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Original Research Article

Randomized Prospective Double-Blind Study Assessing Efficacy of the Dexmedetomidine on Haemodynamic Stress Response during Laryngoscopy and Intubation

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Conflict of interest: Nil

Abstract

Aim: The aim of the present study was to assess the efficacy and safety of dexmedetomedine in attenuating haemodynamic stress response to laryngoscopy and endotracheal intubation.

Methods: This randomized prospective double-blind study carried out in 200 patients aged 20-60 years of asa physical status of I and II scheduled for elective surgery under general anaesthesia requiring endotracheal intubation at Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar, India for one year.

Results: Patient characteristics in terms of age, gender and weight were comparable in both the groups. On comparing the changes in heart rate between group c and group d at various specific timing, there was significant difference between the two groups ($p<0.05$). On comparing the changes in SBP and DBP between group c and group d at various specific timings, there was statistically significant difference between the two groups ($p<0.05$). The difference in sedation score was significant between group c and group d after drug administration ($p<0.001$). Sedation did not cause respiratory depression in any patient.

Conclusion: Dexmeditomidine in a dose of 1 mcg/kg given half an hour before induction effectively blunts the hemodynamic response to laryngoscopy and endotracheal intubation and provides stable hemodynamic through the surgery and provides good and safe level of sedation without respiratory depression in routine surgery.

Keywords: Dexmedetomidine, Hemodynamic Changes, Hypertension, Intubation, Laryngoscopy, Tachycardia

Introduction

Laryngoscopy and tracheal intubation lead to tachycardia and hypertension due to increase in the plasma concentration of catecholamines subsequent to sympathetic stimulation. The elevation in arterial pressure generally peaks in 1-2 minutes and returns to normal levels within five minutes. [1] This may be inconsequential in normal people but may lead to serious morbidity in patients with co-existing cerebrovascular or cardiovascular conditions. [2] The laryngoscopic response in these patients can increase myocardial oxygen demand and may lead to complications in susceptible individuals. Various prophylactic interventions have been tried to blunt this stress response; administration of local anesthetics, opioids, beta blockers, alpha 2 adrenergic agonists, vasodilators, magnesium, or increased concentrations of volatile anesthetic. [3]

Direct laryngoscopy during tracheal intubation in patients undergoing general anesthesia is noxious stimuli that produce adverse hemodynamic responses, due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. Increased plasma catecholamine concentration leads to hypertension, tachycardia, and arrhythmia. [4] The magnitude of hemodynamic response is greater with increasing force and duration of laryngoscopy and endotracheal intubation. [5] In geriatric age group owing to decreased reserve capacity of cardiovascular structure and function, it is important for anesthesiologists to attenuate sympathoadrenal response during tracheal intubation which can be detrimental, especially in geriatric age group if not taken care of. [6] There is increase in life expectancy due to the better medical

facility, which leads to increasing number of patients presenting for surgery in geriatric age group. With increase in age, there is alteration in autonomic system, diminution in physiological reserve, increasing the risk of coexisting cardiac disease, and increased sensitivity to opioids and anesthetic drugs. [7,8]

The series of physiological changes (the pressure response to laryngoscopy and tracheal intubation) leads to an endocrine response as adrenaline and noradrenaline secretion by the stimulation of sympathetic nervous system. [9,10] The elevated catecholamine concentration in plasma due to sympathetic discharge increases the arterial blood pressure, heart rate and oxygen consumption, leading to haemodynamic instability. [11,12] The rise in blood pressure and heart rate usually occurs about 15 seconds after laryngoscopy and becomes maximal after 30-45 seconds. Thus, limiting laryngoscopy to 15 seconds or less can minimize blood pressure elevation. Usually these changes are transient and well tolerated by healthy individuals, but may be fatal in patients with hypertension, coronary artery diseases and cerebrovascular diseases. [12]

Dexmedetomidine is a highly selective alpha-2 adrenoceptor (α2-AR) agonist. It has been introduced to anaesthesia practice relatively recently. It produces sedation, anxiolysis and analgesia without respiratory depression. It involves spinal and supraspinal sites. [13] It is said that dexmedetomidine significantly reduces the incidence of postoperative cognitive dysfunction (POCD) and improves Mini-Mental State Examination (MMSE) score. [14] It is equally effective in all age groups and is being used in pediatric age as well as elderly patients. [15]

The aim of the present study was to assess the efficacy and safety of dexmedetomedine in attenuating haemodynamic stress response to laryngoscopy and endotracheal intubation.

