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Comparative Study of Dexmedetomidine and Fentanyl for Attenuation of Hemodynamic Response to Laryngoscopy and Intubation

Sabin Gauchan,[1] Chitra Thapa[1]

[1]Department of Anesthesiology, Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal.

ABSTRACT

Background: Laryngoscopy and intubation cause hypertension and tachycardia which can lead to myocardial ischemia or cerebrovascular hemorrhage in patients with raised intracranial pressure, hypertension. The objective of this study was to compare the efficacy of dexmedetomidine (1 mcg/kg) and fentanyl (2 mcg/kg) in attenuating hemodynamic response to laryngoscopy and intubation. **Methods:** Sixty patients scheduled for elective surgeries under general anaesthesia were randomly divided into two groups: Group D and Group F. Group D received dexmedetomidine 1 mcg/kg and group F received fentanyl 2 mcg/kg intravenously over 10 min prior to induction of anesthesia. All the drugs and techniques of anesthesia were standardized in patients in both the groups. Heart rate, systolic, diastolic and mean arterial pressure were recorded at following intervals: at baseline, after drug administration (at 2 and 5 min), after induction, and at 1, 2 and 5 min after intubation. **Results:** Heart rate and blood pressure was found to be significantly lower in dexmedetomidine group as compared to fentanyl group at 1, 2 and 5 min after intubation. **Conclusions:** Dexmedetomidine 1 mcg/kg is superior to fentanyl 2 mcg/kg for attenuation of hemodynamic response to laryngoscopy and intubation.

Keywords: attenuation; dexmedetomidine; fentanyl; intubation; laryngoscopy.

INTRODUCTION

The major responsibility of anesthesiologists towards their patient is provision of a patent airway. Even after the development of various types of airway devices, tracheal intubation still remains the gold standard in airway management Intubation is preceded by laryngoscopy, which is done to visualize the larynx and adjacent structures. Both laryngoscopy and intubation are noxious stimuli and are associated with hemodynamic stress response.[1] Laryngeal stimulation during laryngoscopy gives rise to the laryngo-sympathetic reflexes with an increase in plasma concentration of adrenaline and noradrenaline leading to tachycardia, arrhythmias and acute rise in blood pressure.[2,3] Although the corresponding increases in blood pressure and heart rate are transitory and variable, they are more pronounced and unpredictable in patients with raised intracranial tension and cardiovascular disease like hypertension. Hence this study was conducted to compare the efficacy of dexmedetomidine and fentanyl for attenuation of the hemodynamic response during laryngoscopy and intubation.

METHODS

This was a randomized double blind cross sectional study conducted at Nepal Medical College and Teaching hospital from June to August 2019. After Ethical approval from the Institutional review committee of Nepal Medical College and Teaching Hospital, the process of data collection was initiated. A thorough pre-operative evaluation of the patients was done a day before surgery. 60 Adult patients aged 18-55 years of both genders, American Society of Anesthesiologist Physical status (ASA PS) I and II, posted for elective surgeries under general anesthesia who gave willful consent 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 hypopthyroidism, patients allergic to the study drug, patients with baseline heart rate < 60beats/minute and patients on beta blockers were excluded. The patients in whom intubation attempt lasted longer than 15 seconds or had multiple intubation attempts (2 or more) were also excluded from the study. An informed written consent was obtained from all the patients. Premedication was done with tab. lorazepam 2 mg for patients weighing 50 kg or more and tab. lorazepam 1mg for patients weighing less than 50 kg on a night before surgery. The patients were kept nil per oral for at least 8 hours for solid food and sips of clear liquid till 2 hours prior to surgery. The patients were allocated into two groups by on duty anesthesiologist: Group F and Group D, 30 in each

Correspondence: Dr. Sabin Gauchan, Nepal Medical College and Teaching Hospital, Jorpati, Kathmandu, Nepal. **Email:** sabingauchan@hotmail.com. **Phone:** +977-9851058474. **Article received:** 2019-06-30. **Article accepted:** 2019-08-14.

