

A COMPARATIVE STUDY BETWEEN TWO DIFFERENT DOSES OF DEXMEDETOMIDINE FOR ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION

Thapa C, Gauchan S

Department of Anesthesiology, Nepal Medical College and Teaching Hospital, Attarkhel, Kathmandu, Nepal

ABSTRACT

Laryngoscopy and endotracheal intubation are stressful situation for the patients, as these procedures are capable of producing tachycardia, hypertension and arrhythmias. This study was conducted with the objective of arriving at an optimal dose of dexmedetomidine that can attenuate the hemodynamic response to laryngoscopy and intubation with minimal side effects. The current study was conducted in 60 patients, posted for elective surgery under general anesthesia with endotracheal intubation. The patients were divided into two groups: Group A and Group B. Group A received dexmedetomidine 0.5 µg/kg and group B received dexmedetomidine 1 µg/kg intravenously over 10 min prior to induction of anesthesia. The anesthesia technique was standardized in both the groups. Heart rate, systolic, diastolic and mean arterial pressure were monitored and recorded at 5 min and 10 min of completion of infusion of study drug, after induction, and at 1 min, 2 min, 5 min after intubation. The baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were statistically similar in both the groups. After the infusion of the study drug the mean heart rate, mean systolic blood pressure, mean diastolic blood pressure, mean arterial pressure at all times were comparable in both the groups. Episodes of hypotension and bradycardia were also statistically similar in both the groups. Attenuation of hemodynamic response to laryngoscopy and intubation by dexmedetomidine is similar with the two doses: 0.5 µg/kg and 1 µg/kg. Both the doses of dexmedetomidine were devoid of any significant adverse effects.

KEYWORDS

Attenuation, dexmedetomidine, laryngoscopy, tracheal intubation

CORRESPONDING AUTHOR

Dr. Chitra Thapa, Lecturer,
Department of Anesthesiology,
Nepal Medical College Teaching Hospital,
Attarkhel, Gokarneshwor-8, Kathmandu, Nepal
Email: tchitra50@yahoo.com
ORCID ID: 0000-0002-0778-8596
DOI: <https://doi.org/10.3126/nmcj.v21i3.26444>

INTRODUCTION

Endotracheal intubation is the trans-laryngeal placement of a tube in the trachea via nose or mouth. Introduced in the last quarter of the 19th century, it is one of the most frequently performed procedures.¹ Along with provision of ventilation it also helps prevent aspiration in patients. But the clinical benefits of endotracheal intubation are not without undesirable side effects. Direct laryngoscopy and tracheal intubation leads to tachycardia, hypertension, and various types of arrhythmias which may prove fatal in patients with untreated hypertension, coronary artery disease, intracranial hypertension or aneurysm.²

Recently dexmedetomidine has been reported to be very useful in blunting the hemodynamic effects of laryngoscopy and intubation. It has been studied in different doses. But the dose of dexmedetomidine at which it blunts the stress response with minimal side effects is yet to be established in our population. So in search of an optimal dose of dexmedetomidine for attenuation of stress response in Nepalese population, this study was planned.

MATERIALS AND METHODS

This was a randomized double blind study conducted at Nepal Medical College and Teaching Hospital from June to August 2019. Ethical approval from the Institutional Review Committee of Nepal Medical College and Teaching Hospital was obtained. Thorough pre-operative evaluation of the patients was done a day before surgery. A total of 60 patients, aged 18-55 years of either sex, ASA PS I and II posted for elective surgery under general anesthesia were included in this study. Patients with hypertension and cardiac disease, patients with difficult airway (Mallampatti Grade III and IV), obese patients (BMI >25), patients with endocrinal diseases like hyperthyroidism and hypothyroidism, patients allergic to the study drug, patients with baseline heart rate < 60 beats/minute and patients on beta blockers were excluded from the study. Those patients who had intubation attempt lasting longer than 15 sec, and multiple intubation attempts (2 or more) were also excluded from the study. An informed written consent was obtained from all the patients who meet the inclusion criteria. Premedication was done with tab. Lorazepam 2 mg for patients weighing 50 kg or more and tab. Lorazepam 1 mg for patients weighing less than 50 kg on the night before surgery. The patients were kept nil per oral for at least 8 hours for solid food and sips of clear liquid were allowed till 2 hours prior to surgery. The patients were allocated into two groups: Group A and Group B, 30 patients in each

