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Original Article

Effect of Different Doses of Dexmedetomidine on Hemodynamic Response During Laryngoscopy and Tracheal Intubation in Endoscopic Neurosurgeries

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ABSTRACT

Background: Direct laryngoscopy and endotracheal intubation are the most frequently performed procedure. The noxious stimuli generated by the process of intubation leads to a period of extreme hemodynamic stress which is accompanied by intense sympathetic activity. This response mechanism to laryngoscopy and orotracheal intubation is somatovisceral reflexes.

Aim of the Study: The aim of this study is to assess the optimal dose of dexmedetomidine for the purpose of attenuation of hemodynamic response during laryngoscopy and tracheal intubation.

Materials and Methods: This study is prospective, randomized, and double-blind study on 144 patient divided into four groups. Groups I, II, III, and VI comprise dexmedetomidine 0.5 μg/kg, 0.75 μg/kg, 1 μg/kg, and 20 ml of NS. The study solution was infused 10 min before the standard general anesthesia in endoscopic neurosurgical procedure. Heart rate, blood pressure, and oxygen saturation were measured at specified time interval and analyzed. Sedation was also assess using Richmond Agitation Sedation Scale (RASS) just after dexmedetomidine infusion and at 10 min after completion of dexmedetomidine infusion.

Result: Neurosurgical patients are subset of patients in which induction from anesthesia is met with hemodynamic perturbations which, in turn, may lead to disastrous complication such as intracranial hematoma and raised intracranial pressure. Our study demonstrated that dexmedetomidine when used preoperatively as a premedicament in doses at 0.75 ug/kg in infusion from, provided the most acceptable hemodynamics in the peri induction period with an acceptable level of twilight.

Key words: Intubation, Laryngoscopy, Dexmedetomidine

INTRODUCTION

In 1921, Rowbatham and Magill had studied and practiced endotracheal intubation. The noxious stimuli generated by the process of intubation leading to a period of extreme hemodynamic stress which is accompanied by intense sympathetic activity.[1]

The hemodynamic changes brought about by laryngoscopy and intubation was first described by Reid and Brace.[2]

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Direct laryngoscopy and endotracheal intubation are the most frequently performed procedures, but their clinical benefits are not without a few undesirable effects due to afferent vagal stimulation and an efferent sympathoadrenal response.[3] These response mechanism to laryngoscopy and orotracheal intubation is somatovisceral reflexes.[4] Proprioceptors at the base of the tongue are stimulated during laryngoscopy leads to impulse dependent increases of systemic blood pressure, heart rate, and plasma catecholamine concentrations. Subsequent orotracheal intubation and passage of tube recruits additional receptor that elicit augmented hemodynamic and epinephrine responses as well as some vagus mediated inhibition of the heart.[5] The magnitude of response is directly proportional to the force and duration of laryngoscopy.[6] The response is initiated within 5 s of laryngoscopy, peaks in 1–2 min and returns to normal

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levels by 5 min. This is called vascular contraction reflex.[7] These changes are usually short lived and well tolerated by normal patients. However, in patients with cardiovascular disease, it can incite harmful effects such as myocardial ischemia, ventricular dysrhythmias, ventricular failure, and pulmonary edema. It can also lead to cerebrovascular accidents in susceptible patients.[8] The circulatory responses evolved by endotracheal intubation is not adequately suppressed by intravenous anesthetic induction agents.[9]

Alpha-2 agonists such as dexmedetomidine and clonidine reduce operational stimulus during surgery which is caused by sympathetic outflow and decreases cardiovascular behavior.[10] These drugs decreases sympathetic activity, which are beneficial for the cases.[11]

Its hemodynamic effects are predictable and dose-dependent. Dexmedetomidine, at clinically effective dosages, does not depress respiration, and therefore does not interfere with extubation. This pharmacological profile renders it suitable for premedication for general anesthesia in intravenous doses varying from 0.25 to 1 μg/kg for the attenuation of intubation responses, but the optimal dose not yet established.[12] Our study is to assess the effect of different doses of dexmedetomidine on hemodynamic response during laryngoscopy and tracheal intubation in endoscopic neurosurgeries at the Department of Anaesthesiology, N.S.C.B. Medical College Jabalpur (M.P.).

Aims and Objectives

Primary objectives

The primary objective of the study is to assess the optimal dose of dexmedetomidine for the purpose of attenuation of hemodynamic response during laryngoscopy and tracheal intubation.

Secondary objectives

1. The secondary objective of the study is to assess the sedation after 10 min of completion of dexmedetomidine infusion.
2. Any adverse effect of dexmedetomidine such as hypotension, bradycardia, respiratory depression, and fall in oxygen saturation.

MATERIALS AND METHODS

After obtaining approval from Institutional Ethics Committee, this study was conducted at Govt. N.S.C.B. Medical College and Hospital, Jabalpur.

Design of Study

- This was a prospective double-blind randomized study.

Conduct of Study

- The study was conducted in the Department of Anaesthesiology of N.S.C.B. Medical College, Jabalpur M.P.

Duration of Study

The duration of the study was from March 1, 2018, to August 31, 2019

Sample Size

- In our study, the total sample size of 144 was divided into four groups of 36 patients each. Following formula was used to estimate the require sample size in the study.

$$n = \frac{Z^2\ p\ q}{d^2}$$

where
n = Sample size
Z = 1.96 at 95% CI, 80% power and 5% alpha
p = Probability which was assumed 0.63
q = 1 − p
d = Marginal error which was 25% relative precision top, i.e. 0.16.

Selection Criteria of Cases

Inclusion criteria

1. Patient of ASA Grades I and II in the age group of 18–60 years of either gender was enrolled.

METHODOLOGY

After approval from the Institutional Ethics Committee, this study was conducted inside Neurosurgery operation theatre at N.S.C.B. Medical College and Hospital, Jabalpur. Written informed consent was obtained from all patients enrolled in the study.

All 144 patients of age 18–60 years, ASA physical Statuses I and II of either sex who were scheduled for elective neurosurgery were included in this study. Patient was equally divided into four groups of 36 patients each.

- Group I: Dexmedetomidine 0.5 μg/kg diluted with 0.9% NS to 20 ml IV.
- Group II: Dexmedetomidine 0.75 μg/kg diluted with 0.9% NS to 20 ml IV.
- Group III: Dexmedetomidine 1 μg/kg diluted with 0.9% NS to 20 ml IV.
- Group IV: 20 ml of 0.9% normal saline IV.

Careful pre-anesthetic evaluation was done and it was made sure that the patients met the inclusion

and exclusion criteria. Patients were kept nil per oral from midnight for at least 8 h before surgery. After shifting the patient to the operation theater, two large bore (18 G) intravenous access were obtained, and normal saline was started at the rate of 10 ml/kg/h. Monitors such as pulse oximeter, noninvasive blood pressure, and 3-lead electrocardiogram were connected and pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO2) were recorded at that time.

The study solution was infused over 10 min. The general anesthesia technique was standardized in all four groups. Patients were premedicated with intravenous glycopyrrolate (0.2 mg) half an hour before induction. After preoxygenation for 3 min, general anesthesia was induced with inj. propofol (2–2.5 mg/kg) i.v, fentanyl (1.5 mcg/kg), followed by inj. vecuronium bromide (0.1 mg/kg) to facilitate direct laryngoscopy and orotracheal intubation (high-volume/low-pressure cuffed endotracheal tubes). The internal diameter of the endotracheal tube was 7–7.5 mm for women and 8–8.5 mm for men.

Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and oxygen saturation (SPO_2) were measured at:

- Baseline
- After 10 min of dexmedetomidine infusion (over 10 min) or just before intubation
- At 1 min after intubation.
- At 5 min after intubation.
- At 10 min after intubation.
- At 20 min after intubation.