group, by slips of paper in a box technique. The same anesthesiologist prepared the intravenous infusion and coded them. The infusions were handed to the resident anesthetist, who was unaware of its content, to be administered to the patients. The same resident recorded all the hemodynamic parameters of the patients. All the intubations were done by the co-author of the study. On shifting the patient to the operating room ECG, heart rate (HR), pulse oximetry and non-invasive blood pressure (NIBP) were attached and monitored. Baseline cardiovascular parameters ie heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO2) were recorded. IV access was secured with appropriate size cannula. Patients belonging to the Group F (n=30) received fentanyl 2 µg/kg diluted with 0.9% normal saline to a total 20 ml volume, slowly IV over 10 minutes via syringe pump. Patients belonging to the Group D (n=30) received dexmedetomidine 1 µg/kg diluted with 0.9% normal saline to a total 20 ml volume, slowly IV over 10 minutes via syringe pump. Vitals (HR, SBP, DBP, MAP and SpO2) were monitored during infusion of the drug. After 10min, induction was done with Propofol 1% intravenously 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 intravenously. 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 administration of the test drug at 2 and 5 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 anesthesia was recorded. Clinically relevant hypotension was defined as decrease in systolic arterial blood pressure by 20% or more from baseline value. It was treated with 200 ml of Ringer's lactate solution. If ineffective, 5 mg mephentermine was given intravenously.

Clinically relevant bradycardia was defined as heart rate < 50 b eats/min and was treated with atropine 0.6 mg intravenously. Sample size calculation was done by the following formula Number of cases in each group (n) = $2(z_\alpha+z_\beta)^2\ S^2/d^2$ On the basis of study done by Jain et al,[4] the mean std deviation of heart rate at 5 min after intubation was 6.96 and the difference in mean was 7.57. Sample size (n) = 2 ($1.96 + 1.28)^2\ (6.96)^2/(7.57)^2$= 17.73. So, the minimum sample size required is 18 in each group. As the data collection period for this study was three months, we included all the patients who met the inclusion criteria from june to August, 2019 so the sample size increased to 60 (30 in each group). The data was compiled and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS), version 16.

RESULTS

Total 60 patients were enrolled in this study. None of the patient had laryngoscopy duration >15 secs and multiple attempts. Demographic datas (age, weight, gender) were comparable in both the groups (Table 1).

Table 1. Demographic data.

Parameter	Group D	Group F	p-value
Age (years)	32.87 ± 10.34	33.60 ± 11.33	0.794
Weight (Kg)	67.10 ± 7.44	67.03 ± 7.87	0.973
Gender (male: female)	10:20	5:25	0.235

Heart rate at baseline was comparable in both the groups. After the administration of the test drugs heart rate was statistically significantly lower in dexmedetomidine group as compared to fentanyl group at all the studied intervals (Table 2).

Table 2. Comparison of heart rate (bpm) between fentanyl and dexmedetomidine group

Parameter	Group D	Group F	p-value
HR baseline	84.60 ± 13.67	77.63 ± 14.35	0.059
HR 2 min of infusion	65.80 ± 9.546	77.50 ± 12.89	<0.001
HR 5 min of infusion	65.43 ± 10.56	76.03 ± 11.44	<0.001
HR after induction	66.53 ± 10.494	73.23 ± 11.04	0.02
HR 1 min after intubation	78.23 ± 9.951	92.03 ± 14.41	<0.001
HR 2 min after intubation	73 ± 9.649	82.07 ± 12.03	0.002
HR 5 min after intubation	68.73 ± 10.395	76.07 ± 11.59	0.012

The two groups when compared for systolic blood pressure (SBP), the baseline SBP and SBP till 2 min of drug infusion was comparable. After 5 min of infusion, SBP was significantly lower in dexmedetomidine group than in fentanyl group. SBP after induction was again comparable in both the groups. However the SBP values were significantly lower in dexmedetomidine group at 1, 2 and 5 min after intubation as compared to fentanyl group (Table 3).

The baseline diastolic blood pressure (DBP) were comparable in both the groups. After the

Table 3. Comparison of SBP (mmHg) between fentanyl and dexmedetomidine group.

Parameter	Group D	Group F	p-value
SBP baseline	127.90 ± 12.28	130.43 ± 13.69	0.454
SBP 2 min of infusion	118.57 ± 10.51	123.57 ± 13.59	0.116
SBP 5 min of infusion	112.60 ± 9.91	121.13 ± 14.83	0.011
SBP after induction	106.73 ± 10.66	111.80 ± 11.92	0.088
SBP 1 min after intubation	121.87 ± 14.38	136.57 ± 19.57	0.001
SBP 2 min after intubation	105.70 ± 12.01	117.90 ± 15.41	0.001
SBP 5 min after intubation	102.07 ± 11.50	111.03 ± 10.64	0.003

administration of study drugs the DBP values were significantly lower in dexmedetomidine group as compared to fentanyl group (Table 4).

