



## Original Article

# IV Nalbuphine vs IV Fentanyl in attenuating pressor response: A Comparison

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## Abstract

**Introduction:** Laryngoscopy and tracheal intubation are noxious stimuli that evoke a transient but exaggerated hemodynamic response and increased intracranial pressure. This response may manifest as tachycardia, hypertension, and dysrhythmias with deleterious respiratory, neurological and cardiovascular effects. It is lethal to patients with preexisting coronary artery disease, recent myocardial infection, hypertension, geriatric population, pre-eclampsia and cerebrovascular pathology. Fentanyl is opioid receptor agonist that blocks the stress response to surgical stimuli and it is cardiovascular stable. Nalbuphine is a semi-synthetic opioid analgesic that does not increase systemic blood pressure, pulmonary artery blood pressure, heart rate, or arterial filling pressure. These drugs are compared in attenuating pressor response to laryngoscopy and intubation.

## Aims and Objectives

- 1) To assess the effect of IV Nalbuphine (0.2mg/kg) and IV Fentanyl (2µg/kg) during laryngoscopy and intubation on Pulse rate(PR), Systolic blood pressure(SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP), ECG changes, SPO2 and Respiratory rate(RR)
- 2) To compare the changes in above factors before intubation, at the time of intubation, after intubation, 1min after intubation, 3mins after intubation, 5mins after intubation, 10 mins after intubation & 15 mins after intubation.
- 3) To observe and compare for side effects if any

**Material and Methods:** In a prospective, randomized, comparative study, 60 patients ASA I and II, aged 20-55 years, weight 40-70 kgs undergoing elective surgeries requiring general anaesthesia were included.

Group N – 30 patients were given IV Nalbuphine 0.2 mg/kg diluted in 10ml distilled water.

Group F - 30 patients were given IV Fentanyl 2 µg/kg diluted in 10ml distilled water.

**Results:** Hemodynamic variations after intubation was more in group F as compared to group N.

**Conclusions:** From present study it is concluded that both drugs show almost equal rise in heart rate at intubation, but increase in both systolic blood pressure and diastolic blood pressure was more with Fentanyl than Nalbuphine. Hence Nalbuphine can be preferred to control the pressor response to laryngoscopy and intubation with no significant adverse effects.

**Keywords:** Nalbuphine, Fentanyl, endotracheal intubation, pressor response.

## Introduction

Laryngoscopy and tracheal intubation are noxious stimuli that evoke exaggerated hemodynamic response and increased intracranial pressure. This response may manifest as tachycardia, hypertension and dysrhythmias with deleterious respiratory, neurological and cardiovascular effects<sup>[1]</sup>. These changes are maximum immediately after intubation and lasts for 5-10 minutes<sup>[1]</sup>. They are generally well tolerated by healthy patients but can be lethal to patients with preexisting coronary artery disease, recent myocardial infarction, hypertension, geriatric population, pre-eclampsia, and cerebrovascular pathology.

Attenuation of stress response to laryngoscopy and intubation has been practiced either by non-pharmacological or pharmacological methods. The non-pharmacological methods used are smooth and gentle intubation with a shorter duration of laryngoscopy, insertion of laryngeal mask airway (LMA) or advanced airways and blocking glossopharyngeal and superior laryngeal nerves. Pharmacological methods include topical Lignocaine sprays, deeper planes of anaesthesia by inhalational/intravenous (IV) agents or narcotics, beta blockers; calcium channel blockers; vasodilators, alpha-2 agonists with its own limitations<sup>[2]</sup>.

Fentanyl was first synthesized in 1960 and was found to be significantly potent than Morphine or Meperidine. The large safety margin, relatively short duration of action, and minimal respiratory depression at analgesic doses observed for Fentanyl has made it the drug of choice for intravenous anaesthesia<sup>[3]</sup>. Its ability to provide cardiovascular stability and to block the stress response to surgical stimuli at high doses made it the mainstay of cardiac anaesthesia.

Nalbuphine a semi-synthetic opioid analgesic is agonist at kappa receptor and antagonist at  $\mu$  receptor. Nalbuphine is a potent analgesic. essentially equivalent to that of Morphine on a milligram basis<sup>[4]</sup>.

Nalbuphine, does not increase systemic blood

pressure, pulmonary artery blood pressure, heart rate, or arterial filling pressure. Hence Nalbuphine may be useful to provide sedation and analgesia in patients with heart disease, as during cardiac catheterization<sup>[5,6]</sup>.

The present study was designed to compare the effects of Fentanyl and Nalbuphine on hemodynamic responses to endotracheal intubation in patients requiring general anaesthesia.