group, by slips of paper in a box technique. One of the anesthesiologist prepared the intravenous infusion and coded them. The coded infusion was given to the resident anesthetist, who was unaware of its content, to be administered to the patients. The same resident was given the responsibility of monitoring the patient intraoperatively and recording all the hemodynamic parameters of the patients. All the intubations were done by the co-author of the study.

In the operating room ECG, pulse oximeter and non-invasive blood pressure (NIBP) cuff were attached. Baseline cardiovascular parameters i.e. heart rate, blood pressure (systolic, diastolic and mean) and oxygen saturation were recorded. Intravenous (IV) access secured with appropriate sized cannula. Patients belonging to the Group A (n=30) received dexmedetomidine 0.5 µg/kg diluted with 0.9% normal saline to make a total 20 ml volume, slowly IV over 10 minutes via syringe pump. Patients belonging to the Group B (n=30) received dexmedetomidine 1 µg/kg diluted with 0.9% normal saline to make 20 ml volume, slowly IV over 10 minutes via syringe pump. Vitals heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO₂) were monitored during infusion of the drug. General anesthesia technique was standardized for both the groups. Inj. Fentanyl 2 µg/kg was given, induction was done with Propofol 1% injection in incremental dose until loss of eyelash reflex was attained. Isoflurane at 0.5% was turned on. After confirmation of bag and mask ventilation, vecuronium 0.1 mg/kg was given. One minute after vecuronium injection, isoflurane was increased to 2% to deepen the anesthesia. Three minutes after vecuronium injection, direct laryngoscopy and intubation was done. Heart rate, systolic, diastolic and mean arterial pressure was recorded before giving the test drug, after completion of the administration of the test drug at 5 and 10 minutes, after induction, after intubation at 1 minute, 2 minutes and 5 minutes. Maintenance of anesthesia was done with isoflurane, oxygen, vecuronium with IPPV and fentanyl as needed. At the end of the surgery, residual effect of neuromuscular blockade was reversed by Neostigmine 2.5 mg and glycopyrolate 0.4 mg. Patients were then extubated and transferred to the post-operative ward. The duration of surgery and the duration of anaesthesia were also recorded.

Clinically relevant hypotension was defined as a decrease in systolic arterial blood pressure by 20% or more from baseline value. It was treated with 200 ml Ringer's lactate solution. If ineffective, 5 mg mephentermine was given. Clinically relevant bradycardia was defined as heart rate < 50

beats/min and was treated with atropine 0.6 mg intravenously.

Data were entered in Microsoft Excel and analyzed with the Statistical Package for the Social Science (SPSS). A p value < 0.05 was considered to indicate statistical significance in all tests.

RESULTS

Total 60 patients were enrolled in the study. None of the patients were excluded from the study. The demographic characteristics and ASA grading was comparable in both the study groups. (Table 1)

The results of comparison of mean heart rate showed that the baseline heart rate was comparable in both the groups. After the infusion of the drug there was a decline in heart rate in both the groups till post induction period. After 1 min of intubation there was a rise in the

heart rate in both the groups. In group A there was a 5.6% raise in the heart rate as compared to baseline whereas in group B the rise was by 2.0% as compared to baseline. The values were comparable in the groups. Thereafter at 2 min and 5 min there was a decline in heart rate below the baseline value. (Table 2)