Materials and Methods

This randomized prospective double-blind study carried out in 200 patients aged 20-60 years of ASA physical status of I and II scheduled for elective surgery under general anaesthesia requiring endotracheal intubation at Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar India for one year

After detailed pre-anaesthetic evaluation, systemic examination and routine investigations, patient with major systemic disease like COPD, renal disease, cardiac diseases, diabetes, patients on antipsychotic drugs, pregnant patient and anticipated difficult intubation were excluded from this study. In pre-anesthetic preparation room, monitoring for heart rate, non-invasive blood pressure (systolic, diastolic and mean arterial pressure), and peripheral oxygen saturation were established and baseline vital parameters were recorded, including Ramsay sedation score. Intravenous line was secured and premedication consisting of Ondansetron 0.08 mg/kg IV and Glycopyrrolate 0.004 mg/kg IM, were given 30 minutes before induction of anesthesia.

Patients were randomly divided into two groups (each of 100 patients) using random number table method.

Group D, (n=100): Inj.dexmedetomidine 1mcg/kg in 100 ml NS.

Group C, (n=100): 100 ml NS.

Intravenous infusion over 10-15 minutes, 30 minutes before induction of anesthesia.

Ramsay Sedation score

Score	Level of sedation
0	Awake and agitated.
1	Awake and comfortable.
2	Asleep but arousable.
3	Asleep with sluggish response to verbal command and touch.
4	Asleep with no response to verbal command and touch.

Patients were monitored for hemodynamic changes at various specific timing as per protocol, and sedation was monitored according to Ramsay Sedation Score (as mentioned below) immediately and at 5, 10, 15 and 20 minutes after drug administration.

1. In the operation theatre multipara monitor was attached and vital parameters were recorded.
2. Standard general anaesthesia was given to all patients.
3. All the parameters were recorded at various specific timings as per protocol.
4. Hypotension was defined as a decrease in systolic blood pressure > 30% of the baseline value or systolic blood pressure < 100 mm Hg and treated with intravenous blouses of 6 mg ephedrine and crystalloid fluids.
5. Hypertension was defined as increase in blood pressure > 30% of the baseline value and treated with Inj. NTG i.v. Infusion

6. Bradycardia was defined as a pulse rate of < 60 beat/ min and will be treated with bolus of 0.6 mg atropine.
7. Tachycardia was defined as pulse rate of > 100 beats /min and was treated with beta-blockers.
8. Any treatment required and complication if any, was recorded till 30 min after intubation.
9. At the end of surgery, neuromuscular blockade was reversed with neostigmine 50 microgram/kg and glycopyrrolate 10 microgram/kg IV.
10. After satisfying the extubation criteria, trachea was extubated, and patients were transferred to post anaesthesia care unit.

Statistical Analysis

The data obtained in the study for various parameters were presented in the tabulated form. Using statistical software (graph pad prism statistical software) mean and standard deviation were calculated for all the quantitative variables. Intra group comparison was made using paired student t-test and comparison among different groups (inter group comparison) was done using unpaired t-test. P value <0.05 was considered statistically significant.

Results

Table 1: Demographic profile of patients

Demographic profile	Group C	Group D	p value
Age(yrs)	34.36±8.24	35.75±8.60	>0.05
Gender (M:F)	60/40	64/36	>0.05
Weight(kg) (Mean ± SD)	57.63±7.53	55.35±7.73	>0.05
ASAPS (I:II)	80/20	86/14	>0.05

Patient characteristics in terms of age, gender and weight were comparable in both the groups.

