

## Original Research Article

# A prospective randomized controlled trial comparing the effects of dexmedetomidine and fentanyl on attenuation of pressor response during laryngoscopy and intubation in neurosurgical patients

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### ABSTRACT

**Background:** Laryngoscopy is associated with a sympathetic response that results in a rapid increase in blood pressure and heart rate in these patients. The mechanisms underlying these hemodynamic changes are incompletely understood. They may be caused by a reflex sympathetic discharge due to stimulation of the upper respiratory tract. It has been observed that hemodynamic responses to tracheal intubation are associated with an increase in plasma catecholamine concentrations and are attenuated by  $\beta$ -adrenergic blockade. These hemodynamic changes may be undesirable particularly in neurosurgical patients. Aim of the study is the present study was prospective, randomized, double-blind conducted to evaluate the efficacy of dexmedetomidine and fentanyl in attenuation of pressor responses to laryngoscopy and intubation in neurosurgical patients undergoing lumbar spine surgeries.

**Methods:** A total of 60 patients of 18–65 years, American Society of Anaesthesiologists Class I/II of undergoing elective neurosurgical procedures were included in the study. The patients were divided into two groups of 30 patients each. Group D received dexmedetomidine and Group F received Fentanyl. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) were recorded preoperatively (baseline), at 5 and 8 minutes after infusion of study drug, before induction, 1 minute after induction, 2 minute after intubation, 5 minute after intubation, 10 minute after intubation and 15 minute after intubation.

**Results:** There was a better control of Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure in Group D when compared to Group F during laryngoscopy and after intubation.

**Conclusions:** The present study shows that dexmedetomidine suppresses hemodynamic responses effectively than fentanyl.

**Keywords:** Dexmedetomidine, Fentanyl, Intubation, Laryngoscopy, Sympathetic response

### INTRODUCTION

Induction of general anesthesia, laryngoscopy, tracheal intubation, and extubation are associated with various hemodynamic changes. Laryngoscopy and tracheal intubation may be associated with sympathetic stimulation and lead to tachycardia and hypertension.<sup>1</sup> These hemodynamic changes may predispose to

myocardial ischemia. Therefore, there is a need to blunt these noxious responses effectively.<sup>2</sup> Various drug combinations have been used with variable success to attenuate the sympathetic responses during laryngoscopy and intubation.<sup>3,4</sup> Alpha two agonists have hypnotic, sedative, analgesic, anxiolytic, sympatholytic and analgesic properties without producing significant respiratory depression. Opioids also blunt the

hemodynamic response to intubation effectively, but they may lead to nausea, vomiting, and respiratory depression.<sup>5</sup> The aim of the present study was to evaluate and compare the effect of low dose infusion of dexmedetomidine and fentanyl in attenuation of pressor response to laryngoscopy and intubation in neurosurgical patients undergoing elective surgery.

## METHODS

The study was a prospective, randomized, double-blind study. Sixty American Society of Anaesthesiologists (ASA) Class I and II patients, aged 18-65 years and undergoing elective neurosurgical patients undergoing lumbar spine surgeries were randomly assigned to one of the two groups).

In Group D (dexmedetomidine group) 30 patients received dexmedetomidine and in the Group F (fentanyl group) 30 patients received fentanyl. Patients with any cardiac, renal and hepatic disease were excluded from the study.

On arrival to operation theatre all standard monitors (electrocardiogram, pulse oximetry, non-invasive blood pressure were attached and baseline vital parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP), and arterial oxygen saturation (SpO<sub>2</sub>) were noted. An intravenous (IV) line was secured and 10 ml/kg/h of normal saline infusion was started.

The drug to be infused (dexmedetomidine or fentanyl) was prepared by an anesthesiologist who was blinded to the computerized generated randomization schedule in 20 ml syringes. In Group D intravenous infusion of dexmedetomidine (1 µg/kg) was administered intravenously over 10 min using an infusion pump before induction of anesthesia.

In Group F, fentanyl (2 µg/kg) was administered intravenously over 10 min using an infusion pump before induction of anesthesia.

Induction was done 10 min after start of loading infusion of dexmedetomidine or fentanyl. Propofol was given slowly in incremental doses till loss of verbal response. Endotracheal intubation was facilitated by injection atracurium 1 mg/kg. Maintenance of anesthesia was done with O<sub>2</sub> in N<sub>2</sub>O, isoflurane and repeated intermittent bolus doses of atracurium and fentanyl. Residual neuromuscular blockade was reversed by neostigmine and glycopyrrolate followed by tracheal extubation when the patient was fully conscious responding to verbal commands.

Intraoperatively, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), oxygen saturation (SpO<sub>2</sub>), and electrocardiogram (ECG) were recorded at the following

intervals: at baseline, after drug administration (at 5, and 8 min), before induction, after induction, and after laryngoscopy (2, 5, 10 and 15 min).

## RESULTS

It was seen that the age, body weight, and duration of the surgery was comparable in between the two groups. (Table 1).