Sedation was assessed using Richmond agitation sedation scale (RASS):

- Just after dexmedetomidine infusion.
- At 10 min after completion of dexmedetomidine infusion.

An event of hypotension (SBP <70 mm of Hg) was managed with 6 mg mephentermine IV and bradycardia (HR < 45 bpm) with 0.6 mg of atropine IV.

All the patients were mechanically ventilated at a fresh gas flow of 6 L/min and anesthesia was maintained with isoflurane (minimum alveolar concentration 0.8–1.0) and vecuronium (0.02 mg/kg every 20–30 min) throughout the surgical procedure. Intraoperative analgesia was supplemented with incremental doses of fentanyl every hour. Intraoperatively $etCO_2$ and urine output were also monitored. During mechanical ventilation, a respiratory rate and tidal volume were adjusted to keep normocapnia and normoxia with oxygen saturation ≥98%. Ringer lactate and normal saline were used for replacement and maintenance. Colloids, blood and blood products were used as and when required.

After surgery, reversal was achieved using IV neostigmine 0.05 mg/kg and IV glycopyrrolate 0.01 mg/kg. Once patient became conscious and responded to verbal commands, extubation was performed. After extubation, the patients were oxygenated with 100% oxygen for 5 min and after assessing adequate recovery, patient was shifted to post anesthesia care unit or wards and was monitored for 12 h.

Data Analysis and Statistics

Data were collected, summarized, and classified in the form of master chart in MS Excel worksheet. Quantitative data were expressed in Mean ± SD. Weightage of association of various factors was inferred by logistic regression. Data analyzed with the help of ANOVA test and other appropriate statistical test to find the significance of study parameters between the study groups.

Tools in the Study

The Richmond Agitation-Sedation Scale was used for assessment of sedation after dexmedetomidine infusion.

The Richmond agitation–sedation scale

	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient–ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	Spontaneously pays attention to caregiver
−1	Drowsy	Not fully alert, but has sustained (more than 10 s) awakening, with eye contact, to voice
−2	Light sedation	Briefly (<10 s) awakens with eye contact to voice
−3	Moderate sedation	Any movement (but no eye contact) to voice
−4	Deep sedation	No response to voice, but any movement to physical stimulation
−5	Unarousable	No response to voice or physical stimulation

OBSERVATION AND RESULTS

Table 1:Sex distribution

Sex		Group				Total
		Dexmedetomidine 0.5 mcg/kg	Dexmedetomidine 0.75 mcg/kg	Dexmedetomidine 1 mcg/kg	NS 0.9%	
Female	*n*	14	12	15	15	56
	%	38.9	33.3	41.7	41.7	38.9
Male	*n*	22	24	21	21	88
	%	61.1	66.7	58.3	58.3	61.1
Total	*n*	36	36	36	36	144
	%	100.0	100.0	100.0	100.0	100.0

Chi square = 0.701; *P* = 0.873

Table 2: Age distribution

Age group		Group				Total
		Dexmedetomidine 0.5 mcg/kg	Dexmedetomidine 0.75 mcg/kg	Dexmedetomidine 1 mcg/kg	NS 0.9%	
≤20 years	*n*	0	3	0	0	3
	%	0.0	8.3	0.0	0.0	2.1
21–30 year	*n*	3	8	10	8	29
	%	8.3	22.2	27.8	22.2	20.1
31–40 years	*n*	20	7	8	15	50
	%	55.6	19.4	22.2	41.7	34.7
41–50 years	*n*	6	11	12	12	41
	%	16.7	30.6	33.3	33.3	28.5
51–60 years	*n*	7	7	6	1	21
	%	19.4	19.4	16.7	2.8	14.6
Total	*n*	36	36	36	36	144
	%	100.0	100.0	100.0	100.0	100.0

Chi square = 28.86; *P* = 0.004

Table 3: ASA distribution

ASA		Group				Total
		Dexmedetomidine 0.5 mcg/kg	Dexmedetomidine 0.75 mcg/kg	Dexmedetomidine 1 mcg/kg	NS 0.9%	
I	*n*	21	23	22	20	86
	%	58.3	63.9	61.1	55.6	59.7
II	*n*	15	13	14	16	58
	%	41.7	36.1	38.9	44.4	40.3
Total	*n*	36	36	36	36	144
	%	100.0	100.0	100.0	100.0	100.0

Chi square = 0.577; *P* = 0.902

Table 4: RASS just after infusion

RASS 10 min after infusion		Group				Total
		Dexmedetomidine 0.5 mcg/kg	Dexmedetomidine 0.75 mcg/kg	Dexmedetomidine 1 mcg/kg	NS 0.9%	
−5	*n*	0	2	28	0	30
	%	0.0	5.6	77.8	0.0	20.8
−4	*n*	1	28	8	0	37
	%	2.8	77.8	22.2	0.0	25.7
−3	*n*	31	6	0	0	37
	%	86.1	16.7	0.0	0.0	25.7
−2	*n*	4	0	0	0	4
	%	11.1	0.0	0.0	0.0	2.8
0	*n*	0	0	0	36	36
	%	0.0	0.0	0.0	100.0	25.0
Total	*n*	36	36	36	36	144
	%	100.0	100.0	100.0	100.0	100.0

Chi square = 320.63; *P* < 0.0001

Table 5: RASS 10 min after infusion

RASS just after infusion		Group				Total
		Dexmedetomidine 0.5 mcg/kg	Dexmedetomidine 0.75 mcg/kg	Dexmedetomidine 1 mcg/kg	NS 0.9%	
−5	*n*	0	0	8	0	8
	%	0.0	0.0	22.2	0.0	5.6
−4	*n*	0	7	28	0	35
	%	0.0	19.4	77.8	0.0	24.3
−3	*n*	1	29	0	0	30
	%	2.8	80.6	0.0	0.0	20.8
−2	*n*	32	0	0	0	32
	%	88.9	0.0	0.0	0.0	22.2
−1	*n*	3	0	0	0	3
	%	8.3	0.0	0.0	0.0	2.1
0	*n*	0	0	0	36	36
	%	0.0	0.0	0.0	100.0	25.0
Total	*n*	36	36	36	36	144
	%	100.0	100.0	100.0	100.0	100.0

Chi square = 379.47; $P < 0.0001$.

Table 6: Changes in heart rate (mean, standard deviation) before and after intubation in different treatment groups