Table 4. Comparison of DBP (mmHg) between fentanyl and dexmedetomidine group.

Parameter	Group D	Group F	p-value
DBP baseline	80.47 ± 8.83	85.03 ± 9.12	0.054
DBP 2 min of infusion	72.23 ± 7.77	80.43 ± 9.54	0.001
DBP 5 min of infusion	68.87 ± 7.36	78.90 ± 10.45	<0.001
DBP after induction	66.63 ± 9.24	72.27 ± 11.66	0.043
DBP 1 min after intubation	76.03 ± 12.74	93.40 ± 15.61	<0.001
DBP 2 min after intubation	63.60 ± 6.53	75.83 ± 11.85	<0.001
DBP 5 min after intubation	60.80 ± 7.27	69.93 ± 8.47	<0.001

The baseline Mean arterial pressure (MAP) were comparable in both the groups. The values at 2 and 5min after administration of study drug were significantly lower in dexmedetomidine group as compared to fentanyl group. MAP immediately after induction was comparable in both the groups. However at 1,2 and 5 min after intubation, MAP values were significantly lower in dexmedetomidine group as compared to fentanyl group (Table 5). In dexmedetomidine group, two patients developed hypotension, which was managed by decreasing volatile anesthetic concentration and infusing intravenous fluid. Four patients had bradycardia, out of which one patient required atropine injection. No such effect was seen in fentanyl group.

Table 5. Comparison of MAP (mmHg) between fentanyl and dexmedetomidine group.

Parameter	Group D	Group F	p-value
MAP baseline	98.13 ± 9.56	103.47 ± 11.52	0.056
MAP 2 min of infusion	88.73 ± 7.20	96.73 ± 11.63	0.002
MAP 5 min of infusion	84.23 ± 7.74	94.97 ± 12.65	<0.001
MAP after induction	81.80 ± 10.60	86.50 ± 11.76	0.109
MAP 1 min after intubation	92.23 ± 13.62	111.17 ± 15.30	<0.001
MAP 2 min after intubation	79.63 ± 7.10	92.10 ± 12.16	<0.001
MAP 5 min after intubation	75.90 ± 7.49	85.43 ± 9.02	<0.001

DISCUSSION

The hemodynamic response to laryngoscopy and tracheal stimulation following laryngoscopy and tracheal intubation was first documented by Reid and Brace in 1940.[5] Various modalities have been tried in an effort to attenuate adverse hemodynamic responses to intubation, but no single technique is ideal. Some of the pharmacological attempts made are topical anesthesia of the oropharynx,[6] drugs like lignocaine,[7] sedatives, vasoactive drugs like sodium nitroprusside, calcium channel blockers, beta blockers[8] and other drugs especially alpha 2 agonist like clonidine and dexmedetomidine.[9] Shribman[2] in 1987 described two components of pressor response: the first being the response to laryngoscopy and the second, the response to intubation. Laryngoscopy and intubation have been reported to be associated with a rise in plasma nor epinephrine levels by as much as 61%.[9] The marked sympathoadrenal response manifest in patients as hypertension and tachycardia.[10] Hence they are regarded as the most critical events during administration of general anesthesia. The changes in hemodynamics starts five seconds after laryngoscopy, reaches the maximum within 1-2 minutes and lasts 5 minutes.[11] Therefore in this study we compared the effect of the study drugs on heart rate and blood pressure till 5 min of intubation. Fentanyl is one of the most studies drug for attenuation of hemodynamic response to laryngoscopy and intubation. It is a short acting synthetic opioid. Fentanyl exhibits a dose dependent blunting of sympathetic response. At 6 mcg/kg fentanyl is known to completely abolish arterial pressure and HR increase during laryngoscopy and intubation.[12] But these higher doses produce tissue accumulation, respiratory depression requiring mechanical respiratory support.[13] At 2 mcg/kg, though not completely, it has been reported to significantly attenuate the hemodynamic response.[12] To be on safer side we used fentanyl in a dose of 2 mcg/kg in our study. Dexmedetomidine is another drug, which is increasingly being used for the same purpose. It is relatively new alpha 2 agonist approved by FDA in 1999. Dexmedetomidine causes activation of alpha

