RESEARCH PAPER

A comparative study of two different doses of dexmedetomidine on haemodynamic responses to induction of anaesthesia and tracheal intubation

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ABSTRACT

Tracheal intubation and direct laryngoscopy are considered as the most critical event during administration of general anaesthesia. Dexmedetomidine is an alfa-2 adrenergic agonist use for control of haemodynamic response to laryngoscopy and tracheal intubation. Our study consisted 60 patients of ASA grade I or II, scheduled for elective gynaecological, general and ENT surgery, divided into two groups of 30 patients each. Group A received injection dexmedetomidine 1.0 µg.kg^{-1} over 10 minutes and Group B received injection dexmedetomidine 0.5 µg.kg^{-1} over 5 min, both diluted in 10 ml normal saline. One min after dexmedetomidine, injection thiopental sodium 5 mg.kg $^{-1}$ and injection vecuronium bromide 0.1 mg.kg $^{-1}$ were administered intravenously for induction. Intubation was performed after 3 min. The parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and O_2 saturation (SpO2) were recorded at pre-induction, 60 seconds (sec) after dexmedetomidine (t1), 60 sec after induction (t2), during laryngoscopy and tracheal intubation (t3), 1 min after intubation (t4), 2 min after intubation (t5) and 5 min after intubation (t6). Data obtained was analysed using unpaired t-test. We have observed statistically highly significant ($p<0.01$) increase in mean SBP, DBP and MAP in Group B as compare to Group A at t3 and t4 while at pre-induction, t1, t2, t5 and t6, mean SBP, DBP and MAP were comparable in both groups ($p>0.05$). There were statistically highly significant ($p<0.01$) increases in mean HR in Group B as compare to Group A at t3, t4, t5 and t6 while it was comparable ($p>0.05$) at pre-induction, t1 and t2 in both groups. There was no significant changes in SpO2 in both groups at all intervals ($p>0.05$). We conclude that dexmedetomidine 1 µg.kg^{-1} is more effective than 0.5 µg.kg^{-1} in attenuating haemodynamic responses to laryngoscopy and tracheal intubation, without any systemic side effects.

Key words: Dexmedetomidine, endotracheal intubation, haemodynamic response, laryngoscopy

INTRODUCTION

Tracheal intubation is placement of a flexible plastic tube into the trachea to maintain an open airway, to facilitate ventilation of the lung and prevention of aspiration in critically ill or anesthetized patients. Direct laryngoscopy and passage of an endotracheal tube are noxious stimuli produces adverse hemodynamic responses, due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. Increases plasma catecholamines concentration [1] leads to hypertension, tachycardia and arrhythmia. The magnitude of hemodynamic response is greater with increasing force and duration of laryngoscopy and endotracheal intubation.[2] The elevation of blood pressure typically starts within 5 sec of laryngoscopy, reached pick in 1-2 min and returns to control level within 5 min.[3] Transient hypertension and tachycardia are probably of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency and cerebrovascular disease. At least in such individuals there is a necessity to blunt this response. Reid and Brace [4] in 1940 were the first to report the circulatory responses to laryngeal and tracheal stimulation in an anesthetized man. Dexmedetomidine, a highly selective alfa-2 adrenergic agonist has sedative, anxiolytic, sympatholytic and analgesic effect. In addition, dexmedetomidine has been shown to

decrease perioperative catecholamines concentration and promote hemodynamic and adrenergic stability, as well as it decrease induction doses of intravenous anaesthetic and also decrease intra operative opioid and volatile anaesthetic requirements for maintenance of anaesthesia.[5,6] The purpose of our study was to investigate and compare the effects of two different doses of dexmedetomidine on controlling hemodynamic response to induction of anaesthesia and tracheal intubation.

MATERIALS AND METHODS

The study protocol was approved by institutional ethical committee and written informed consent was obtained from all the patients. Sixty normotensive patients (ASA Grade I or II, age between 19-60 years, weight between 40-80 kg, Mallampatti Grade I or II) were randomly allocated in two groups (30 patients each). Group A received inj. dexmedetomidine 1µg/kg in 10 ml normal saline, IV over 10 min. While Group B received inj. dexmedetomidine 0.5µg/kg in normal saline, IV over 5 min.