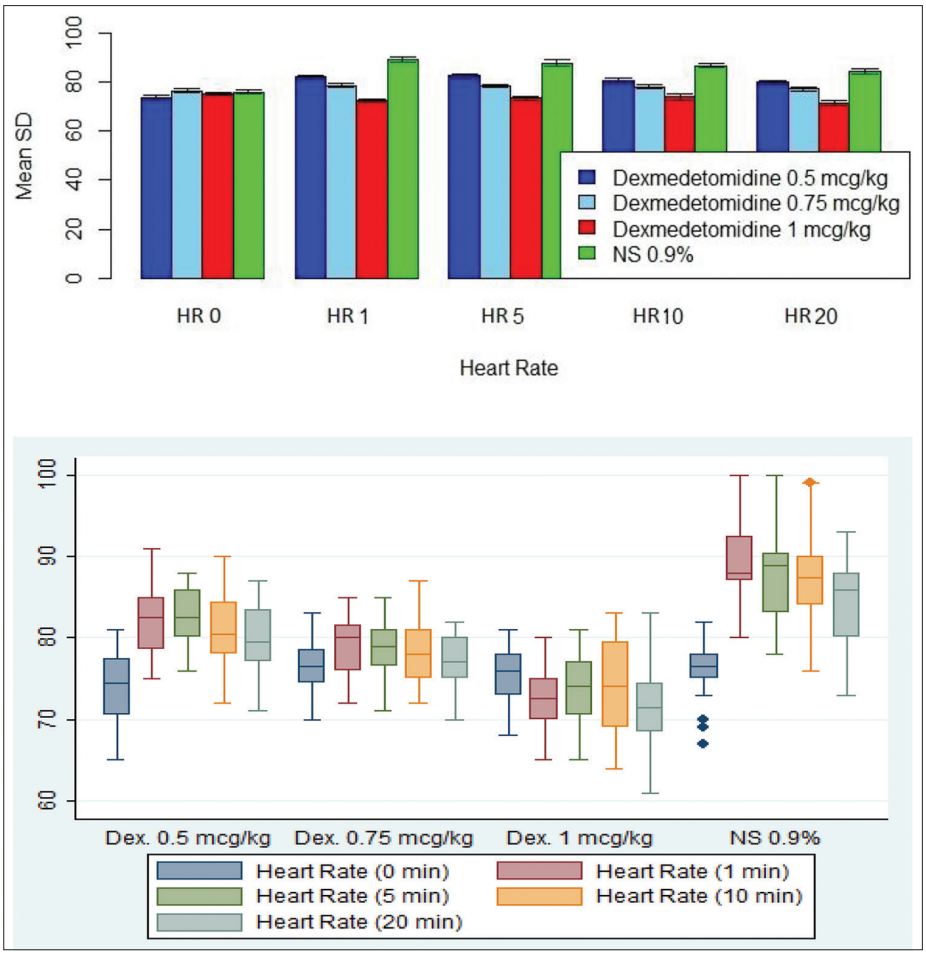
Variable	Follow-up	Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Heart rate	Before intubation	73.75	4.43	76.58	3.29	75.25	3.45	76.11	3.59
Heart rate	1 min After intubation	82.11	4.52	78.75	3.49	72.69	3.57	89.31	5.77
Heart rate	5 min After intubation	82.67	3.71	78.44	3.15	73.61	4.28	87.94	5.86
Heart rate	10 min After intubation	80.67	4.51	78.17	3.78	73.97	5.86	86.78	4.71
Heart rate	20 min After intubation	79.94	3.76	77.28	3.23	71.58	5.15	84.42	4.81

Variables	Follow-up	ANOVA	
		F statistics	*P*
Heart rate	1	150.209	<0.0001
Heart rate	5	99.582	<0.0001
Heart rate	10	62.025	<0.0001
Heart rate	20	62.449	<0.0001

DISCUSSION

Derbyshire *et al.*[13] correlated the stress response to laryngoscopy and intubation with concomitant measurement of plasma adrenaline and noradrenaline. There was significant increase in plasma noradrenaline concentration and this was more when a non-depolarizer neuromuscular blocking agent is used for endotrachael tube placement (141% vs. 74% in depolarizer). Plasma adrenaline levels also increased significantly (18% vs. 39% in depolarizer group). The levels of the catecholamines did correlate well with rise in mean arterial pressure. Low *et al.*[14] also demonstrated significant adrenergic and noradrenergic response to laryngoscopy and intubation. They measured plasma catecholamine concentrations in 16 normotensive and 10 hypertensive patients undergoing elective vascular surgery. Following laryngoscopy, there was a moderate increase in arterial pressure in both normotensive and hypertensive patients. In normotensive patients, laryngoscopy was associated with a moderate increase in plasma noradrenaline concentration. There was no change in adrenaline concentration. By contrast, there was a marked increase in noradrenaline concentration, a moderate increase in adrenaline concentration and an arterial pressure response in the group of hypertensive patients. These data are consistent with transient sympathetic over activity in hypertensive patients following noxious stimuli such as laryngoscopy.

In patients with intracranial space-occupying lesion, induction agent alone will usually not attenuate the increases in MAP and CPP produced during laryngoscopy with tracheal intubation. Large increases in CPP can either increase intracranial blood volume, thereby increasing ICP, or disrupt the blood–brain barrier (BBB), causing cerebral edema. The previous studies demonstrated that there is no simple method to maintain a decreased ICP (compared with its awake baseline value) immediately following laryngoscopy and tracheal intubation in patients with intracranial hypertension. Although propofol is beneficial in attenuating the increase in ICP secondary to



Graph 1: Changes in heart rate (mean, standard deviation) before and after intubation in different treatment groups

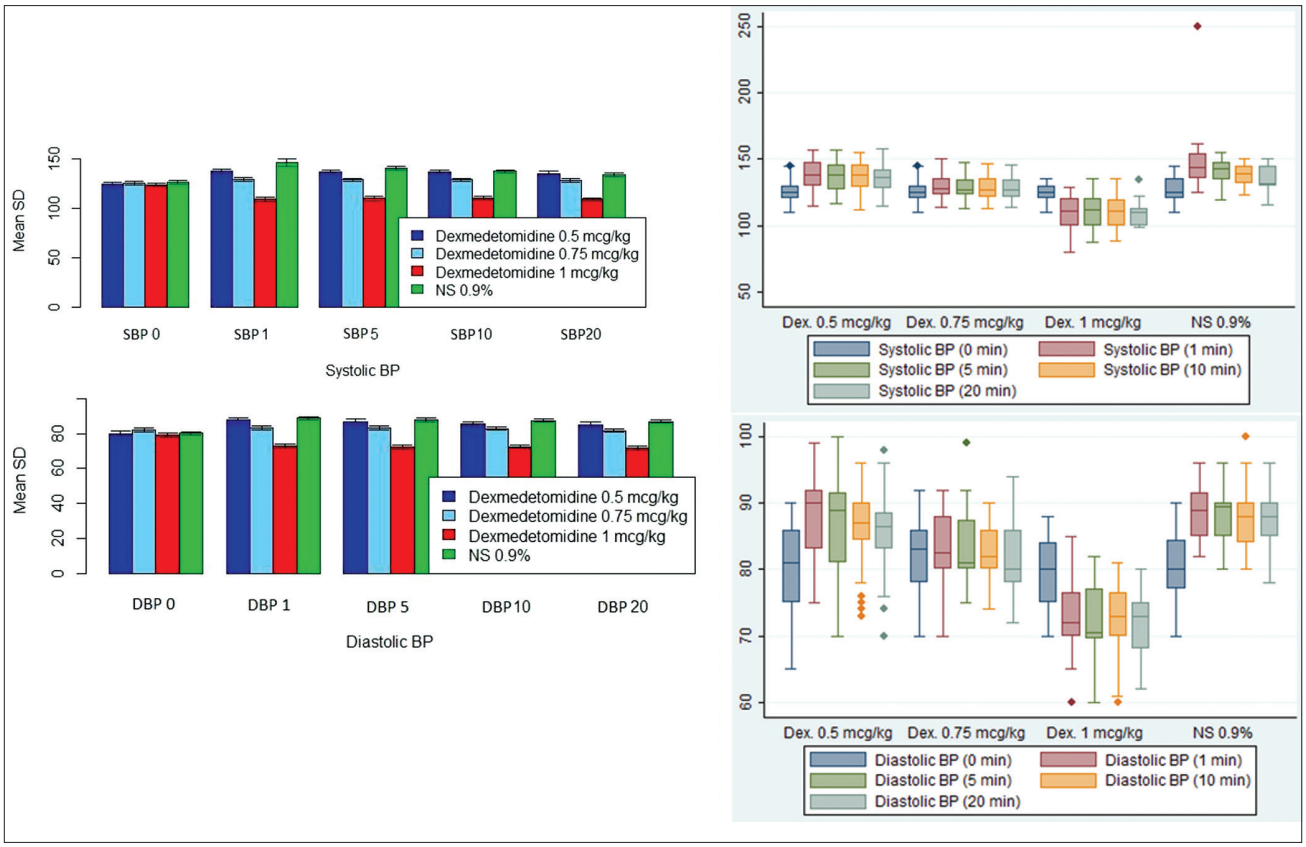
Table 7: Changes in blood pressure (mean, standard deviation) before and after intubation in different treatment groups

