Original Research Article

To evaluate two different doses of Dexmedetomidine for attenuating the hemodynamic response to tracheal intubation

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Abstract

Introduction: The hemodynamic response associated with laryngoscopy and tracheal intubation is a common concern for the anesthesiologist, especially in high-risk patients. The use of dexmedetomidine has found favor in obtunding this response, in addition to providing better intubating conditions and reducing the dose of other anesthetic drugs. Most of the current literature states a loading dose of 1 µg/kg dexmedetomidine to be superior to lower doses in this regard. **Material and Methods**: This is a comparative, prospective and observational study conducted at a tertiary care teaching hospital among 40 patients in each group. American Society of Anaesthesiologists (ASA) physical status I and II of either sex aged between 18 to 60 years, scheduled for elective surgeries were enrolled for the present study. The total 80 patients were randomly assigned to two groups of 40 patients each, according to computer generated random number table. Dexmedetomidine infusion was discontinued and residual neuromuscular blockade was antagonized by appropriate doses of neostigmine and glycopyrrolate and tracheal extubation was performed. **Result:** Mean HR in Group A was 82.6 ± 5.64 per min and in group B it was 81.74 ± 5.74 per min at baseline level, which was comparable ($p>0.05$). At 5 minutes and 10 minutes of drug infusion, both Group A and Group B had fall in mean HR, but Group B had statistically significant fall in HR as compared to Group A ($p<0.05$). Baseline SBP between two groups was comparable and found insignificant ($p>0.05$). There was fall in SBP from baseline value in group A while drug infusion was going on, while Group B showed transient rise from baseline value in SBP at 1 minutes of drug infusion which was statistically insignificant difference. **Conclusion:** Dexmedetomidine at 0.5 µg/kg loading dose provides significantly better attenuation of haemodynamic responses of endotracheal intubation unaccompanied by transient hypertension and bradycardia, which is observed at 1 µg/kg loading dose.

Keywords: Dexmedetomidine, **E**ndotracheal intubation, Hypertension

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Introduction

Dexmedetomidine, the S-enantiomer of medetomidine, a relatively newer alpha-2 adrenoreceptor agonist was first used in 1999 as a sedative during premedication primarily in the Intensive Care Units. [1] However, with the passage of time, dexmedetomidine has proved to be a novel drug which is currently used for the purpose of analgesia, day-care surgeries, short procedures such as colonoscopies, and as an adjunct to general anesthesia for the purpose of co-induction. [2] The term co-induction of anesthesia has been applied to the use of two or more drugs to induce anesthesia. Co-induction of anesthesia is practiced by anesthesiologists exploiting drug interactions, particularly synergism. It can produce an improvement in all phases of anesthesia including induction, maintenance, and recovery. [3]

Till date, no perfect drug or drug combination that would blunt the hemodynamic response completely without causing unwanted side effects has been found, but dexmedetomidine promises to be a good option. [4] It was found that patients sedated with dexmedetomidine could be easily aroused for cooperation with procedures and it may protect against myocardial ischemia and reduces the requirement of opioid analgesia. Furthermore, the dose of induction agents such as propofol and thiopentone for sedation and induction of anesthesia may have to be reduced in the presence of dexmedetomidine. [5] The hemodynamic response to laryngoscopy and intubation is also decreased with the administration of dexmedetomidine. [6]

Existing comparative studies of different doses of dexmedetomidine in blunting the hemodynamic response have found the use of a higher loading dose of 1 µg/kg to be more effective compared to lower doses and advocated the use of higher dose. [7] However, this advantage may be offset by adverse effects such as hypotension and bradycardia which are likelier to occur with higher dose. A lower dose of 0.5 µg/kg, besides blunting the hemodynamic response, would be safer in terms of having a reduced incidence of adverse effects and being more cost-effective. [8]

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Material and Methods

This is a comparative, prospective and observational study conducted at a tertiary care teaching hospital among 40 patients in each group.

Inclusion Criteria

American Society of Anaesthesiologists (ASA) physical status I and II of either sex aged between 18 to 60 years, scheduled for elective surgeries were enrolled for the present study.

Exclusion criteria

The patients suffering from hepatic, renal, cardio-pulmonary diseases, or endocrinal disease, obesity, uncontrolled hypertension, any neurological disorder and patients with anticipated difficult airway or who required more than one attempt for intubation.

Patients with known hypersensitivity or drug allergies, taking any antihypertensive or antidepressant drugs.