**Table 1: Demographic profile.**

	Group D	Group F	P value
Age (years)	57.40±9.12	56.40±5.4	0.53 (NS)
Weight (kg)	70.72±6.17	68.59±7.63	0.57(NS)
Duration of surgery (min)	60.43±7.36	61.54±8.43	0.61(NS)

NS- Non-significant, Group D- Dexmedetomidine group, Group F-Fentanyl group.

The mean age of patients receiving dexmedetomidine was 57.40 years which was comparable to the mean age of patients in fentanyl (56.40 years) group. The weight of patients in dexmedetomidine group was 70.72 kgs which was similar to those of patients who received fentanyl (68.59 kgs). The duration of surgery between the two groups was also comparable, 60.43 minutes in dexmedetomidine group and 61.54 minutes in fentanyl group.

The baseline heart rate between the two groups was similar (Table 2). In group D (dexmedetomidine), the mean baseline HR was 74.75±7.06 beats per minute (bpm) while in the group F (fentanyl) it was 77.21±6.21 bpm.

After administration of the study drug dexmedetomidine or fentanyl it was observed that the mean HR at 5 and 8 minutes after administration of the study drug decreased in both groups. However, on comparing the two groups there was no significant difference in heart rates in patients receiving dexmedetomidine or fentanyl. However, it was observed that Heart rate, after induction, and after laryngoscopy at 2, 5, 10 and 15 min was lower in the dexmedetomidine group when compared with the fentanyl group.

It was observed from this study that the baseline systolic, diastolic and mean blood pressures between the two groups were similar. After administration of the study drug dexmedetomidine or fentanyl it was observed that the systolic, diastolic and mean blood pressure at 5 and 8 minutes after administration of the study drug decreased in both groups.

However, on comparing the two groups there was no significant difference in systolic, diastolic or mean blood pressures in patients receiving dexmedetomidine or fentanyl. However, it was observed that systolic, diastolic and mean blood pressures after induction, and

after laryngoscopy at 2, 5, 10, and 15 min was lower in the dexmedetomidine group when compared with the fentanyl group. (Tables 3, 4 and 5) None of the patients

in dexmedetomidine group or fentanyl group developed hypotension or bradycardia during duration of the study.

**Table 2: Comparison of mean heart rate at different time intervals in the dexmedetomidine and fentanyl groups.**

Time	Heart rate (Mean±SD) Group D	Heart rate (Mean±SD) Group F	p value	Difference
Baseline (bpm)	74.75±7.06	77.21±6.21	>0.05	NS
<b>After drug</b>				
5 minutes	71.23±6.17	73.35±5.59	>0.05	NS
8 minutes	71.22±6.21	72.31±6.01	>0.05	NS
Before Induction	72.75±5.11	70.33±7.02	>0.05	NS
After induction	73.81±6.96	82.81±6.96	<0.05	S
<b>After intubation</b>				
2 minutes	76.15±6.01	84.87±8.10	<0.05	S
5 minutes	77.32±6.32	85.88±7.14	<0.05	S
10 minutes	75.39±6.31	83.12±7.12	<0.05	S
15 minutes	74.17±6.96	82.75±6.96	<0.05	S

NS-Non significant, S- Significant, bpm-beats /minute, Group D- Dexmedetomidine group, Group F-Fentanyl group

**Table 3: Comparison of systolic blood pressure at different time intervals in the dexmedetomidine and fentanyl groups.**

Time	Systolic blood pressure (Mean ±SD) Group D	Systolic blood pressure (Mean ±SD) Group F	p value	Difference
Baseline (mm Hg)	126.15±6.76	124.63±5.98	>0.05	NS
<b>After drug</b>				
5 minutes	123.65±5.47	125.13±5.48	>0.05	NS
8 minutes	123.59±6.21	124.53±5.78	>0.05	NS
Before Induction	121.66±6.27	123.41±6.12	>0.05	NS
After induction	119.76±6.36	120.66±5.88	<0.05	S
<b>After intubation</b>				
2 minutes	123.18±6.93	127.43±7.19	<0.05	S
5 minutes	122.55±6.36	128.54±6.95	<0.05	S
10 minutes	121.45±6.91	125.66±6.86	<0.05	S
15 minutes	121.35±6.17	126.05±6.16	<0.05	S

NS – Non significant, S- Significant, Group D- Dexmedetomidine group, Group F-Fentanyl group

**Table 4: Comparison of diastolic blood pressure at different time intervals in the dexmedetomidine and fentanyl groups.**

Time	Diastolic blood pressure (Mean±SD) Group D	Diastolic blood pressure (Mean±SD) Group F	p value	Difference
Baseline (mm Hg)	79.21±7.17	79.16±6.88	>0.05	NS
<b>After drug</b>				
5 minutes	76.15±5.07	77.25±6.39	>0.05	NS
8 minutes	75.76±7.19	75.71±6.88	>0.05	NS
Before Induction	75.98±7.19	76.65±6.76	>0.05	NS
After induction	73.69±7.29	77.39±6.58	<0.05	S
<b>After intubation</b>				
2 minutes	76.31±5.19	82.13±6.21	<0.05	S
5 minutes	76.35±5.45	81.15±5.89	<0.05	S
10 minutes	74.14±6.09	80.66±6.86	<0.05	S
15 minutes	74.35±6.17	79.05±6.16	<0.05	S