Variable	Follow-up	Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Systolic BP	Before intubation	124.58	9.59	125.83	9.45	123.89	7.47	126.53	9.09
Systolic BP	1 min After intubation	137.81	11.69	129.14	8.98	109.11	12.36	146.42	20.71
Systolic BP	5 min After intubation	137.03	10.91	129.06	9.22	110.31	11.09	140.97	9.30
Systolic BP	10 min After intubation	136.94	11.44	129.03	8.94	110.42	10.95	137.67	7.72
Systolic BP	20 min After intubation	135.44	10.72	128.25	8.91	109.36	7.85	134.50	8.91
Diastolic BP	Before intubation	80.11	6.85	82.25	5.64	79.31	5.15	80.17	5.35
Diastolic BP	1 min After intubation	87.64	6.69	83.22	5.27	72.86	5.68	89.00	4.18
Diastolic BP	5 min After intubation	86.69	7.75	83.25	5.21	72.28	5.76	87.94	4.65
Diastolic BP	10 min After intubation	85.72	5.81	82.78	4.27	72.64	5.09	87.53	5.25
Diastolic BP	20 min After intubation	85.25	6.76	81.81	5.45	71.86	5.44	87.03	4.41

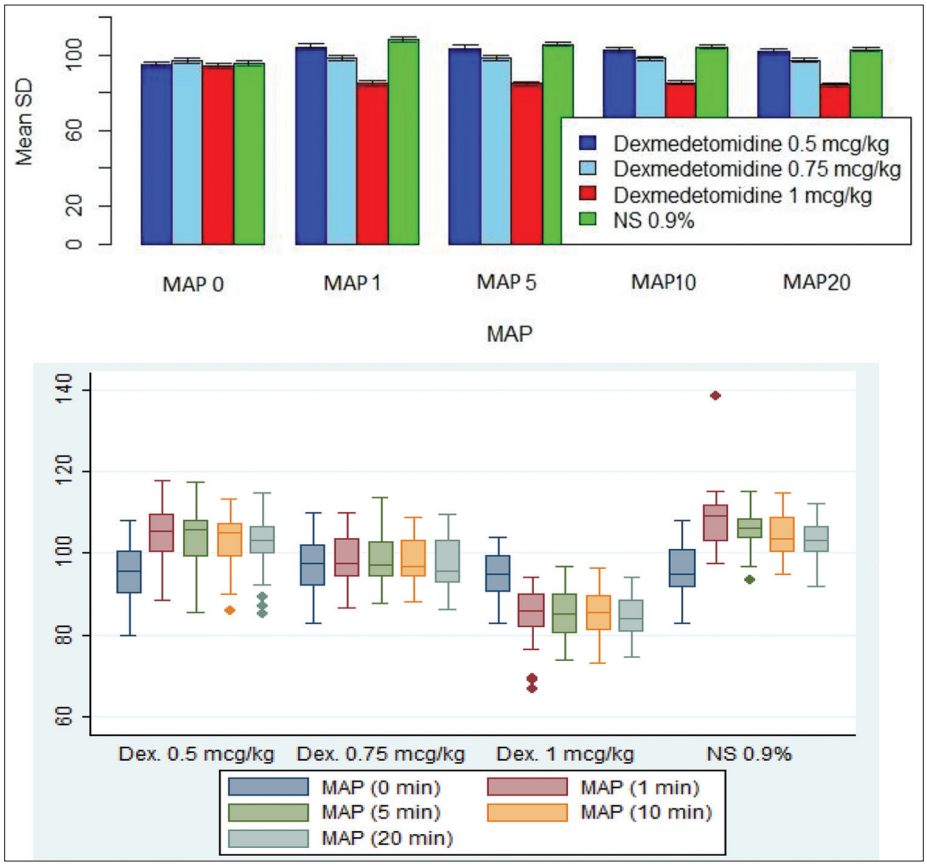
Variables	Follow-up	ANOVA	
		F statistics	P value
Systolic BP	1	63.757	<0.0001
Systolic BP	5	138.365	<0.0001
Systolic BP	10	109.691	<0.0001
Systolic BP	20	114.359	<0.0001
Diastolic BP	1	246.903	<0.0001
Diastolic BP	5	158.797	<0.0001
Diastolic BP	10	107.588	<0.0001
Diastolic BP	20	107.784	<0.0001

tracheal stimulation, it failed to show to maintain a decreased ICP effectively soon after intubation.

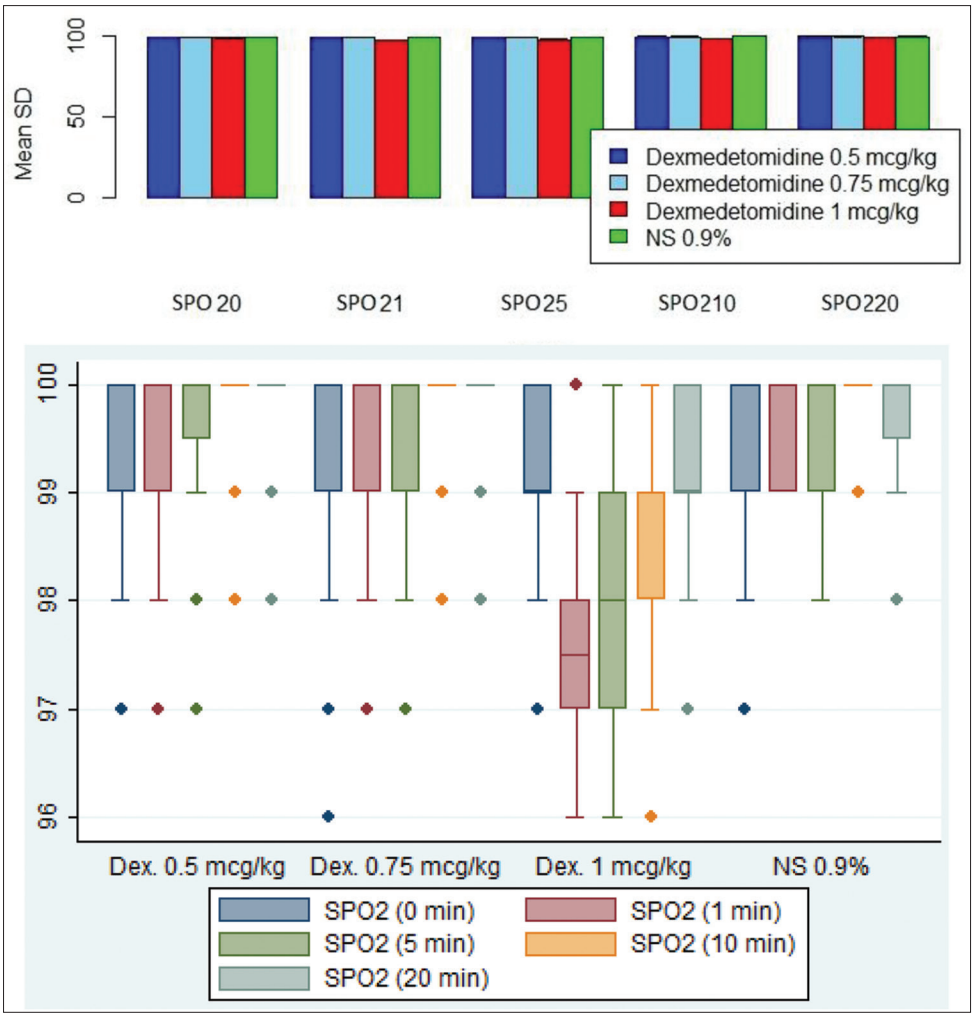
Dexmedetomidine has distribution half-life of approximately 6 min, so can be used successfully for attenuating the stress response to laryngoscopy. It has also been evaluated by several authors as an adjuvant to anesthesia for neurosurgery with favorable perioperative hemodynamic control.[15-20] Dexmedetomidine has been liberally and extensively used in