The comparison of SBP between the groups showed that the baseline mean systolic blood pressure was comparable in the two groups. Following infusion of study drug, both the group showed a gradual decline in SBP values till the period of induction. Following intubation there was a rise in SBP in both the groups but the values were lower than the baseline value in both the groups. At 2 min and 5 min SBP values again declined in both the groups. No statistically meaningful distinction was noted in mean SBP values at all measured intervals in both the groups. (Table 3)

Table 1: Demography and ASA PS grading

Variables	Group A	Group B	P value
Age (years)	34.13 ± 9.74	36.47 ± 10.90	0.38
BMI	23.16 ± 1.63	23.52 ± 1.58	0.39
Gender (M:F)	10:20	9:21	0.78
ASA grading (I:II)	24:6	23:7	0.75

Table 2: Comparison of Heart Rate (HR)

Variables	Group A (bpm)	Group B (bpm)	P value
HR Baseline	73.97 ± 12.09	78.47 ± 10.78	0.13
HR 5 mins of infusion	67.50 ± 10.12	69.50 ± 10.73	0.46
HR 10 mins of infusion	69.20 ± 10.98	68.60 ± 10.43	0.82
HR after induction	68.03 ± 11.86	67.33 ± 7.94	0.78
HR 1 min after intubation	78.17 ± 8.17	80.07 ± 7.48	0.35
HR 2 mins after intubation	72.03 ± 6.34	74.47 ± 9.07	0.23
HR 5 mins after intubation	69.33 ± 9.484	72.20 ± 10.11	0.26

Min: Minute, bpm: Beats per minute

Table 3: Comparison of Systolic Blood Pressure (SBP)

Variables	Group A (mmHg)	Group B (mmHg)	P value
SBP Baseline	130.20 ± 14.92	128.30 ± 12.66	0.59
SBP 5 mins of infusion	118.03 ± 15.11	113.60 ± 14.89	0.25
SBP 10 mins of infusion	115.37 ± 15.56	112.67 ± 14.71	0.49
SBP after induction	104.53 ± 15.07	120.47 ± 16.69	0.43
SBP 1 min after intubation	120.47 ± 16.69	118.67 ± 14.08	0.65
SBP 2 mins after intubation	107.63 ± 14.78	104.47 ± 13.82	0.39
SBP 5 mins after intubation	101.17 ± 15.25	97.43 ± 12.74	0.30

The results of comparison of DBP between the groups showed the baseline values to be comparable in both the groups. The infusion of the study drug caused a fall in DBP in both the groups. The DBP values were low in both the groups till induction. In the first minute after intubation there was a rise in DBP but the values were lower than the baseline DBP. Thereafter at 2 and 5 mins after intubation there was again a gradual decrease in DBP. All the DBP values were comparable in both the groups. (Table 4)

The baseline MAP values were comparable in both the groups. MAP value showed a gradual decrease in both the groups after the infusion of study drug till immediately after induction. Intubation caused an increase in MAP in both the groups. But at no time the mean MAP value was higher than the baseline MAP value. At all the studied intervals the mean MAP values were statistically similar in both the groups. (Table 5)

Three patients in Group B developed hypotension, which was absent in Group A. Four patients in group B and 2 patients in group A developed bradycardia. Episodes of hypotension and bradycardia were statistically similar in both the groups. (Table 6)

Table 6: Side effects

Variables	Group A	Group B	p-value
Hypotension	0	3	0.23
Bradycardia	2	4	0.67

DISCUSSION

The cardiovascular effects of laryngoscopy and intubation were first described by Reid and Brace in 1940.³ The peak rise in blood pressure and heart rate is usually transient, occurring 30 seconds after intubation and lasting for less than 10 min.³ Usually well tolerated by healthy individuals. But the patients with untreated hypertension, coronary artery disease, intracranial hypertension or aneurysm are the ones at risk. Laryngoscopy reaction in such individuals may predispose to development of pulmonary edema, myocardial insufficiency and cerebrovascular accident.^{4,5}