NS – Non significant, S- Significant, Group D- Dexmedetomidine group, Group F-Fentanyl group

**Table 5: Comparison of mean blood pressure at different time intervals in the dexmedetomidine and fentanyl groups.**

Time	Diastolic blood pressure (Mean±SD) Group D	Diastolic blood pressure (Mean ±SD) Group F	p value	Difference
Baseline (mm Hg)	71.11±6.97	71.16±6.98	>0.05	NS
<b>After drug</b>				
5 minutes	70.17±5.18	72.43±6.45	>0.05	NS
8 minutes	69.72±6.91	72.71±6.98	>0.05	NS
Before Induction	69.18±6.99	71.15±6.26	>0.05	NS
After induction	68.20±6.12	73.19±5.35	<0.05	S
<b>After intubation</b>				
2 minutes	68.13±5.17	73.21±6.19	<0.05	S
5 minutes	68.47±6.14	73.25±6.19	<0.05	S
10 minutes	67.34±6.17	72.97±8.91	<0.05	S
15 minutes	67.45±5.77	72.15±5.76	<0.05	S

NS- Non-significant, S- Significant, Group D-Dexmedetomidine group, Group F-Fentanyl group

## DISCUSSION

Laryngoscopy and tracheal intubation are associated with marked sympathetic response associated with release of catecholamines which leads to hypertension and tachycardia.<sup>6</sup> Though these responses are transitory and innocuous in normal healthy individuals, but in patients with cardiac comorbidities like hypertension, ischemic heart disease, and cerebrovascular disease these transient changes in hemodynamics may be undesirable. Many attempts have been made to blunt these noxious sympathoadrenal responses as the use of inhalational anesthetic agents, lidocaine opioids, direct-acting vasodilators,  $\beta$ -blockers, and calcium-channel blockers.<sup>7-14</sup> Although, fentanyl is advocated for attenuation of sympathetic response to laryngoscopy and intubation only a high dose of 6 micrograms per kg completely abolishes the sympathoadrenal response. This dose may lead to respiratory support for surgical procedures of short and intermediate durations.<sup>15</sup>

In this study, fentanyl was given at the dose of 2 micrograms/kg diluted in 20 ml normal saline over 10 min. Rapid administration of a bolus dose of dexmedetomidine may cause transient increase in blood pressure and reflex decrease in HR because of peripheral alpha 2 adrenoceptor stimulation of vascular smooth muscle.<sup>16</sup> To avoid this authors administered dexmedetomidine over 10 minutes.

The main aim of this study was to compare the effectiveness of fentanyl and dexmedetomidine for attenuation of the pressor response to laryngoscopy and endotracheal intubation. It was observed that there was no statistically significant difference in heart rate between the two groups until induction of anesthesia ( $P > 0.05$ ). However, after induction and intubation at 2 minutes, 5 minutes, 10 minutes and 15 minutes the decrease in heart rate in the dexmedetomidine group was more ( $P > 0.05$ )

when compared with the fentanyl group. Our results were similar to a study conducted by Patel et al, who also observed that dexmedetomidine significantly attenuates stress response at intubation with lower increase in HR in the dexmedetomidine group when compared to fentanyl group. Similarly, Kharwar et al, observed that there was a marked decrease in pulse rate from baseline in the dexmedetomidine group as compared with the fentanyl group.<sup>17,18</sup> Similarly, dexmedetomidine caused a marked blunting of sympathetic responses post intubation when compared to the fentanyl group. This was similar to the results obtained in our study.

In this study, there was no statistically significant difference in systolic, diastolic and mean blood pressure between the two groups until induction of anesthesia ( $P > 0.05$ ). However, after induction and intubation at 2 minutes, 5 minutes, 10 minutes and 15 minutes the decrease in systolic, diastolic and mean blood pressure in the dexmedetomidine group was more when compared with the fentanyl group ( $P > 0.05$ ). Our results were similar to a study conducted by Patel et al who also observed that dexmedetomidine significantly attenuates stress response at intubation with lower increase in systolic, diastolic and mean blood pressures in the dexmedetomidine group when compared to fentanyl group.<sup>17</sup> Gupta et al, observed similar findings to this study.<sup>19</sup> They found that Intravenous fentanyl (2  $\mu\text{g}/\text{kg}$ ) failed, addition of clonidine to fentanyl was able to partially blunt it, but the addition of dexmedetomidine to fentanyl completely abolished the hemodynamic response to laryngoscopy and intubation.

## CONCLUSION

Present study demonstrates that dexmedetomidine is superior to fentanyl for attenuation of hemodynamic response during laryngoscopy and intubation. An intravenous infusion of dexmedetomidine at 1

microgram/kg administered before laryngoscopy and endotracheal intubation is effective in blunting the noxious hemodynamic sympathetic response to laryngoscopy and intubation.

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