In all the patients, IV line was secured and routine monitor like pulse oxymeter (SpO2), non-invasive blood pressure (BP) and electrocardiogram were attached. Vital data like B.P. (SBP, DBP), heart rate (HR) and SpO_2 were recorded as pre-induction parameters (basal) and pre-medication inj. Glycopyrrolate 0.2mg IV was given. According to group, inj. dexmedetomidine was given and patients were pre-oxygenated with 100% oxygen via facemask. Anaesthesia was induced with inj. thiopentone 5 mg/kg IV. Laryngoscopy and tracheal intubation was done after 3 min of inj. Vecuronium 0.1mg/kg. Anaesthesia was maintained using 66% nitrous oxide, 33% oxygen, inj. vecuronium and sevoflurane 1%. Measurements of HR, SBP, DBP, and SpO2 were performed as basal, 60 sec after inj. dexmedetomidine (t_1), 60 sec after induction (t_2), during laryngoscopy and intubation (t_3), 60 sec after intubation (t_4), 2 min after intubation (t_5) and 5 min after intubation (t_6).

Data were analyzed with unpaired independent sample t-test to measure difference between the groups. P>0.05 was consider as not significant, P<0.05 was considered as significant and p<0.01 was considered as highly significant. The results were presented as means and standard deviation.

RESULTS

Demographic profile of two groups is given in Table 1.

Table 1: Demographic characteristic of two groups

Characteristic	Group A	Group B
No. of Patients	30 (15 Male, 15 Female)	30 (16 Male, 14 Female)
Age (Mean±SD)	30.66±11.20	28.26±9.13
Weight (Mean±SD)	53.66±6.28	53.83±6.39

Haemodynamic changes: Statistical evaluation between groups shows that mean HR at pre-induction, t1 and t2 were statistically not significant (P value> 0.05). While mean HR at t3 (during laryngoscopy and intubation), t4, t5 and t6 were significantly higher in Group B as compare to Group A (P value<0.01) [Table 2]. At t3 and t4 there were increase in mean SBP, DBP and MAP in Group B as compare to Group A, which was statistically highly significant (P<0.01). The mean SBP and DBP at pre-induction, t1, t2, t5 and t6 were comparable in both groups (P>0.05) [Table 3]. There was no significant changes in SpO2 in both groups (p>0.05) [Table 4].

None of patients in either group had any cardiovascular or respiratory side effects due to dexmedetomidine.

DISCUSSION

Most of general anaesthetic procedures in modern anaesthetic practice are carried out with endotracheal intubation. Tracheal intubation and direct laryngoscopy are considered as the most

Table 2: Showing the inter-group comparison of mean heart rate (bpm) changes at various intervals

Time	Pre-induction (basal)	t_1	t_2	t_3	t_4	t_5	t_6
Group-A	105.9±10.28	82.17±5.58	81.20±7.51	81.77±8.68	77.70±8.63	77.60±8.71	77.77±8.59
Group-B	103.66±4.73	82.37±3.65	84.07±4.25	103.33±5.17	87.27±3.35	87.53±3.40	83.13±2.40
***P*- Value**	0.28	0.87	0.074	0.000	0.000	0.000	0.002

Table 3: Showing the inter-group comparison of mean SBP, DBP and MAP (mmHg) changes at various intervals

Time	Mean SBP		*P*	Mean DBP		*P*	MAP		*P*
	Group-A	Group-B		Group-A	Group-B	N.S.	Group-A	Group-B	N.S.
Basal	127.3±5.59	126.5±3.85	N.S.	83.46±2.09	85.00±3.80	N.S.	98.08±2.82	98.93±3.81	N.S.
t1	115.00±3.95	114.87±3.62	N.S.	74.40±3.87	73.80±3.16	N.S.	87.93±3.83	87.49±3.18	N.S.
t2	113.60±4.73	115.13±3.26	N.S.	74.27±4.32	75.00±3.95	H.S.	87.38±4.12	88.38±3.48	H.S.
t3	113.53±4.25	127.47±2.34	H.S.	72.87±4.19	85.80±3.37	H.S.	86.42±3.52	99.69±2.85	H.S.
t4	113.07±3.85	116.83±3.91	H.S.	73.07±4.29	76.13±2.77	N.S.	86.40±3.58	89.70±2.95	N.S.
t5	112.53±4.06	113.40±3.64	N.S.	72.73±3.61	72.87±3.35	N.S.	86.00±3.53	86.38±3.37	N.S.
t6	113.07±4.57	112.40±3.54	N.S.	72.53±3.19	72.27±3.00	N.S.	86.04±3.52	85.64±3.11	N.S.