## Aims and Objectives

- 1) To assess the effect of IV Nalbuphine (0.2mg/kg) and IV Fentanyl (2 $\mu$ g/kg) during laryngoscopy and intubation on Pulse rate(PR), Systolic blood pressure (SBP), Diastolic blood pressure(DBP), Mean arterial pressure (MAP),ECG changes, SPO2 and Respiratory rate(RR)
- 2) To compare the changes in above factors before intubation, at the time of intubation, after intubation, 1min after intubation, 3mins after intubation, 5mins after intubation, 10 mins after intubation & 15 mins after intubation.
- 3) To observe and compare for side effects if any

## Material and Methods

After obtaining approval from hospital ethical committee, a prospective, randomized, comparative study was carried out in 60 ASA Grade I and II elective patients between age 20 to 55 years and Weight 40-70kgs undergoing elective surgeries requiring general anaesthesia. Patients of ASA grade III and IV, patient's with cardiovascular disease, allergy to opioids, hepatic or renal disease, bronchospastic disease; patients on beta blockers and adrenergic or psychotropic drug were excluded from the study.

Patients were divided into two groups of 30 each.

**Group N:** 30 patients were given IV Nalbuphine (0.2 mg/kg) before induction.

**Group F:** 30 patients were given IV Fentanyl (2  $\mu$ g/kg) before induction.

A detailed pre-anaesthetic evaluation with investigations like Hb, CBC, Urine examination, LFT, RFT, RBSL ECG, CXR were done.

A written informed valid consent was taken and after confirming nil by mouth status multi-parameter monitor was attached and preoperative basal pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, respiratory rate, ECG and SpO<sub>2</sub> was recorded. Intravenous crystalloid 500ml infusion was started. All patients were preoxygenated with 100% oxygen for 3 minutes followed by pre-medication with Inj. Ondansetron 4mg IV, Inj. Ranitidine 50mg IV, Inj. Glycopyrrolate 0.2 mg IV, Inj. Midazolam 1mg IV. After premedication following drugs were given to patients as per their study group:

**Group F:** Received Inj. Fentanyl 2µg/kg IV

**Group N :** Received Inj. Nalbuphine 0.2mg/kg IV.

Both the drugs were diluted in 10ml distilled water and injected IV slowly over 1 min. Vital parameters were recorded after test medication.

Induction was done with Inj. Thiopentone Sodium 2.5% IV 4-6mg/Kg and endotracheal intubation was facilitated with Inj. Suxamethonium 2mg/kg

IV.

Anaesthesia was maintained with O<sub>2</sub>, N<sub>2</sub>O and Isoflurane. Inj. Vecuronium 0.05-1 µg/kg IV is used for muscle relaxation. Patients were not stimulated during the observation period and surgery was allowed to start after 15 minutes of intubation.

Pulse rate, blood pressure, mean arterial pressure, oxygen saturation, ECG was monitored continuously and recorded before intubation, at intubation and then at 3, 5, 10 & 15 minutes post intubation. At the end of surgery anaesthesia was reversed with Inj. Neostigmine 0.05 mg/kg IV and Inj. Glycopyrrolate 0.008mg/kg IV.

Patients were observed intraoperatively and postoperatively for any complications like nausea and vomiting, pruritus, arrhythmias, bradycardia etc.

### Results

Comparative evaluation was done for age, sex, weight and height. P value was calculated using t test and was statistically insignificant. (p>0.05).

**Table 1** Mean Changes in Pulse rate in both groups during procedure

Heart Rate	Group	N	Mean	SD	p- value
Baseline	Fentanyl	30	87.07	8.80	<b>0.30</b>
	Nalbuphine	30	84.67	8.94	
Before Intubation	Fentanyl	30	87.80	9.84	<b>0.35</b>
	Nalbuphine	30	85.23	11.19	
At Intubation	Fentanyl	30	89.40	11.73	<b>0.06</b>
	Nalbuphine	30	86.07	11.35	
After Intubation	Fentanyl	30	86.70	12.56	<b>0.24</b>
	Nalbuphine	30	83.07	10.98	
1 min.	Fentanyl	30	84.40	12.05	<b>0.26</b>
	Nalbuphine	30	81.40	8.19	
3 min.	Fentanyl	30	83.40	9.96	<b>0.08</b>

	<b>Nalbuphine</b>	30	79.17	8.63	
<b>5 min.</b>	<b>Fentanyl</b>	30	83.97	10.06	<b>0.10</b>
	<b>Nalbuphine</b>	30	79.97	8.56	
<b>10 min.</b>	<b>Fentanyl</b>	30	83.50	9.69	<b>0.07</b>
	<b>Nalbuphine</b>	30	79.23	7.87	
<b>15 min.</b>	<b>Fentanyl</b>	30	80.80	9.11	<b>0.09</b>
	<b>Nalbuphine</b>	30	77.30	6.61	

Mean

Baseline heart rate was comparable between both groups (p=0.3). Heart rate changes in patients remained comparable before and after intubation and hence were statistically insignificant (p>0.05). The mean HR after drug administration was

slightly

increased in both groups (F:87.07 to 87.8; N:84.67 to 85.23) which further increased during intubation (F:89.4; N:86.07). However post-intubation, HR was gradually decreased in both the groups.