The total 80 patients were randomly assigned to two groups of 40 patients each, according to computer generated random number table. After the loading dose of dexmedetomidine (1.0µg/kg), patients of Group A were given maintenance infusion of dexmedetomidine in dose of 1.0 µg/kg/h and patients of Group B were given maintenance infusion of dexmedetomidine in dose of 0.5µg/kg/h, continued till the end of surgery. Study drug preparation was done by an assistant who was blinded to the study protocol and was not involved for any data collection. All patients received premedication with pantoprazole 40 mg perorally, a proton-pump inhibitor for acid prophylaxis and midazolam 7.5 mg, a benzodiazepine for anxiolysis perorally on the eve of surgery. All the patients were kept fasting overnight for 8 h.

On the day of surgery, all the patients (n = 80) included in the study were started with Ringer's lactate infusion at the rate of 60 ml/h. Subsequently, injection fentanyl (a potent synthetic opioid analgesic with a short duration of action) in the dose of 1 µg/kg body weight, followed by injection ondansetron (a serotonin $5HT_3$ receptor antagonist for the prevention of postoperative nausea and vomiting) in the dose of 0.1 mg/kg body weight and injection ranitidine (a histamine H_2 receptor antagonist) in the dose of 50 mg were administered intravenously.

Study drug was infused intravenously over a period of 10 min, and all the patients were preoxygenated during this time using a face mask. As soon as the study drug infusion was over, the induction of anesthesia began with 1% propofol intravenously at the rate of 0.5 ml/s which continued till the patient's verbal response was abolished. The dose of propofol required for abolishing this response was noted after which neuromuscular blockade was achieved with injection rocuronium administered intravenously in the dose of 0.9 mg/kg body weight. Subsequently, endotracheal intubation was attempted after 90 s. While intubation was performed, all patients were assessed for five variables – face mask ventilation, jaw relaxation, positioning of vocal cords, movement of vocal cords on intubation, and reflex movement on tracheal intubation.

Baseline systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), mean blood pressure (MBP), and oxygen saturation (SPO_2) were recorded at the time of starting study drug and then after every 2 min till intubation. Subsequently, vitals were recorded at 2, 5, and 10 min after intubation. Any variation in BP and HR was recorded.

Statistical analysis

The variables were expressed as Mean ±SD. The statistical analysis was done using SPSS version 20. The parameters were compared using the Chi-square test for categorical data, one-way analysis of variance (ANOVA) for intergroup comparison, and paired t-test for intragroup comparison.

Result

In table 1, maximum number of male in both groups, Group A has 62.5% and Group B has 67.5%.

Table 1: Gender distribution of patients

Gender	Group A		Group B	
	No	%	No	%
Male	25	62.5	27	67.5
Female	15	37.5	13	32.5
Total	**40**	**100.0**	**40**	**100.0**

Table 2: Age distribution of patients

Age in years	Group A		Group B	
	No	%	No	%
<20	1	2.5	2	5.0
21-30	7	17.5	8	20.0
31-40	14	35.0	13	32.5
41-50	10	25.0	11	27.5
51-60	8	20.0	6	15
Total	**40**	**100.0**	**40**	**100.0**
Mean ± SD	36.37±4.74		35.94±4.69	

*data are expressed as Mean± standard deviation, p=0.696.

In table 2, the mean age in Group A and B were 36.37±4.74 and 35.94±4.69 respectively with a P value of 0.696.

Table 3: Comparison of types of surgical procedure in study groups

Surgery	Group A		Group B	
	No	%	No	%
Thoracic spine procedures	3	7.5	2	5.0
Cervical spine procedures	14	35.0	16	40.0
Lumbar spine procedures	23	57.5	22	55.0
Total	**40**	**100.0**	**40**	**100.0**

The types of surgery included lumbar spine surgeries (57.5% and 55% in Group A and B respectively), cervical spine surgeries (35.0% and 40% in Groups A and B respectively), thoracic spine surgeries (7.5%, 5% in groups A, B respectively) and were comparable between the groups. The average duration of surgery was 153.53±14.53 and 164.53±14.74 minutes in Groups A and B respectively which was comparable, with a P value of 0.644 in table 3.

