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Original Research Article

Randomized Prospective Double Blind Clinical Evaluation of Dexmedetomidine on Haemodynamic Stress Response during Laryngoscopy and Intubation

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Conflict of interest: Nil

Abstract

Aim: The present study was aimed at attenuation of haemodynamic sress response to laryngoscopy and intubation in patients posted for elective surgeries under GA.

Methodology: This randomized prospective double-blind study carried out in 140 patients aged 20-60 years of ASA physical status of I and II scheduled for elective surgery under general anaesthesia requiring endotracheal intubation. After detailed pre-anaesthetic evaluation, systemic examination and routine investigations were done. In pre-anesthetic preparation room, monitoring for heart rate, non-invasive blood 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 Ondensetran 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 70 patients) using random number table method. Group B, (n=70): Inj. dexmedetomidine 1mcg/kg in 100 ml NS and Group A, (n=70): 100 ml NS Intravenous infusion over 10-15 minutes, 30 minutes before induction of anesthesia. Patients were monitored for hemodynamic changes at various specific timing as per protocol, and sedation was monitored according to Ramsay Sedation Score immediately and at 5, 10, 15 and 20 minutes after drug administration.

Results: 52 and 59 were ASA physical status I in group A and B respectively, and 18 and 11 were ASA physical status II in group A and B respectively. Patient characteristics in terms of age, gender and weight were comparable in both the groups. On comparing the changes in heart rate, SBP, DBP, SpO2, MAP, and sedation sore between group A and group B at various specific timing, there was significant difference between the two groups. Sedation did not cause respiratory depression in any patient. There was significant fall in heart rate in dexmedetomidine group after drug administration as compared to baseline. There was increase in heart rate at the time of laryngoscopy and intubation, but this increase was not significant. After intubation, heart rate returned below baseline value and remained so throughout the study period. While in control group, heart rate significantly increased during laryngoscopy and intubation and remained above baseline throughout the study period. In group A, 18 patients (25.7%) had tachycardia, 16 patients (22.9%) had hypertension and 4 patients (5.7%) had arrhythmia intraoperative. In group B, 6 patients (8.6%) had bradycardia and 3 patients (4.3%) had hypotension, preoperatively. Intraoperative, 5 patients (7.1%) had tachycardia and 3 patients (4.3%) had hypertension. Respiratory depression was not seen in any patient of either group.

Conclusion: Dexmeditomidine given before induction effectively blunts the hemodynamic response to laryngoscopy and endotracheal intubation and provides stable hemodynamic throught the surgery and provides good and safe level of sedation without respiratory depression in routine surgery.

Keywords: Dexmeditomidine, laryngoscopy, endotracheal intubation, bradycardia, tachycardia.

Introduction

Induction of general anaesthesia, laryngoscopy, tracheal intubation, and extubation are associated with various haemodynamic changes due to increased sympathoadrenal activity, which may result in hypertension and/or tachycardia [1, 2]. 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 [3, 4]. The elevated catecholamine concentration in plasma due to sympathetic discharge increases the arterial blood pressure, heart rate and oxygen consumption, leading to haemodynamic instability [5, 6].

Although transient, this exaggerated response may precipitate hypertensive crises, myocardial ischemia, arrhythmias, or increases in intracranial pressure in susceptible individuals [1]. To attenuate sympathetic discharge and provide hemodynamic stability various agents such as volatile anaesthetics [7], topical and IV lidocaine, opioids [8], vasodilators like Sodium nitroprusside [9], Nitroglycerine [10], Calcium channel blockers [11], Beta blockers [12] and alpha 2 agonist [13] have been used in general anaesthesia.

It has become evident by various studies that, $\alpha 2$ adrenoceptor agonists may be a useful class of drugs in conjunction with anesthesia. Dexmedetomidine (DEX) is such a potent and highly selective alpha-2 receptor agonist with sympatholytic, sedative, amnestic, and analgesic properties [14]. It is an ideal agent for relieving anxiety or nervousness before anaesthesia. It is established that preoperative intravenous (IV) DEX can successfully attenuate the laryngoscopic stress response [15]. The efficacy of dexmedetomidine in decreasing the hemodynamic response to laryngoscopy and intubation has been studied through intravenous [16, 17], intranasal [18, 19], and intramuscular routes [20].

However, intravenous administration may cause bradycardia and hypotension, and intranasal administration may be associated with irritation [21]. Beside IV route, DEX is also effective through intramuscular, oral and intranasal (IN) routes. The intranasal route is more convenient and effective than others [22]. Intranasal DEX has been shown to have a high rate of patient acceptance. Recently, several studies in paediatric age group have reported beneficial perioperative outcomes of intranasal DEX premedication as an alternative to traditional premedication [22, 23]. To the best of our knowledge, there are no recent studies demonstrating the effects of dexmedetomidine on the hemodynamic response to laryngoscopy and intubation. The present study was aimed at attenuation of haemodynamic sress response to laryngoscopy and intubation in patients posted for elective surgeries under GA.

Materials and Methods

This randomized prospective double-blind study carried out in 140 patients aged 20-60 years of ASA physical status of I and II

scheduled for elective surgery under general anaesthesia requiring endotracheal intubation.

After detailed pre-anaesthetic evaluation, systemic examination and routine investigations were done. Patients 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 Ondensetran 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 70 patients) using random number table method. Group B, (n=70): Inj. dexmedetomidine 1mcg/kg in 100 ml NS and Group A, (n=70): 100 ml NS Intravenous infusion over 10-15 minutes, 30 minutes before induction of anesthesia. Patients were monitored for hemodynamic changes at various specific timing as per protocol, and sedation was monitored according to Ramsay Sedation Score immediately and at 5, 10, 15 and 20 minutes after drug administration.