Graph 2: Changes in blood pressure (mean, standard deviation) before and after intubation in different treatment groups



Graph 3: Changes in mean arterial pressure (mean, standard deviation) before and after intubation in different treatment groups



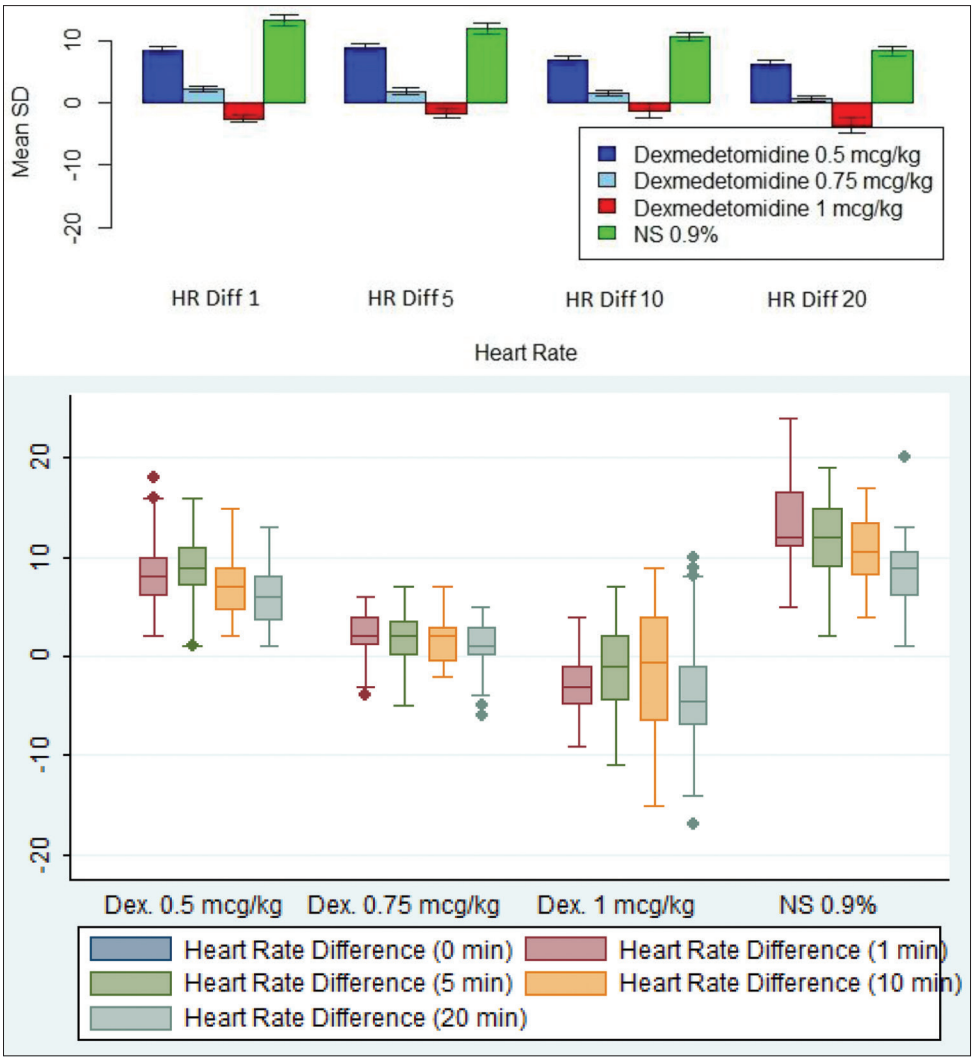
Graph 4: Changes in SPO_2 (mean, standard deviation) before and after intubation in different treatment groups

Table 8: Changes in mean arterial pressure (mean, standard deviation) before and after intubation in different treatment groups

Variable	Follow-up	Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
MAP	Before intubation	94.86	7.50	97.03	6.74	94.17	5.77	95.56	6.44
MAP	1 min after intubation	104.36	7.84	98.53	6.20	84.94	7.04	108.14	7.54
MAP	5 min after intubation	103.47	8.19	98.52	6.07	84.95	6.03	105.62	5.34
MAP	10 min after intubation	102.80	7.07	98.19	5.56	85.23	5.75	104.24	5.18
MAP	20 min after intubation	101.98	7.05	97.29	6.25	84.36	5.12	102.85	4.98

Variables	Follow-up	ANOVA	
		F statistics	*P*
MAP	1	188.847	<0.0001
MAP	5	283.434	<0.0001
MAP	10	174.723	<0.0001
MAP	20	190.556	<0.0001

neurosurgical operation due to its favorable profile to afford neuroprotection. Drummond *et al.*[21] evaluated the effect of dexmedetomidine on cerebral blood flow velocity (CBFV), cerebral metabolic rate (CMR), and CO_2 response in normal humans. The vasoconstrictive seems to occur principally at the level of plial arterioles and activation of intrinsic noradrenergic neural pathways originating in the locus ceruleus projecting to the microvasculature of the CNS. They found that CBFV and CMRe decreased in dose-related manner. CBFV/CMRe ratio remains unchanged. Georgia *et al.*[22] used transcranial Doppler imaging and tested the effect of loading dose of 1mcg/kg dexmedetomidine on cerebral hemodynamics in patients scheduled to undergo



Graph 5: Mean difference in heart rate before and after intubation in different treatment groups