Table 2: Changes in heart rate in two groups

Heart Rate	Group C	Group D
Baseline	81	81
AD-5 minutes	80	80
AD- 10 minutes	82	79
AD- 15 minutes	83	80
AD- 20 minutes	84	82
During laryngoscopy and intubation	103	86
AI- 1 minute	101	81
AI- 2 minutes	100	80
AI- 5 minutes	99	78
AI- 10 minutes	98	77

On comparing the changes in heart rate between group C and group D at various specific timing, there was significant difference between the two groups ($p<0.05$).

Table 3: Changes in systolic blood pressure in two groups

Systolic blood pressure	Group C	Group D
Baseline	120	121
AD-5 minutes	119	120
AD- 10 minutes	118	118
AD- 15 minutes	118	119
AD- 20 minutes	119	121
During laryngoscopy and intubation	142	124
AI- 1 minute	140	120
AI- 2 minutes	139	119
AI- 5 minutes	138	118
AI- 10 minutes	136	116

On comparing the changes in SBP between group C and group D at various specific timings, there was statistically significant difference between the two groups ($p<0.05$).

Table 4: Changes in diastolic blood pressure in two groups

Diastolic blood pressure	Group C	Group D
Baseline	75	75
AD-5 minutes	76	73
AD- 10 minutes	77	71
AD- 15 minutes	76	70
AD- 20 minutes	90	72
During laryngoscopy and intubation	88	76
AI- 1 minute	86	74
AI- 2 minutes	84	70
AI- 5 minutes	82	69
AI- 10 minutes	80	70

On comparing the changes in DBP between group C and group D at various specific timings, there was statistically significant difference between the two groups ($p<0.05$).

Table 5: Changes in SpO_2 in two groups

Changes in SpO2	Group C	Group D
Baseline	99	99.5
AD-5 minutes	98.5	98
AD- 10 minutes	99	99
AD- 15 minutes	99.5	98
AD- 20 minutes	99	99
During laryngoscopy and intubation	98.5	99.5
AI- 1 minute	98	99
AI- 2 minutes	98.5	99.5
AI- 5 minutes	98	98
AI- 10 minutes	98	99

SpO_2 remained stable and comparable in both the groups throughout the study period ($p>0.05$).

Table 6: Sedation score in two groups

Sedation score	Group C	Group D
Baseline	0	0
After drug infusion	0	1.16
5 minutes	0	1.22
10 minutes	0	1.42
15 minutes	0	1.18
20 minutes	0	1.72

The difference in sedation score was significant between group C and group D after drug administration ($p<0.001$). Sedation did not cause respiratory depression in any patient.

Table 7: Complications

Complications	Group C		Group D	
	No.	%	No.	%
Bradycardia	0	0	12	12
Hypotension	0	0	5	5
Arrhythmias	5	5	0	0
Tachycardia	30	30	4	4
Hypertension	28	28	3	3
Respiratory depression	0	0	0	0

In group C, 30 patients (30%) had tachycardia, 28 patients (28%) had hypertension and 5 patients (5%) had arrhythmia intraoperative. In group D, 12 patients (12%) had bradycardia and 5 patients (5%) had hypotension, preoperative. Intraoperative, 4 patients (4%) had tachycardia and 3 patients (%) had hypertension. Respiratory depression was not seen in any patient of either group.

