patients' demographics and clinical data, such as age, weight, and gender, were recorded.

Standard monitors were connected to all patients which included 5-lead electrocardiogram, pulse oximetry, non-invasive blood pressure, and capnography. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP) were measured before induction of anesthesia as a baseline reading. A standard protocol of anesthetic management was used for all patients. Pre-oxygenation by O_2 100% for 3 min after intravenous access. Sodium chloride 0.9% was infused at rate of 4 ml/kg/h. The study drug (dexmedetomidine 0.5 mcg/kg or sodium chloride 0.9%) was administered intravenously using a syringe pump over 10 min. It started and finished just before induction of anesthesia.

General anesthesia was induced by fentanyl 1μg /kg, propofol 1.5–2 mg/kg, intravenous lignocaine 1 mg/kg, and cisatracurium 0.15 mg/kg for endotracheal intubation. Trachea was intubated after 3 min of mask ventilation with oral endotracheal tube of appropriate size under direct laryngoscopy. Isoflurane inhalational anesthetic with 50% oxygen in air and cisatracurium 0.03 mg/kg was used for maintenance of anesthesia. The lungs were mechanically ventilated to keep intra-operative end-tidal carbon dioxide ($EtCO_2$) between 35 and 40 mmHg. At the end of surgery and discontinuing isoflurane inhalation, neostigmine 2.5 mg and atropine 1 mg were used for muscle relaxant reversal.

Table 1 Demographic data of both studied groups

	Dexmed group (*n*=35)		Control group (*n*=35)		*P* value
	No.	%	No.	%	
Gender					
Male	18	51.4	19	54.3	0.811
Female	17	48.6	16	45.7	
Age					
Mean± SD	52.23±4.15		51.37±4.13		0.389
Weight					
Mean± SD	88.14±5.9		89.51±5.66		0.325

Data expressed as mean (SD), frequency (percentage). *P* value was significant if < 0.05 No significant differences between the two groups