2 receptors located in the post synaptic terminals in the central nervous system, leading to reduced neuronal activity and augmentation of vagal activity.[14–17] It has been used in different doses for attenuation of hemodynamic reflexes to laryngoscopy and intubation. There are studies in which the dose of dexmedetomidine ranges from 0.1 to 10 mcg/kg/hr, but the higher doses have been associated with bradycardia and hypotension.[18,19] Ozair et al.[9] and Jain et al.[4] in their studies of comparison of dexmedetomidine and fentanyl found the use of dexmedetomidine in the dose of 1 mcg/kg to be effective in controlling the pressor response to intubation without significant side effects. Taking these studies as references we gave dexmedetomidine in the dose of 1 mcg/kg in our study. In our study following infusion of study drug there was decrease in HR in both the groups. Laryngoscopy and intubation caused an increase in HR in both the groups and maximum increase in HR was noted at 1 min post intubation. In the dexmedetomidine group the HR values though higher as compared to post infusion period, were still lower than the baseline HR values whereas in fentanyl group HR at 1 and 2 min post intubation were higher than the baseline value, at 5 min HR reached the baseline.

At 1 min after intubation HR values were lower than the baseline value by 7.5% in dexmedetomidine whereas in fentanyl group there was an increase in HR at 1 min post intubation by 18.54% as compared to baseline HR. When the two groups were compared, HR was significantly lower in dexmedetomidine group than in fentanyl group starting from the drug infusion till 5 min post intubation. In our study dexmedetomidine had better control on HR as compared to fentanyl. Jain et al[4] compared dexmedetomidine 1 mcg/kg and fentanyl 2 mcg/kg, dose similar to our study. They found postintubation HR value increased in both the groups when compared to postinduction values but in dexmedetomidine group HR was lower than the baseline value whereas in fentanyl group the postintubation values were higher than the baseline values. The findings in their study were similar to our study. From their study they concluded that dexmedetomidine completely abolishes the chronotropic response to laryngoscopy and intubation compared to fentanyl. Kharwar et al[20] also showed similar findings in their study. They observed a decrease in HR from baseline in dexmedetomidine as well as fentanyl group after induction. At 1 min after intubation, they observed an increase in HR of 9.85% from baseline in the fentanyl group and whereas a decrease of 7.03% from baseline was noted in the dexmedetomidine group. When we compared SBP, DBP and MAP, all the values gradually decreased after the infusion of study drugs in both the groups. Intubation caused a rise in systolic, diastolic and mean arterial pressure. The blood pressure values at 1 min after intubation were higher as compared to postinduction pre laryngoscopy values in both the groups. In dexmedetomidine group the rise in systolic, diastolic and mean arterial pressure did not reach the baseline value. The systolic, diastolic and mean arterial pressure were lower than the baseline value by 4.7%, 5.5% and 6% respectively. But in fentanyl group the rise in blood pressure at 1 min after intubation reached a level higher than the baseline value. The systolic, diastolic and mean arterial pressure were higher than the baseline value by 4.7%, 9.8% and 7.4% respectively.

The systolic, diastolic and mean arterial pressure values at 2 and 5 min after intubation were lower than the baseline values in both the groups. However the systolic, diastolic and mean arterial pressure at 1, 2 and 5 min after intubation were statistically lower in dexmedetomidine group as compared to fentanyl group. Laha et al.[21] conducted a study on the effects of dexmedetomidine 1 mcg/kg on attenuation of sympathoadrenal responses and requirements of anesthetic agents. Their findings were similar to ours. They found that administration of dexmedetomidine attenuates the rise in mean HR and blood pressure at 1, 2, 3 and 5 min. Scheinin et al[22] studied the effect of dexmedetomidine on tracheal intubation and dose of thiopentone and fentanyl needed for the surgery. Their findings regarding attenuation of hemodynamic response to intubation was similar to ours. They observed that dexmedetomidine reduces the doses of thiopentone and fentanyl. However it was not included in our study objective. In their study plasma catecholamine concentration was also measured and they found that the concentration of noradrenaline in mixed venous plasma was lesser in the dexmedetomidine group during all phases of induction. Measuring plasma catecholamine was not feasible in our institute.

Similarly, Gunalan et al[23] in their study of comparative evaluation of bolus administration of dexmedetomidine and fentanyl for stress attenuation during laryngoscopy and endotracheal intubation have concluded that dexmedetomidine (1 mcg/kg) given prior to intubation provided protection against the pressor response during laryngoscopy and intubation when compared to fentanyl.

CONCLUSION

Based on this study it is concluded that dexmedetomidine 1 mcg/kg is superior to fentanyl 2 mcg/kg for attenuation of hemodynamic response to laryngoscopy and intubation.

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Conflict of interest:

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