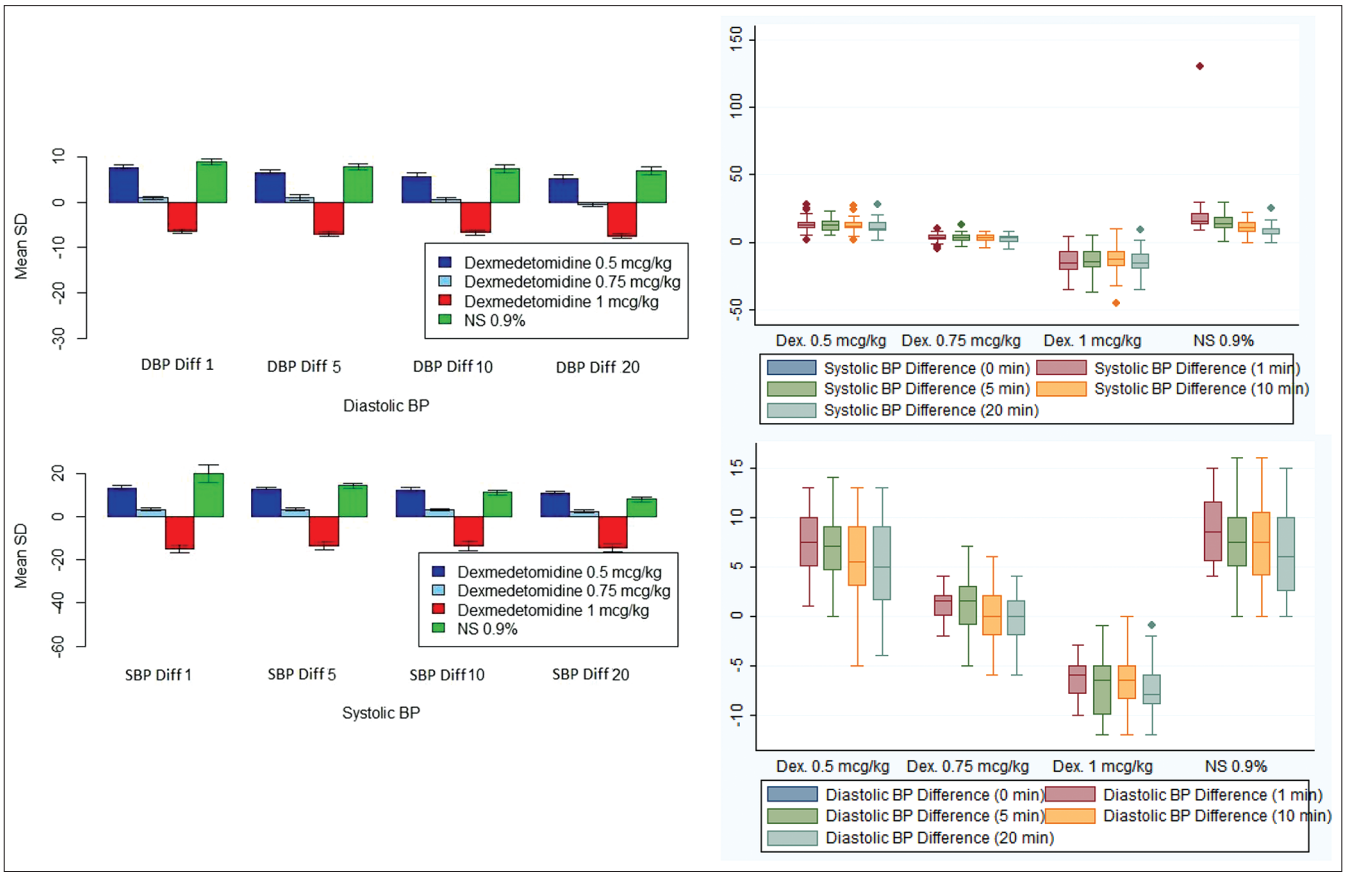
Table 9: Changes in SPO_2 (mean, standard deviation) before and after intubation in different treatment groups

Variable	Follow-up	Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
SPO_2	Before intubation	99.44	0.88	99.25	1.08	99.11	0.95	99.33	0.86
SPO_2	1 min after intubation	99.53	0.77	99.28	1.00	97.58	1.18	99.64	0.49
SPO_2	5 min after intubation	99.64	0.72	99.53	0.81	97.86	1.17	99.50	0.61
SPO_2	10 min after intubation	99.75	0.60	99.75	0.60	98.42	1.11	99.89	0.32
SPO_2	20 min after intubation	99.86	0.42	99.81	0.47	99.31	0.75	99.72	0.51

Variables	Follow-up	ANOVA	
		F statistics	*P*
SPO_2	1	41.10	<0.0001
SPO_2	5	35.44	<0.0001
SPO_2	10	33.70	<0.0001
SPO_2	20	7.47	0.0001

lumbar discectomy. They observed a decline of FV (flow velocity) in MCA along with augmentation of PI (pulsability index) and cerebral vascular resistance index. Prielipp *et al.*[23] evaluated the effect of dexmedetomidine on regional and global cerebral blood flow in healthy human volunteers. They used PET (positron emission tomography) to determine CBF. Global CBF decreased significantly from 91 ml/100 gm/min to 61 ml/100 gm/min.

Its hemodynamic effects are predictable and dose-dependent. Dexmedetomidine, at clinically effective dosages, does not depress respiration, and therefore does not interfere with extubation. This pharmacological profile renders it suitable



Graph 6: Mean difference in blood pressure before and after intubation in different treatment groups

Table 10: Mean difference in heart rate before and after intubation in different treatment groups

Variable	Follow-up	Mean difference from Intubation							
		Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Heart rate	1 min after intubation	8.36	3.42	2.17	2.42	−2.56	3.1	13.19	4.31
Heart rate	5 min after intubation	8.92	3.15	1.86	2.55	−1.64	4.3	11.83	4.56
Heart rate	10 min after intubation	6.92	3.29	1.58	2.26	−1.28	6.18	10.67	3.5
Heart rate	20 min after intubation	6.19	3.22	0.69	2.67	−3.67	5.94	8.31	3.86

Table 11: Mean difference in blood pressure before and after intubation in different treatment groups

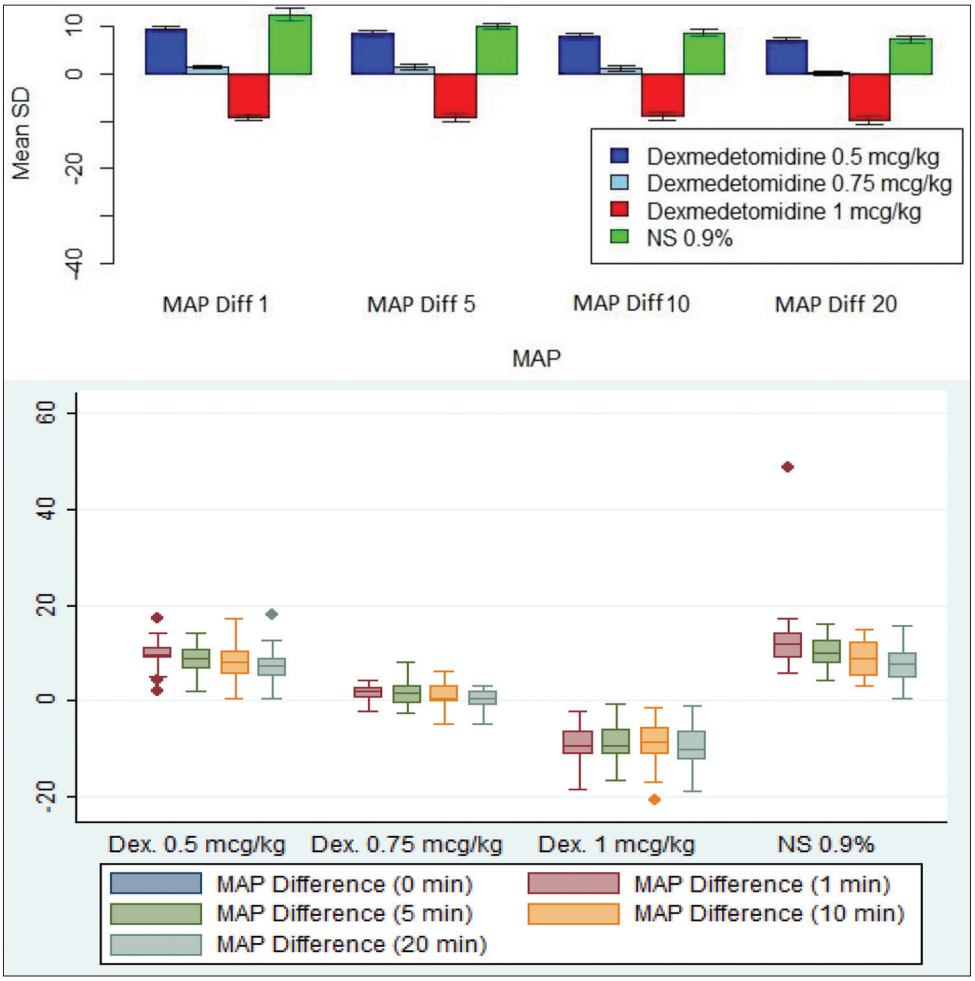
Variable	Follow-up	Mean difference from Intubation							
		Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Systolic BP	1 min after intubation	13.22	5.28	3.31	2.9	−14.78	9.39	19.89	19.74
Systolic BP	5 min after intubation	12.44	4.99	3.22	3.31	−13.58	10	14.44	5.84
Systolic BP	10 min after intubation	12.36	5.05	3.19	2.7	−13.47	11.09	11.14	5.5
Systolic BP	20 min after intubation	10.86	5.17	2.42	3.28	−14.53	9.96	7.97	5.08
Diastolic BP	1 min after intubation	7.53	3.08	0.97	1.72	−6.44	2.24	8.83	3.35
Diastolic BP	5 min after intubation	6.58	3.25	1	3.02	−7.03	2.9	7.78	3.64
Diastolic BP	10 min after intubation	5.61	4.4	0.53	2.82	−6.67	2.8	7.36	4.22
Diastolic BP	20 min after intubation	5.14	4.69	-0.44	2.38	−7.44	2.59	6.86	4.61