Table 4: Showing the inter-group comparison of mean SpO2 (%) changes at various intervals

Time	Basal	t1	t2	t3	t4	t5	t6
Group-A	99.03±0.18	99.13±0.34	99.07±0.36	99.13±0.43	99.23±0.43	99.27±0.45	99.10±0.30
Group-B	98.96±0.18	99.06±0.25	99.03±0.18	99.03±0.18	99.17±0.37	99.17±0.37	99.20±0.40
***P*-Value**	0.162	0.398	0.656	0.250	0.527	0.356	0.286

critical event during administration of general anesthesia as they provoke transient but marked sympathoadrenal response as hypertension and tachycardia.[7] These responses are transitory variable and may not be significant in otherwise normal individuals. But in patient with cardiovascular compromise like hypertension, IHD, Cerebrovascular disease and in patient with intracranial aneurysms, even these transient changes in haemodynamics can result in potentially harmful effects like left ventricular failure, pulmonary oedema, myocardial ischemia[3], ventricular dysrrhythmias and cerebral haemorrhage.[8] This is by far the most important indication for attenuation of haemodynamic response to laryngoscopy and tracheal intubation during general anaesthesia.

Many methods like use of inhalational anaesthetic agents, lidocaine[9], opioids[10,11], direct acting vasodilator[12,13], calcium channel blockers[14,15], and β-blockers[16] have been tried by various authors for blunting haemodynamic response to laryngoscopy and tracheal intubation. But all such manoeuvres had their own limitations. For example, with opioids respiratory depression [17] and chest wall rigidity [18] were potential problems, use of halothane was associated with dysrhythmias[19], calcium channel blocker produced reflex tachycardia [20], direct acting vasodilator needed invasive haemodynamic monitoring and lidocaine did not give consistent result in blunting the haemodynamic responses to laryngoscopy and intubation. Beta blockers are also one group of pharmacological agents employed for blunting haemodynamic response to laryngoscopy and intubation but they blunt HR response better than BP response.[16]

The α-2 adrenoreceptor are involved in regulating the autonomic and cardiovascular systems, which are located on blood vessels, where they mediate vasoconstriction and on sympathetic terminals they inhibit norepinephrine release. The α-2 receptors are also located within the central nervous system (CNS) and their activation leads to sedation, a reduction of tonic levels of sympathetic outflow and an augmentation of cardiac-vagal activity. This can result in a decrease in HR and cardiac output. The use of α-2 agonists in the perioperative period has been associated with reduced anaesthetic requirements and attenuated HR and BP responses to stressful events. In addition α-2 receptors within the spinal cord modulate pain pathways, providing some degree of analgesia.[21,22] The analgesic, sedative, anxiolytic, sympatholytic and blunting of exaggerated haemodynamic responses by administration of dexmedetomidine are being extensively studied and are mainly mediated by the activation of alpha-2 receptors located in the post-synaptic terminals in the CNS, which causes decreased neuronal activity and augmentation of the vagal activity.[23] Another α -2 agonist Clonidine, is also used by various authors to blunt the haemodynamic response for laryngoscopy and intubation.[24] Recently, the use of dexmedetomidine has been dramatically increased. This highly selective α-2 agonist has a set of unique effects that include titratable sedation, sympatholysis and analgesia without significant respiratory depression.[25]

The present study was undertaken to know two different doses of dexmedetomidine (0.5µg/kg and 1µg/kg), in attenuation of haemodynamic response to laryngoscopy and tracheal intubation during general anaesthesia.

In our study after giving dexmedetomidine the mean HR, SBP, DBP and MAP were decreased in both groups. In Group B, we have observed increases in mean SBP, DBP and MAP as compare to Group A at t3 (during laryngoscopy and intubation) and t4, which was statistically highly significant. ($p<0.01$) At pre-induction, t2, t4, t5 and t6 mean SBP, DBP and MAP were comparable in between both groups ($p>0.05$). There were increases in mean HR in Group B as compare to Group A at t3 (during laryngoscopy and intubation), t4, t5 and t6 which was statistically highly significant ($p<0.01$), while mean HR at pre-induction, t1 and t2 were comparable in between groups ($p>0.05$).There was no significant change in Spo2 in both groups at all intervals ($p>0.05$).