Table 1: 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.

Procedure:

In the operation theatre multipara monitor was attached and vital parameters were recorded. Standard general anaesthesia was given to all patients. All the parameters were recorded at various specific timings as per protocol. 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. Hypertension was defined as increase in blood pressure > 30% of the baseline value and treated with Inj. NTG i.v. Infusion. Bradycardia was defined as a pulse rate of < 60 beat/ min and will be treated with bolus of 0.6 mg atropine. Tachycardia was defined as pulse rate of > 100 beats min and was treated with beta blockers. Any treatment required and complication if any, was recorded till 30 min after intubation. At the end of surgery, neuromuscular blockade was reversed with neostigmine 50 microgram/kg and glycopyrrolate 10 microgram/kg IV. After satisfying the extubation criteria, trachea was extubated, and patients were transferred to post anaesthesia care unit.

Results:

Table 2: Demographic profile of patients

Demographic profile	Group A	Group B	p value
Age(years)	35.75±9.46	37.35±10.63	>0.05
Gender (M: F)	38/32	41/29	>0.05
Weight(kg) (Mean ± SD)	58.45±8.57	54.85±9.47	>0.05
ASAPS (I: II)	52/18	59/11	>0.05

52 and 59 were ASA physical status I in group A and B respectively, and 18 and 11 were ASA physical status II in group A and B respectively. Patient characteristics in terms of age, gender and weight were comparable in both the groups. On comparing the changes in heart rate, SBP, DBP, SpO2, MAP, and sedation sore between group A and group B at various specific timing, there was significant difference between the two groups ($p<0.05$). Sedation did not cause respiratory depression in any patient.

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 group A, 18 patients (25.7%) had tachycardia, 16 patients (22.9%) had hypertension and 4 patients (5.7%) had arrhythmia intraoperative. In group B, 6 patients (8.6%) had bradycardia and 3 patients (4.3%) had hypotension, preoperatively. Intraoperative, 5 patients (7.1%) had tachycardia and 3 patients (4.3%) had hypertension. Respiratory depression was not seen in any patient of either group.

Table 3: Complications (Adverse Events)

Complication	Group A		Group B	
	No.	%	No.	%
Bradycardia	0	0	6	8.6
Hypotension	0	0	3	4.3
Arrhythmias	4	5.7	1	1.4
Tachycardia	18	25.7	5	7.1
Hypertension	16	22.9	3	4.3

In group A, 11 patients (15.7%) needed Inj. NTG infusion in titrated dose to achieve baseline MAP value, intraoperative and 13 patients (18.6%) were given beta blockers. In group B, 4 patients (5.7%) needed Inj. Atropine (0.6 mg) IV to overcome bradycardia after drug administration. Intraoperative, 2 patient (2.9%) needed Inj. NTG infusion.

Table 4: Patients needed treatment for complications in two groups

Treatment	Group A		Group B	
	Number of pts	%	Number of pts	%
Beta blockers	13	18.6	1	1.4
Inj. Atropine	0	0	4	5.7
Inj. NTG Infusion	11	15.7	2	2.9

Discussion:

DEX, a centrally acting α2agonists, is widely used in the intensive care unit for its unique sedative, hypnotic, anxiolytic, sympatholytic, antisecretory and analgesic properties. It has unique pharmacological property of conscious sedation and is devoid of any respiratory depression. It is responsible for producing dose dependant co-operative sedation that allows early interaction and early postoperative

neurological assessment [24]. Dex also has a reversal drug for its sedative effect called as atipamizole, which acts by increasing the central turnover of noradrenaline [25]. Due to all of these specific characteristics, nowadays DEX become popular as an ideal premedication agent [26, 27].

Dexmedetomidine acts on various brain stem and medullary nuclei (nucleus tractus solitarus, lateral reticular nucleus) and the hypothalamus to decrease the sympathetic nervous activity and attenuate the hemodynamic response to laryngoscopy and intubation [28]. Various studies have investigated the effects of intravenous dexmedetomidine on the hemodynamic response to laryngoscopy and intubation [28-31]. While doses of 1–2 μg/kg have been found to be effective in attenuating this hemodynamic response, they are associated with significant side effects, such as bradycardia, hypotension, or respiratory depression [29, 30]. Lawrence and De Lange [29], found that a single dose of 2 μg/kg dexmedetomidine caused a higher incidence of bradycardia and hypotension compared with the placebo treatment. Similarly, Mahajan et al. [30], found that with the same depth of anesthesia, there was a significant fall in HR and SBP and DBP in the dexmedetomidine group (1 μg/kg) versus the placebo group, and that this effect lasted until 30 min following drug administration.

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. A.E. Sagroglu et al [32] compared the two doses of dexmedetomidine (1 microgram/kg and 0.5 microgram/kg) in patients posted for elective gynecological surgery. They observed that SBP, DBP,MAP values were significantly lower during intubation and at 1 and 2 min after intubation in group receiving dexmedetomidine 1 microgram/kg than group receiving dexmedetomidine 0.5 microgram/kg ($P<0.05$).

Kallio et al[33] showed that the maximum inhibition of sympathetic nervous system activity occurred at 50 and 75μg doses of dexmedetomidine. Aho M, et al[34] 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.

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 [35], 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. [36] 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 given before induction effectively blunts the hemodynamic response to laryngoscopy and endotracheal intubation and provides stable hemodynamic throught the surgery and provides good and safe level of sedation without respiratory depression in routine surgery.

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