Table 12: Mean difference in map before and after intubation in different treatment groups

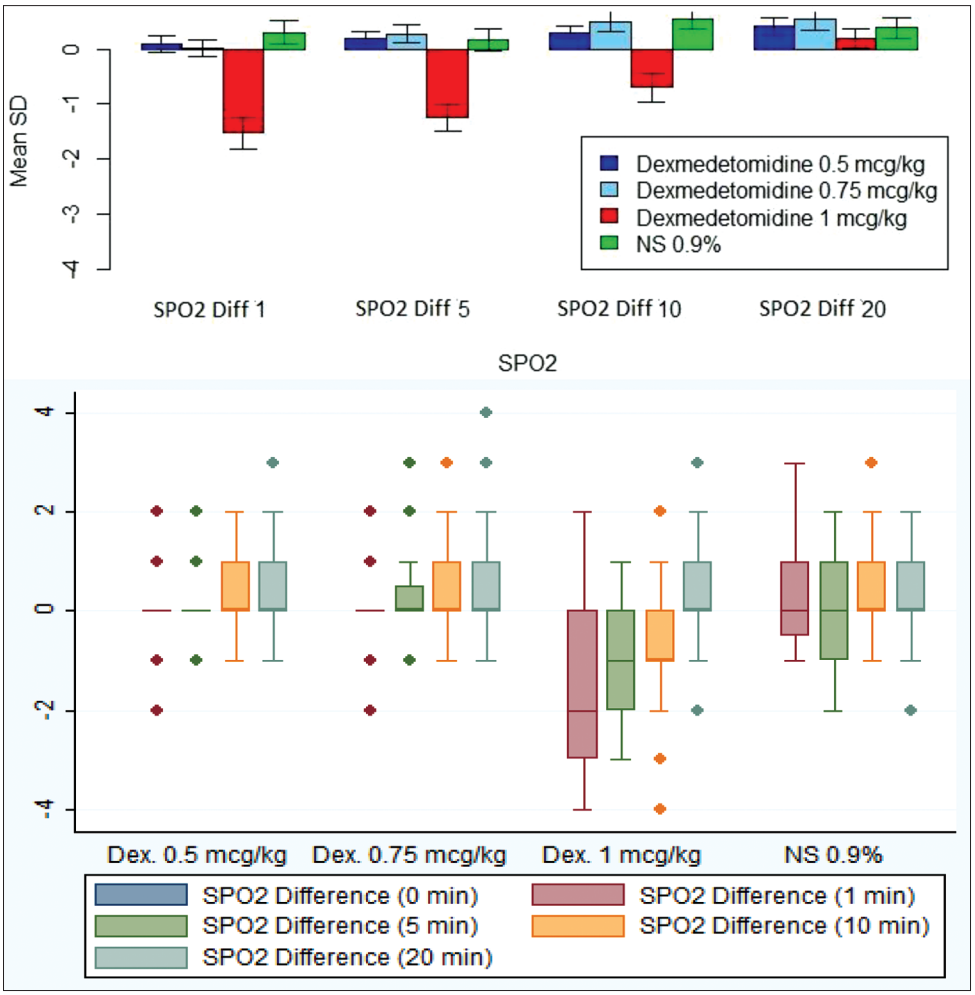
Variable	Follow-up	Mean difference from Intubation							
		Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
MAP	1 min after intubation	9.5	2.96	1.5	1.58	−9.22	3.67	12.58	6.9
MAP	5 min after intubation	8.61	3.01	1.49	2.35	−9.21	3.87	10.06	3.13
MAP	10 min after intubation	7.94	3.64	1.17	2.56	−8.94	4.58	8.69	3.77
MAP	20 min after intubation	7.12	3.61	0.26	2.11	−9.81	4.23	7.3	3.68

Table 13: Mean difference in SPO_2 before and after intubation in different treatment groups

Variable	Follow-up	Mean difference from Intubation							
		Dexmedetomidine 0.5 mcg/kg		Dexmedetomidine 0.75 mcg/kg		Dexmedetomidine 1 mcg/kg		Normal Saline 0.9%	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
SPO_2	1 min after intubation	0.08	0.77	0.03	0.77	−1.53	1.50	0.31	1.09
SPO_2	5 min after intubation	0.19	0.58	0.28	0.81	−1.25	1.18	0.17	1.06
SPO_2	10 min after intubation	0.31	0.62	0.50	0.97	−0.69	1.37	0.56	0.94
SPO_2	20 min after intubation	0.42	0.84	0.56	1.03	0.19	0.92	0.39	0.96



Graph 7: Mean difference in map before and after intubation in different treatment groups



Graph 8: Mean difference in SPO_2 before and after intubation in different treatment groups

for premedication for general anesthesia in intravenous doses varying from 0.25 to 1 μg/kg for the attenuation of intubation responses, but the optimal dose not yet established.[24] Our study is to assess the effect of different doses of dexmedetomidine on hemodynamic response during laryngoscopy and tracheal intubation in endoscopic neurosurgeries.

Our study was carried in neurosurgery operation theater of NSCB Medical College. It was a prospective double blind randomized study in which the study population of 144 was divided into four groups of 36 each. One was the control group and other three groups received dexmedetomidine in infusion form preoperatively in varying doses, namely, 0.5 mcg/kg, 0.75 mcg/kg, and 1.0 mcg/kg. We assessed the optimal dose of dexmedetomidine which attenuated the hemodynamic response during laryngoscopy and tracheal intubation as well as which provided the most stable hemodynamics.

Demographically all four groups were comparable, these were 38.6% female and 61.1% males of ASA physical Statuses I and II who were enrolled in our study. Most of the patients belong to the age group between 31 and 40 years.