Various pharmacological and non-pharmacological methods have been tried to attenuate the hemodynamic response to laryngoscopy and endotracheal intubation. The non-pharmacological methods like shorter duration of laryngoscopy, smooth and gentle intubation, whenever possible insertion of LMA in place of endotracheal intubation⁵ have been

Table 4: Comparison of Diastolic Blood Pressure (DBP)

Variables	Group A (mmHg)	Group B (mmHg)	P value
DBP Baseline	83.13 ± 6.53	83.93 ± 9.05	0.69
DBP 5 mins of infusion	72.70 ± 9.73	73.50 ± 10.28	0.75
DBP 10 mins of infusion	72.10 ± 9.58	71.83 ± 10.35	0.91
DBP after induction	63.33 ± 14.18	65.07 ± 14.22	0.37
DBP 1 min after intubation	81.83 ± 15.70	81.10 ± 9.95	0.83
DBP 2 mins after intubation	67.87 ± 12.56	69.30 ± 10.05	0.62
DBP 5 mins after intubation	63.73 ± 15.35	64.10 ± 7.07	0.90

Table 5: Comparison of Mean Arterial Pressure (MAP)

Variables	Group A (mmHg)	Group B (mmHg)	P value
MAP Baseline	103.50 ± 10.67	101.50 ± 9.69	0.45
MAP 5 mins of infusion	90.40 ± 11.42	89.37 ± 11.38	0.72
MAP 10 mins of infusion	89.43 ± 11.89	87.87 ± 11.27	0.60
MAP after induction	81.93 ± 13.21	79.47 ± 16.07	0.51
MAP 1 min after intubation	98.90 ± 17.48	96.97 ± 11.18	0.61
MAP 2 mins after intubation	83.23 ± 11.628	83.77 ± 12.13	0.86
MAP 5 mins after intubation	78.83 ± 15.48	76.93 ± 10.67	0.58

used to attenuate the cardiovascular response to laryngoscopy and endotracheal intubation. Various pharmacological methods that have been in use are deeper plane of anesthesia with intravenous anesthetic induction agents,⁶ inhalational anesthetic agent,⁷ topical and IV lidocaine,^{8,9} narcotic analgesics,¹⁰ beta blockers,^{11,12} calcium channel blockers,¹³ vasodilators such as sodium nitroprusside,¹⁴ nitroglycerin,¹⁵ etc. but with variable results and side effects. Alpha 2 agonists like clonidine and dexmedetomidine are also one of the groups of drugs being used for attenuation of hemodynamic response to laryngoscopy and intubation. Dexmedetomidine is a highly selective and potent α_2 adrenoceptor agonist ($\alpha_2:\alpha_1$ receptor binding selectivity ratio 1620:1), compared to 220:1 for clonidine, which imparts it a unique property of providing sedation and analgesia without respiratory depression. Various studies have found that dexmedetomidine can decrease the hemodynamic response to laryngoscopy and intubation^{16,17} and has shown better results than clonidine.^{18,19} Dexmedetomidine has a reversal drug for its sedative effect i.e. atipamezole, making dexmedetomidine a superior drug compared to clonidine.