In a similar study done by A Esra Sağıroğlu et al[26], they found that after giving dexmedetomidine 1 $\mu g.kg^{-1}$ (Group A) and 0.5 $\mu g.kg^{-1}$ (Group B), SAP, DAP, MAP and HR levels were significantly lower at 60 sec after induction and 5 min after intubation than baseline levels. But in Group B, these levels were significantly higher at 60 sec after tracheal intubation (t3) while in Group A, SAP, DAP, MAP were significantly lower in at t_3 ($p<0.01$). They conclude that dexmedetomidine 1 $\mu g.kg^{-1}$ is effective to suppress haemodynamic responses to tracheal intubation but dexmedetomidine 0.5 $\mu g.kg^{-1}$ hasn't the same effect. In this study any hypotension or bradycardia were not observed and any medical intervention was not required. Significant respiratory depression, apnea, muscle rigidity or decrease in SpO_2 were also not seen in any patient.

In study done by Ferdi Menda et al[27], they demonstrated that in dexmedetomidine 1µg/kg group, SAP, DAP and MAP were lower at all times in comparison to baseline values. While in the placebo group, SAP, DAP and MAP decreased after the induction of general anesthesia and five min after the intubation compared to baseline values. They also demonstrated that after induction of general anaesthesia, the drop in HR was higher in dexmedetomidine 1µg/kg group than placebo group. Whereas, 1 min after intubation HR increased significantly in placebo group, while it decreased in dexmedetomidine group.

Tanyoung Pipanmekaporn et al[28] demonstrated that during intubation and 10 min afterward (T1-T10), the mean HR, SBP, DBP and MAP in the control Group were significantly higher than those in the dexmedetomidine 0.7µg/kg Gr throughout the study period except at T1.

In similar study by Varshali M. Keniya et al.[29], the increase in SBP after intubation was 40% in control Group as compared to 8% in dexmedetomidine 1µg/kg Gr (P=0.00). While the increase in DBP after intubation was 25% in control Group as compared to 11% in dexmedetomidine 1µg/kg Group (P=0.001). They also found that 1 µg/kg of dexmedetomidine Group received more treatments for bradycardia than patients in the control Group. Arpita Laha et al.[30] demonstrated that pretreatment with dexmedetomidine 1µg/kg attenuated but did not totally abolish cardiovascular and catecholamine responses to tracheal intubation after induction of anaesthesia. They found increase in HR, SBP and DBP after intubation and at 1, 2, 3 and 5 min in both dexmedetomidine and control Gr, but this rise was significantly less with dexmedetomidine. Bajawa SS et al[31] found that the dose of 1 µg/kg of dexmedetomidine attenuate but did not completely obtund the haemodynamic responses to laryngoscopy and tracheal intubation. In a similar study done by Jeong Han Lee et al[32],they observed that in dexmedetomidine 1 µg/kg Group, the increase in SBP and DBP due to tracheal intubation were significantly lower than that of control Group.

Scheinin et al[33] reported that the use of α-2 agonist leads to bradycardia. Basar et al[34] had also reported that the incidence of bradycardia after single dose of 0.5µg/kg of dexmedetomidine was about 5%.

In our study, there was no significant changes in Spo_2 in both groups at all intervals. Similar to our study, Ebert et al[11] didn't observe any apnea, airway obstruction or hypoxemia with bolus doses of dexmedetomidine. They reported that depression of respiration may be seen due to deep sedation, for the reason that α-2 adrenergic agonists don't have active role on the respiration centres. In contrary to our study, Belleville et al[21] found that dexmedetomidine, given as bolus dose of 1-2 $\mu g kg^{-1}$, intravenously within two minutes, causes irregular ventilation and apnea episodes.

Limitation: There were three important limitations regarding this study.

1. Not assessed the quality of intubation.
2. We had not measured the plasma catecholamines levels.
3. We have not studied extubation response, postoperative sedation and hemodynamic variations.

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