On assessing the Richman Agitation Sedation Scores in different group just after completion of study drug infusion, it was found that the majority of patients receiving dexmedetomidine 1.0 mcg/kg, 0.75 mcg/kg, and 0.5 mcg/kg the scores were −5, −4, and −3, respectively, but when analyzed 10 min after infusion, the sedation scores of the respective groups rose to −4, −3, and −2, respectively, which depicts that patients were more arousable. Similarly Hall *et al.*[24] using a loading dose of 6 μg/kg/h for 1 min followed by constant infusion at two doses either 0.2 μg/kg/h or 0.6 μg/kg/h for 50 min observed significant sedation (in 50–60%) using BIS, VAS sedation, and OAA/S, impairment of memory in 50% using DSST and MEM and impairment of psychomotor performance in 28–41% using DSST in infusing dexmedetomidine to human volunteers. Yildiz *et al.*[25] observed Ramsay Sedation Score to be 6 in 56% of patients just after the infusion. Dhanachandra *et al.*[26] observed significant sedation using 0.75 μg/kg

dexmedetomidine. Thus, there was discrepancy between our study and the study done by Dhanachandra *et al.*[26]

Analysis of variance showed that heart rate after 1, 5, 10, and 20 min compared from before intubation changed significantly in all treatment groups except for the group using normal saline. Dexmedetomidine group using 0.75 mcg/kg dose showed most stable heart rate when compared with other groups ($P < 0.0001$). Group wise multiple comparison also showed significance except for dexmedetomidine 0.5 mcg/kg and normal saline at 20 min which were not different ($P > 0.05$) in our study. Dexmedetomidine in 0.75 μg/kg showed minimum deviation from mean (beats/min). Smitha *et al.*[27] showed highly significant reduction in heart rate using 1microgram/kg dexmedetomidine when compared to 0.5 μg/kg. This is congruent to our study results. Yildiz *et al.*[25] observed after 1 μg/kg dexmedetomidine the postoperative heart rate to be less than preoperative levels but it did increase after intubation. Sebastian *et al.*[28] when compared 0.75 μg/kg with 0.5 μg/kg dexmedetomidine showed that heart rate was better controlled with 0.5 μg/kg dose. This was in contrast to the results of our study in which the most stable heart rate was provided with dexmedetomidine 0.75 μg/kg. Kumari *et al.*[29] used 0.5 μg/kg to show significant reduction in heart rate (19.6) till 15 min postoperatively on inter comparison among the study groups. Mahajan *et al.*[30] showed that dexmedetomidine 1 μg/kg was more effective in controlling heart rate when compared to 30 mg/kg magnesium sulfate. Hall *et al.*,[24] when compared two regimens of infusing dexmedetomidine (0.2 or 0.6 μg/kg/h), found a significant reduction in heart rate (16% and 20%) and at higher concentration, the drug paradoxically resulted in increase of blood pressure due to alpha-2 stimulation. Saraf *et al.*[31] using pre-operative 0.6 μg/kg dexmedetomidine found a mean drop of heart rate of 2.86 bpm and a significant fall in heart rate at 2, 5, and 8 min of drug infusion. Talke *et al.*[32] while infusing dexmedetomidine throughout the perioperative period observed that heart rate was slower than placebo (73+ 11 bpm vs. 83+ 20 bpm).

Systolic blood pressure after 1, 5, 10, and 20 min when compared from before intubation changed significantly in all treatment groups except for normal saline, moreover dexmedetomidine 0.75 mcg/kg doses showed most stable systolic blood pressure. Group wise multiple comparison also showed significant change from baseline during follow-up period except for dexmedetomidine 0.5 mcg/kg and normal saline at 1, 5, 10, and 20 min which did not significantly differ ($P > 0.05$).

Diastolic blood pressure after 1, 5, 10, and 20 min when compared from before intubation changed significantly in all treatment groups except for normal saline, moreover dexmedetomidine 0.75 mcg/kg doses showed most stable diastolic blood pressure. Group wise multiple comparison also showed significant changes during follow-up period except for dexmedetomidine 0.5 mcg/kg and normal saline at 1, 5, 10, and 20 min which did not significantly differ ($P > 0.05$).

Mean arterial pressure (MAP) after 1, 5, 10, and 20 min when compared from before intubation changed significantly in all treatment groups except for normal saline, moreover dexmedetomidine 0.75 mcg/kg doses showed most stable mean arterial pressure. Group wise multiple comparison also showed significant changes during follow-up period except for dexmedetomidine 0.5 mcg/kg and normal saline at 5, 10, and 20 min which did not significantly differ ($P > 0.05$).

Smitha *et al.*[27] when comparing 0.5 and 1.0 μg/kg dexmedetomidine showed that the values of SBP, DBP, and MAP were statistically lower at all-time intervals especially 1 min after intubation by 1 μg/kg dexmedetomidine. This is in accordance to our study where dexmedetomidine at 1 μg/kg significantly attenuated the hemodynamic response. Gulabani *et al.*[33] exhibited that dexmedetomidine 1 μg/kg was better than linocaine 1.5 mg/kg and esmolol 100 mg in controlling specifically the diastolic blood pressure. Yildiz *et al.*[25] when infused 1 μg/kg dexmedetomidine proved that the drug was effective in controlling hemodynamic variables. Keniya *et al.*[34] when preloaded the patients with 1 μg/kg dexmedetomidine followed by infusion at 0.2–0.7 μg/kg/h in the operative period found that it better controlled diastolic pressure (11%) than systolic (8%). Thus, the studies by Gulabani *et al.*[33] and Keniya *et al.*[34] showed that dexmedetomidine was more effective in controlling the diastolic blood pressure. Sulaiman *et al.*[15] compared dexmedetomidine 0.5 μg/kg with normal saline and showed that there was statistical difference between them at 1st, 2nd, and 3rd min post-intubation in terms of attenuating SBP, DBP, and MAP. Sebastian *et al.*[28] when comparing normal saline and dexmedetomidine in doses 0.5 and 1.0 μg/kg showed that by 1 μg/kg dose the hemodynamic variables fell below baseline at 3rd min post-intubation. Our study is in accordance to the study by Sulaiman *et al.*[15] and Sebastian *et al.*[28] where the use of dexmedetomidine was better than the placebo in attenuating the hemodynamic response and when used at 1 mcg/kg, maximally abolishes the pressor response to laryngoscopy and intubation. Ravikumar Keshari *et al.*[35] on comparing 0.5 and 1 mcg/kg dexmedetomidine showed that mean SBP was significantly low using 1 mcg/kg dose at 5 and 10 min post-intubation. Thus, all the above studies have pointed out that whenever dexmedetomidine was used in the dosages of 1.0 μg/kg, the hemodynamic variables fell considerably below the baseline and if such doses are used in the perioperative

setting of neurosurgical cases, there is potential chance of CPP (cerebral perfusion pressure) reaching to critical levels. Similar to our study, Dhanachandra *et al*.[26] showed that dexmedetomidine when used in dosage of 0.75 μg/kg provided the most stable hemodynamics.

SPO_2 after 1, 5, 10, and 20 min when compared from before intubation changed significantly in all treatment groups except for normal saline ($P < 0.0001$). Group wise multiple comparison also showed that statistical change in SPO_2 observed with dexmedetomidine 1 mcg/kg dose was most significant from all other treatment groups Aho *et al*.[36] using 2.4 μg/kg, Yildiz *et al*.,[25] Sagiroglu *et al*.,[37] and Ying *et al*.[38] in their study observed elevated sedation scores with 1 μg/kg dexmedetomidine which lowered the SPO_2 values just after the commencement of infusion.

SUMMARY AND CONCLUSION

Neurosurgical patients are subset of patients in which induction from anesthesia is met with hemodynamic perturbations which, in turn, may lead to disastrous complications such as intracranial hematoma and raised intracranial pressure.

The control of hemodynamics in the peri induction period can be met with judicious use of various anesthetic protocols.

This study was planned to evaluate the control of pressor response to laryngoscopy and intubation in neuroendoscopic procedures and avoidance of neurological complications such as raised intracranial tension in immediate peri induction period, provision of stable hemodynamic variables, and early recovery from anesthesia.

Our study demonstrated that dexmedetomidine when used preoperatively as a premedicament in doses at 0.75 μg/kg in infusion form, provided the most acceptable hemodynamics in the peri induction period with an acceptable level of twilight.

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