Discussion

In the era of modern anaesthesia and surgery, the key factor is safe outcome. Anaesthetic drugs, complicated surgical procedures and patient's condition due to co-existing medical diseases increase the risk. With the use of newer safe drugs, continuous monitoring and management of perioperative events with excellent care in the post

operative units have reduced the morbidity and mortality for last few decades. Tracheal intubation is associated with catecholamine release and pressor response, leading to an elevation in HR and blood pressure. Many previous studies have reported the use of dexmedetomidine to suppress this response as well as to reduce the dose of anesthetic agent. [16]

Intubation can increase blood pressure by 40%–50% and HR by 20%. [17] This transient hypertension and tachycardia can be tolerated in young patients but can be catastrophic in vulnerable patients who are vasoconstricted, volume depleted, or have severe heart block. Geriatric patients are at increased risk because of their aging-associated structural and functional changes in the cardiovascular and cerebrovascular systems, which would affect myocardial and cerebral perfusion. [18] The relatively unstable cardiovascular system in elderly patients owing to lost elastance in the arterial wall, venous vessels, and myocardium leads to hypertensive diseases, especially systolic hypertension with a large pulse pressure, further increasing the systemic vascular resistance. [19,20] Stiffening of the venous system leads to the limited ability to autoregulate preload and myocardial stiffening causes delayed relaxation with impaired early and late diastolic filling, leading to poor tolerability to change in volume and pressure. [21]

Aho M, et al [22] studied the effect of two doses of dexmedetomidine (0.3 μg/kg & 0.6μg/kg) and fentanyl (2μg/kg) on haemodynamic response to laryngoscopy and intubation in women undergoing abdominal hysterectomy. They concluded that dexmedetomidine at a dose of 0.6μg/kg administered before induction blunted the tachycardiac response during endotracheal intubation and the post intubation increase in heart rate was significantly less compared to the fentanyl group. M.L. Jaakola, et al [23] studied the effect of a single intravenous bolus dose of dexmedetomidine (0.6 μg/kg) on intraocular pressure, hemodynamic & sympathoadrenal responses to laryngoscopy & tracheal intubation. They observed that in dexmedetomidine group, there was 34% reduction in intraocular pressure & 62% reduction in plasma nor-adrenaline concentrations. After intubation, maximum heart rate was 18% less in dexmedetomidine group compared with placebo. They also noted that there was decrease in blood pressure in dexmedetomidine group. Similar to above studies, in our study there was significant fall in heart rate in dexmedetomidine group after drug administration ($p<0.05$) as compared to baseline. There was increase in heart rate at the time of laryngoscopy and intubation but this increase was not significant ($p>0.05$). After intubation, heart rate returned below baseline value ($p<0.05$) and remained so throughout the study period. While in control group, heart rate significantly increased during laryngoscopy and intubation and remained above baseline ($p<0.05$) throughout the study period.

In our study there was significant fall in heart rate in dexmedetomidine group after drug administration ($p<0.05$) as compared to baseline. There was increase in heart rate at the time of laryngoscopy and intubation but this increase was not significant ($p>0.05$). After intubation, heart rate returned below baseline value ($p<0.05$) and remained stable throughout the study period. While in control group, heart rate significantly increased during laryngoscopy and intubation and remained above baseline ($p<0.05$) throughout the study period. We also observed mild increase in SBP, DBP and MAP during laryngoscopy and intubation in dexmedetomidine group, which was not significant ($p>0.05$). Thereafter, blood pressure decreased and remained so throughout the study period. While in control group, there was significant rise in MAP during laryngoscopy and intubation and this increase was remained so throughout the study period Similar results were found by Hall et al [24] that biphasic cardiovascular changes, where blood pressure decreased followed by a momentary rise in blood pressure after an injection of dexmedetomidine, occurred after infusion of dexmedetomidine in dose of 0.2-0.6 μg/kg. They reported that an insignificant rise in blood pressure had continuously been exhibited for 10 min after an initial injection of dexmedetomidine, and the heart rate decreased significantly. MAP decreased after drug infusion below baseline value ($p<0.05$) without fluctuation in dexmedetomidine group. Changes in blood pressure during laryngoscopy and intubation was comparable to baseline value.

Conclusion

Dexmeditomidine in a dose of 1 mcg/kg given half an hour before induction effectively blunts the hemodynamic response to laryngoscopy and endotracheal intubation and provides stable hemodynamic through the surgery and provides good and safe level of sedation without respiratory depression in routine surgery.

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