Table 4: Comparison of changes in mean Heart Rate (HR) between Group A and Group B

Time	Group A Mean ± SD	Group B Mean ± SD	P- Value
Base	82.6 ± 5.64	81.74 ± 5.74	0.745
5 min with ongoing drug infusion	66.63 ± 4.64	77.62 ± 4.73	<0.0001
at completion of drug infusion	58.63 ± 4.13	73.53 ± 4.12	<0.0001
during induction	66.63 ± 4.06	65.53 ± 3.74	0.574
during intubation	74.53 ± 4.23	71.51 ± 4.64	0.053
1 min after intubation	71.35 ± 4.72	69.74 ± 4.64	0.061
5 min after intubation	67.53 ± 4.65	63.63 ± 4.62	<0.0001
10 min after intubation	63.53 ± 4.73	54.46 ± 4.73	<0.0001

Mean HR in Group A was 82.6 ± 5.64 per min and in group B it was 81.74 ± 5.74 per min at baseline level, which was comparable (p>0.05). At 5 minutes and 10 minutes of drug infusion, both Group A and Group B had fall in mean HR, but Group B had statistically significant fall in HR as compared to Group A (p<0.05). During induction, during intubation and at 1 minute after intubation, fall from baseline HR value was noted and this fall remained to be statistically insignificant between both group. (p>0.05). Maximum fall in mean HR was observed at 10 minutes after intubation in Group A and it was observed in Group B at 10 minutes of drug infusion in table 3.

Table 5: Comparison of changes in mean systolic blood pressure (SBP) between Group A and Group B

Time	Group A Mean ± SD	Group B Mean ± SD	P- Value
Base	127.53 ± 10.6	126.63 ± 10.3	0.732
5 min with ongoing drug infusion	123.63 ± 8.5	101.73 ± 8.4	<0.0001
at completion of drug infusion	121.53 ± 8.1	93.54 ± 7.9	<0.0001
during induction	116.42 ± 6.6	96.34 ± 4.7	<0.0001
during intubation	107.32 ± 6.6	103.47 ± 5.4	0.023
1 min after intubation	103.53 ± 6.1	102.54 ± 5.1	0.623
5 min after intubation	97.51 ± 5.9	97.83 ± 4.3	0.173
10 min after intubation	97.64 ± 5.8	92.01 ± 4.1	<0.0001

Baseline SBP between two groups was comparable and found insignificant (p>0.05). There was fall in SBP from baseline value in group A while drug infusion was going on, while Group B showed transient rise from baseline value in SBP at 1 minutes of drug infusion which was statistically insignificant difference. The maximum fall in SBP in both groups was observed at 10 minutes following intubation, in group A and group B respectively, and this difference was also statistically highly significant (p<0.0001). Neither of the group showed deviation in SBP beyond 30% of the baseline value.

Table 6: Comparison of changes in mean Diastolic blood pressure (DBP) between Group A and Group B

Time	Group A Mean ± SD	Group B Mean ± SD	P- Value
Base	87.54 ± 9.6	87.74 ± 9.3	0.432
5 min with ongoing drug infusion	71.64 ± 7.1	83.48 ± 8.1	<0.0001
at completion of drug infusion	66.37 ± 7.1	76.64 ± 7.3	<0.0001
during induction	63.53 ± 6.8	73.35 ± 7.8	<0.0001
during intubation	70.62 ± 6.6	73.74 ± 7.2	0.0021
1 min after intubation	72.63 ± 7.3	78.75 ± 7.6	<0.0001
5 min after intubation	68.87 ± 6.8	73.64 ± 5.4	<0.0001
10 min after intubation	63.74 ± 5.5	60.43 ± 4.6	<0.0001

In table 6, the difference in mean DBP between two groups was statistically insignificant (p>0.05). Statistically significant decrease from baseline in DBP was observed in Group A at 5 and 10 minutes of drug infusion as compared to increase from baseline which was observed in Group B. (p < 0.05).

Discussion

Tracheal intubation is associated with catecholamine release and pressor response, leading to elevation in HR and arterial pressure. A number of prior studies have reported the use of dexmedetomidine to suppress this response as well as to reduce the dose of anesthetic agent. [9] In our study, the hemodynamic response was significantly reduced but not completely abolished with the use of dexmedetomidine. This effect of dexmedetomidine could be attributed to its action on postsynaptic α_2 receptors in the locus coeruleus and activation of endogenous sleep-promoting pathway. This effect can be particularly useful in patients suffering from cerebrovascular disorders, cardiovascular disorders, and hypertension.