Dexmedetomidine has been used in intravenous doses ranging from 0.25 $\mu\text{g/kg}$ to 1 $\mu\text{g/kg}$ for attenuation of hemodynamic response.²⁰ There are studies comparing the effect of different doses of dexmedetomidine but the optimal dose has still not been established. Gupta *et al*²¹ have compared three different doses of dexmedetomidine in attenuation of hemodynamic response: 0.5 $\mu\text{g/kg}$, 0.8 $\mu\text{g/kg}$ and 1 $\mu\text{g/kg}$ intravenously. They found that a linear hemodynamic pharmacokinetic is exhibited in the dosage range of 0.5 to 1 $\mu\text{g/kg}$. They concluded that premedication with dexmedetomidine at a dosage of 1 $\mu\text{g/kg}$ adequately attenuated the adverse hemodynamic response to laryngoscopy and intubation. But in our study we did not observe a significant difference between 0.5 $\mu\text{g/kg}$ and 1 $\mu\text{g/kg}$ dosage of dexmedetomidine in controlling HR and blood pressure after intubation. In our study, at 1 minute after intubation a slight increase in heart rate as compared to baseline heart rate was noted in both the groups thereafter at 2 and 5 minutes the heart rate decreased to less than the baseline values. Heart rate at all the intervals was found to be comparable in the two groups. Following infusion of the study drugs there was a fall in systolic, diastolic and mean arterial pressure in both the groups. One minute after intubation there was a rise in systolic, diastolic and mean arterial pressure as compared to prelaryngoscopic values but the values were lower than the baseline values. At 2 and 5 minutes after intubation there was a

gradual decrease in systolic, diastolic and mean arterial pressure. The blood pressure values were comparable at all the intervals in both the groups. Gupta *et al*²¹ in their study have used tramadol as analgesic whereas in our study we used fentanyl in a dose of 2 $\mu\text{g/kg}$ prior to intubation. As fentanyl is also known to attenuate the hemodynamic response to laryngoscopy and intubation this may have been the reason for the effectiveness of 0.5 $\mu\text{g/kg}$ dexmedetomidine in our study.

Similarly Sebastian *et al*²² compared dexmedetomidine in a dose of 0.5 $\mu\text{g/kg}$ and 0.75 $\mu\text{g/kg}$ with placebo for attenuation of hemodynamic response to intubation. They have concluded that both the doses of dexmedetomidine (0.5 $\mu\text{g/kg}$ and 0.75 $\mu\text{g/kg}$) was more effective as compared to normal saline but in a dose of 0.75 $\mu\text{g/kg}$ it attenuated the hemodynamic stress response to laryngoscopy and intubation completely as compared to 0.5 $\mu\text{g/kg}$. In their study they used fentanyl as analgesic prior to intubation. In their study the dose of fentanyl used was 1 $\mu\text{g/kg}$ whereas we used it in higher dose that is 2 $\mu\text{g/kg}$ which might be the reason for the difference in the result of our study. Alireza *et al*²³ compared dexmedetomidine and propofol in controlling the hemodynamic response following intubation in the patients in the emergency department. They used dexmedetomidine in a dose of 0.4 $\mu\text{g/kg}$. In their study they found that dexmedetomidine even in this small dose was better than propofol in controlling hemodynamic effects of laryngoscopy and intubation.

In a similar study done by Jarineshin H *et al*²⁴, where they compared the effect of 0.5 $\mu\text{g/kg}$ and 1 $\mu\text{g/kg}$ dexmedetomidine and placebo on attenuation of hemodynamic effects of laryngoscopy and intubation, found a result similar to ours. They concluded that dexmedetomidine effectively and significantly attenuates cardiovascular responses during endotracheal intubation. They found that the two different doses of dexmedetomidine studied did not cause any significant distinct result in mitigating cardiovascular response. Dexmedetomidine in a dose of 1 $\mu\text{g/kg}$ has been associated with increased incidence of bradycardia and hypotension.¹⁷ Irregular breathing and episodes of apnea have also been reported with doses of 1 and 2 $\mu\text{g/kg}$.²⁵ In our study there was no episode of apnea noted. Three patients in Group B had hypotension and 4 patients had bradycardia where as in group A there was no hypotension and only 2 patients had bradycardia. The episodes of bradycardia and hypotension were found to be comparable in both the groups.

From this study, it can be concluded that attenuation of hemodynamic response to laryngoscopy and intubation by dexmedetomidine is similar with the

two doses: 0.5 µg/kg and 1 µg/kg. Both the doses of dexmedetomidine were devoid of any significant adverse effects.

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