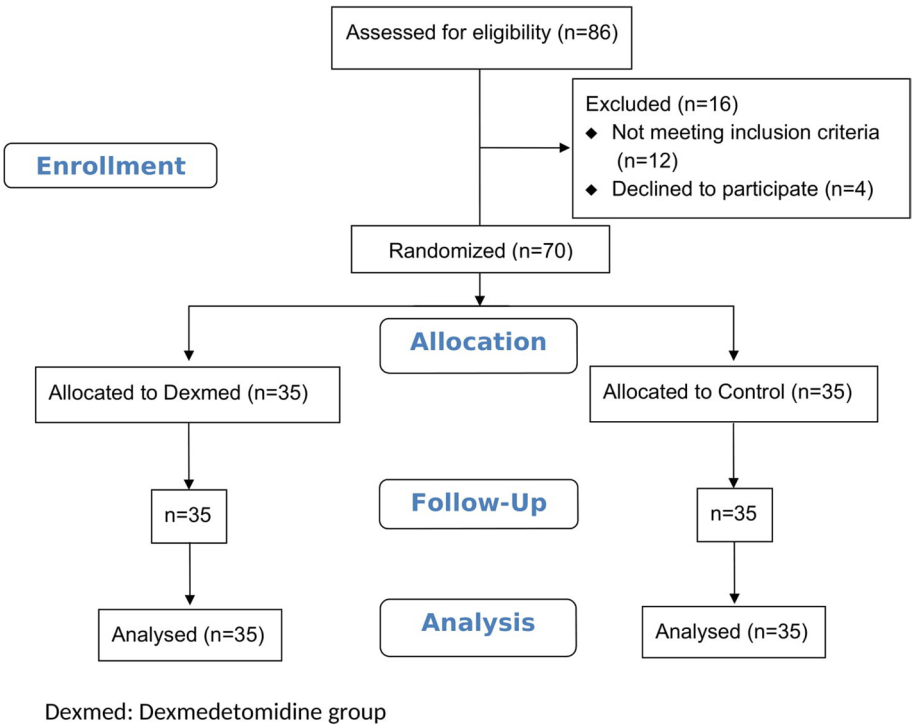

Fig. 1 Consort flow diagram

Assessment parameters

Hemodynamic variables (HR, SBP, DBP, MBP) were recorded at baseline, after 5 min of study drug infusion, 3 min after induction and prior to intubation, 1 min after intubation, 3 min after intubation, and 5 min after intubation. Frequency of hypotension, bradycardia, and change in electrocardiogram were recorded. Bradycardia (heart rate<60 beat\min) was managed with intravenous atropine 0.5 mg while hypotension (mean arterial blood pressure <20% of baseline) was treated with intravenous ephedrine 5 mg. The primary outcomes of this study were the changes in the heart rate pre- and post-induction of anesthesia. Secondary outcomes included systolic blood pressure, diastolic blood pressure, mean arterial pressure, and occurrence of hypotension or bradycardia.

Table 2 Changes in heart rate in both studied groups

Heart rate	Dexmed group (n=35) Mean± SD	Control group (n=35) Mean± SD	P value
TB	87.14±12.62	85.46±11.93	0.568
TA	78.46±9.85	76.2±7.94	0.295
T0	72.63±7.73	71.46±6.77	0.502
T1	76.97±6.96	93.71±10.6	<0.05
T3	71.71±6.1	85.11±7.95	<0.05
T5	69.26±5.56	79.8±7.88	<0.05

Data expressed as mean (SD). *P* value was significant if < 0.05. *TB*, baseline; *TA*, 5 min after study drug infusion; *T0*, 3 min after induction and prior to intubation; *T1*, 1 min after intubation; *T3*, 3 min after intubation; *T5*, 5 min after intubation

Statistical analysis

Data was collected and analyzed using SPSS (Statistical Package for the Social Science, version 20, IBM, Armonk, NY). Continuous data was expressed in the form of mean ± SD or median (range) while nominal data was expressed in the form of frequency (percentage).

Chi-square test was used to compare the nominal data while Student's *t*-test was used to compare means of two groups. *P* value was significant if < 0.05.

Sample size calculation

The primary outcome of this study was the change in the heart rate. The sample size was selected by using estimates of the sample size proportions (α=0.05) and a power of 80%. If dexmedetomidine reduces the heart rate by 20%, the estimated sample size would be 32 patients in each group. We enrolled 35 patients in each group to compensate for possible drop out.

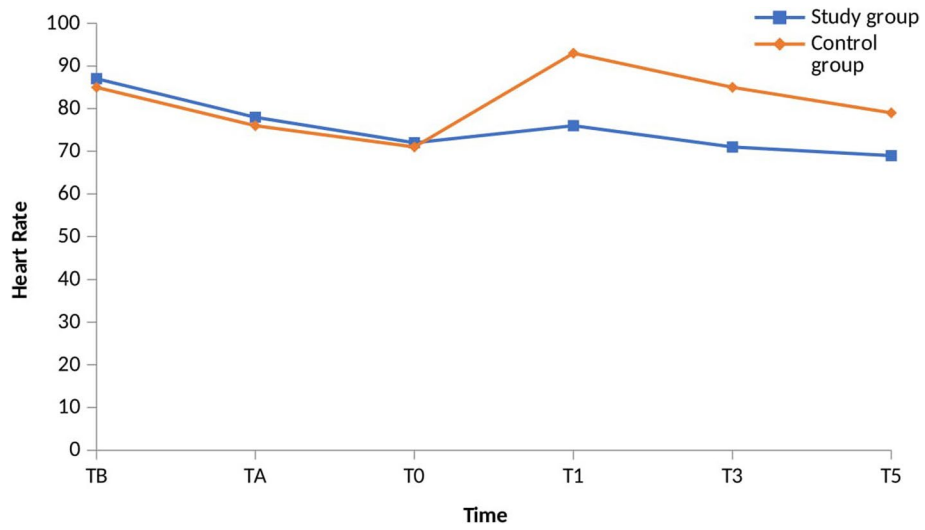

Fig. 2 Changes in heart rate in both studied groups

Results

Figure 1 shows the study flow for the studied patients. No significant differences were present between the two studied groups regarding age, gender, or weight (Table 1).