Heart Rate

The mean baseline of HR in Group A was 82.6 ± 5.64/ minute, whereas it was 81.74 ± 5.74 /minute in Group B, thus, both the groups were comparable with respect of baseline HR value without any significant statistical difference (p>0.05) There was a statistically significant fall in HR from baseline in Group B at 5 and 10 minutes of drug infusion as compared to Group A. The

difference between mean HR in both group at given time interval was also statistically significant ($p<0.05$). Thus, Group A provided more stable haemodynamic condition throughout the stress period. A biphasic cardiovascular response has been described after the administration of Dexmedetomidine which was observed in our study in Group B. Our result is also supported by many earlier studies where they have transient increase in HR initially within 3 to 5 min of dexmedetomidine infusion, which is followed by a decrease and is probably due to the vasoconstriction effect of dexmedetomidine appearing earlier than the central sympathetic action.

Alike to our study, A Smitha KS *et al d* observed a statistically significant fall in mean HR at 1 and 2 minutes of infusion of dexmedetomidine at 1 /kg over 10 minutes. [10] Transient bradycardia was observed by Kenya et al also in their study using infusion of dexmedetomidine at 1 /kg over 10 minutes prior to induction. [11] Significant transient fall in HR at 1st and 5th minute after administration of single dose of 2 /kg was observed by Sagiroglu AE *et al*. [12] Nath SS *et al* have shown decrease in HR after the infusion of 1µg /kg of Dexmedetomidine. [13] During induction and intubation, transient fall in mean HR observed at above time interval in Group B had reversed and it remained comparable to Group A.

Blood Pressure

Baseline SBP in Group A was 127.53 ± 10.6 mmHg and it was 126.63 ± 10.3 mmHg in Group B. Baseline DBP was 87.54 ± 9.6 mm/Hg in Group A. Likewise, the same was 87.74 ± 9.3 mmHg in Group B. Thus, the baseline blood pressure values between two groups were comparable and there was no statistically significant difference ($p>0.05$). Group A showed fall in mean SBP at 5 and 10 minutes of drug infusion, whereas Group B showed rise in SBP at above mentioned time interval, which was statistically highly significant ($p<0.05$), but was transient in nature, as it was followed by fall in mean SBP by 14.3% during induction.

During intubation and 1 min after intubation, rise in DBP from baseline by 73.74 ± 7.2 and 78.75 ± 7.6 mmHg was observed in Group B, whereas DBP remained below baseline by 70.62 ± 6.6 and 72.63 ± 7.3 mmHg for respective time interval in Group A, thus, the difference was statistically quite significant at 1 minute after intubation. Keniya VM *et al* has found 6% rise in DBP after intubation with Dexmedetomidine and Bashir F *et al* noticed only 3% rise in dexmedetomidine treated patients which was similar to our results. [14] In both groups SBP and DBP started falling immediately after intubation but rate of fall in BP was more gradual in group B. Maximum fall in SBP and DBP in both the group was observed at 10 minutes following intubation, but still the difference between both group remained statistically significant ($p<0.05$)

In our study, no patient had bradycardia (HR< 45), hypertension (BP level > 30% over baseline levels), hypotension (BP level< 30% from baseline levels) and any fall in SpO2 level. Similar to our results Chakraborty J et al have also not found any instability of vitals either with clonidine or dexmedetomidine. [15] Patel CR *et al* study also did not show any side effects like bradycardia and sinus pause, which would have warranted the use of atropine. [16] Gupta K *et al* reported that use of α2 agonist leads to bradycardia. [17] Some study reported that when Dexmedetomidine in 1-2 µg/kg given in two minutes causes irregular ventilation and apnoea episodes. [18]

Dexmedetomidine has been established that stimulation of alpha-adrenoreceptors can be beneficial during myocardial ischemia. Dexmedetomidine can cause a reverse steal effect whereby the transmural redistribution of blood flow away from the ischemic endocardium is prevented by specific epicardial vasoconstrictive effects. It can also cause bradycardia thereby decreasing myocardial oxygen consumption. [19] These properties make dexmedetomidine an ideal anesthetic adjuvant for coronary artery bypass grafting. The hypotensive and negative chronotropic effects of dexmedetomidine are theoretical concerns which could limit its use in previously β-blocked ischemic heart disease patients. There was no incidence of bradycardia requiring treatment in our study.

Conclusion

Based on statistical analysis and thereby obtained results, it can be stated that dexmedetomidine at 0.5 µg/kg loading dose provides significantly better attenuation of haemodynamic responses of endotracheal intubation unaccompanied by transient hypertension and bradycardia, which is observed at 1 µg/kg loading dose.

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