Both groups had insignificant differences regarding heart rate at baseline, 5 min of study drug infusion, and 3 min after induction of anesthesia and prior to intubation. However, at 1 min, 3 min, and 5 min after intubation, the dexmed group had significantly lower heart rate (Table 2, Fig. 2).

Both studied groups had insignificant differences regarding SBP, DBP, and MBP at baseline and 3 min after induction of anesthesia. However, the dexmed group had significantly lower values at 5 min after study drug infusion and at 1 min, 3 min, and 5 min after intubation (Table 3, Fig. 3). No side effects have been recorded in both groups such as bradycardia and hypotension. None of the patients needed drug intervention.

Discussion

The present study showed that single dose dexmedetomidine attenuated the hemodynamic response to laryngoscopy and endotracheal intubation in controlled hypertensive patients. Dexmedetomidine causes a variety of pharmacological effects. It has analgesic and dose-dependent sedative effects and decreases sympathetic tone. However, it does not cause respiratory depression. It has been used as an adjuvant in anesthesia practice because of its favorable pharmacological properties (Barak et al. 2003).

The stress response to intubation and surgery may be modulated using dexmedetomidine as it decreases the sympathetic outflow (Barak et al. 2003). It has been found that dexmedetomidine attenuated the sympathoadrenal response to intubation that resulted in the attenuation of heart rate with a dose of 0.6 mcg/kg (Jaakola et al. 1992).

Pre-induction dexmedetomidine attenuated the hemodynamic responses to intubation, reduced the required

Table 3 Changes in blood pressure in both studied groups

	Dexmed group (*n*=35) Mean± SD	Control group (*n*=35) Mean± SD	*P* value
Systolic blood pressure			
TB	133.11±7.53	131.4±9.83	0.416
TA	119±5.72	125.46±7.91	<0.05
T0	108.86±5.61	108.26±5.62	0.656
T1	114.09±6.09	133.43±8.27	<0.05
T3	106.57±6	119.06±6.6	<0.05
T5	103.09±4.26	108.69±5.78	<0.05
Diastolic blood pressure			
TB	84.54±5.24	83.23±6.73	0.365
TA	73.46±4.84	77.77±6.76	0.003
T0	64.8±5.3	62.97±6.82	0.215
T1	69.89±4.57	80.31±9.84	<0.05
T3	64.09±4.45	69.34±7.01	<0.05
T5	59.77±3.57	62.46±5.59	0.020
Mean blood pressure			
TB	100.77±3.99	99.34±4.55	0.167
TA	88.6±4.15	93.66±5.31	<0.05
T0	79.43±4.28	78.03±5.32	0.229
T1	84.69±4.03	97.66±7.75	<0.05
T3	78.2±4.12	86.23±5.76	<0.05
T5	74.09±2.55	77.86±4.32	<0.05

Data expressed as mean (SD). *P* value was significant if < 0.05. *TB*, baseline; *TA*, 5 min after study drug infusion; *T0*, 3 min after induction and prior to intubation; *T1*, 1 min after intubation; *T3*, 3 min after intubation; *T5*, 5 min after intubation

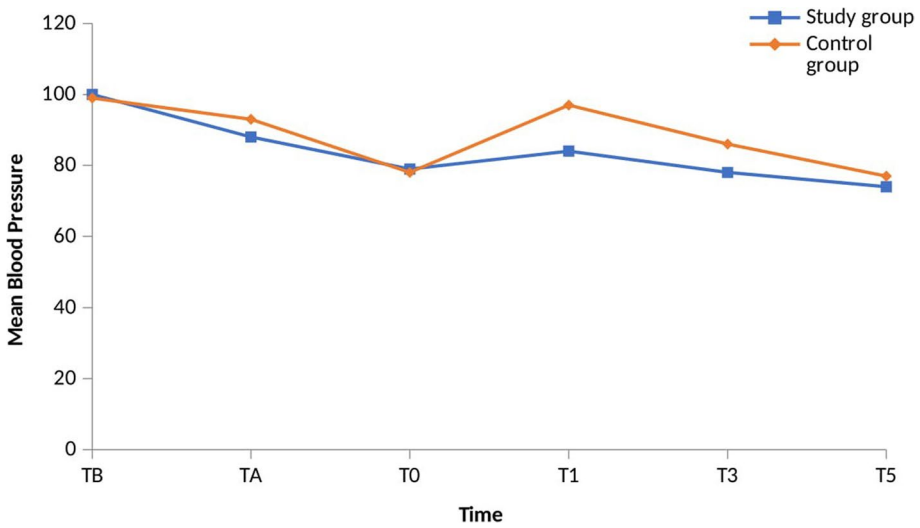

Fig. 3 Changes in mean blood pressure in both studied groups

thiopentone dose, decreased noradrenaline levels in mixed venous blood, and decreased intraoperative and postoperative opioids consumption (Scheinin et al. 1992).

Furthermore, dexmedetomidine attenuated the hemodynamic stimulation to intubation and extubation (Lawrence and De Lange 1997). The bradycardia observed in Lawrence et al.'s (Lawrence and De Lange 1997) study may be attributed to the bolus administration. However, we have used dexmedetomidine as an infusion to avoid the occurrence of side effects. The benefits of dexmedetomidine in blunting the pressor response are advantageous, especially in high risk and hypertensive patients.

Bloor et al. (Bloor et al. 1992) demonstrated that the slow infusion of dexmedetomidine over 10 min could avoid the transient increase in blood pressure caused by bolus administration (Bloor et al. 1992). Moreover, dexmedetomidine was successful in blunting hemodynamic responses in patients undergoing vascular surgery and decreasing the risk of cardiac events (Talke et al. 1995).

Dexmedetomidine is better than clonidine because of the following reasons: Dexmedetomidine has a short elimination half-time of 2 h. It is more selective for alpha 2 receptors than clonidine. Moreover, atipamezole, a sedative agent, may act as a reversal agent for dexmedetomidine by increasing the central turnover of noradrenaline (Yazbek-Karam and Aouad 2006).

The hemodynamic response to intubation is more pronounced in hypertensive patients compared to normotensive one. The complications associated with laryngoscopy and intubation are more common and dangerous in hypertensive patients than normotensive ones (Kovac 1996). Thus, attenuating the pressor response in hypertensive patients to avoid undesirable complications is important.

The limitations of our study include not using invasive blood pressure monitoring, which provides a beat-to-beat recording of the hemodynamics. We did not measure plasma catecholamine because of its cost. Also, our study was for short duration; we did not extend it to include extubation time and postoperative sedation. Finally, we did not compare different doses of dexmedetomidine.

Conclusions

Pretreatment with single-dose dexmedetomidine 0.5 mcg/kg over 10-min infusion prior to induction of anesthesia is a safe and effective method to attenuate the hemodynamic response to laryngoscopy and intubation in controlled hypertensive patients.

Abbreviations

ASA: American Society of Anesthesiologists; HR: Heart rate; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MBP: Mean blood pressure; $EtCO_2$: End-tidal carbon dioxide.

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Authors' contributions

EI: Study design, data analysis, manuscript drafting, and final revision of the manuscript. AM: Patient enrollment, data collection, and final revision of the manuscript. MA: Study design, manuscript drafting, and final revision of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data is available on request.

Declarations

Ethics approval and consent to participate
A written informed consent from all participants was obtained.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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