**Table 2** Mean Changes in Systolic Blood Pressure among both groups during the procedure

SBP	Group	N	Mean	SD	p- value
<b>Baseline</b>	<b>Fentanyl</b>	30	124.37	7.96	<b>0.49</b>
	<b>Nalbuphine</b>	30	122.87	8.54	
<b>Before Intubation</b>	<b>Fentanyl</b>	30	122.73	10.44	<b>0.24</b>
	<b>Nalbuphine</b>	30	119.60	9.76	
<b>At Intubation</b>	<b>Fentanyl</b>	30	122.97	11.20	<b>0.04</b>
	<b>Nalbuphine</b>	30	116.80	11.74	
<b>After Intubation</b>	<b>Fentanyl</b>	30	119.90	9.82	<b>0.07</b>
	<b>Nalbuphine</b>	30	114.97	10.78	
<b>1 min.</b>	<b>Fentanyl</b>	30	121.37	9.63	<b>0.03</b>
	<b>Nalbuphine</b>	30	115.60	10.08	
<b>3 min.</b>	<b>Fentanyl</b>	30	121.33	10.80	<b>0.00</b>
	<b>Nalbuphine</b>	30	113.00	9.59	
<b>5 min.</b>	<b>Fentanyl</b>	30	123.30	9.77	<b>0.00</b>

	Nalbuphine	30	115.10	8.82	
10 min.	Fentanyl	30	122.20	10.97	0.00
	Nalbuphine	30	114.57	8.90	
15 min.	Fentanyl	30	121.43	9.20	0.00
	Nalbuphine	30	111.43	12.36	

Mean Baseline systolic blood pressure was comparable between both groups (p=0.49). However during Intubation and subsequently till 15 minutes after intubation, SBP in patients on

Nalbuphine remained significantly lower than Fentanyl group (p<0.05) and it was statistically significant.

**Table 3** Mean Changes in Diastolic Blood Pressure among both groups during the procedure

DBP	Group	N	Mean	SD	p- value
Baseline	Fentanyl	30	78.53	9.63	0.76
	Nalbuphine	30	77.83	7.84	
Before Intubation	Fentanyl	30	76.53	10.91	0.45
	Nalbuphine	30	74.40	10.93	
At Intubation	Fentanyl	30	77.37	10.03	0.09
	Nalbuphine	30	72.50	11.61	
After Intubation	Fentanyl	30	77.20	8.96	0.07
	Nalbuphine	30	73.17	8.02	
1 min.	Fentanyl	30	77.60	9.73	0.04
	Nalbuphine	30	72.37	9.30	
3 min.	Fentanyl	30	75.27	10.40	0.37
	Nalbuphine	30	73.13	7.55	
5 min.	Fentanyl	30	76.37	10.28	0.15
	Nalbuphine	30	73.20	6.08	
10 min.	Fentanyl	30	74.80	9.84	0.46
	Nalbuphine	30	73.10	7.79	
15 min.	Fentanyl	30	76.13	9.94	0.08
	Nalbuphine	30	72.30	5.94	

Mean Baseline diastolic blood pressure was comparable between both groups (p=0.49). During intubation and subsequently till 1 minute, DBP in patients on Nalbuphine was lower than Fentanyl

group, and was statistically significant (p<0.05). After 1 min, post intubation, diastolic blood pressure was comparable among both groups and was statistically insignificant (p>0.05).

**Table 4** Mean Changes in Mean Arterial Pressure among both groups during the Procedure

MAP	Group	N	Mean	SD	p- value
Baseline	Fentanyl	30	93.81	8.40	<b>0.63</b>
	Nalbuphine	30	92.84	6.75	
Before Intubation	Fentanyl	30	91.93	9.96	<b>0.32</b>
	Nalbuphine	30	89.47	9.19	
At Intubation	Fentanyl	30	92.57	9.37	<b>0.048</b>
	Nalbuphine	30	87.27	10.83	
After Intubation	Fentanyl	30	91.43	8.68	<b>0.047</b>
	Nalbuphine	30	87.10	8.34	
1 min.	Fentanyl	30	92.19	9.14	<b>0.03</b>
	Nalbuphine	30	86.78	9.02	
3 min.	Fentanyl	30	90.62	9.83	<b>0.07</b>
	Nalbuphine	30	86.42	7.25	
5 min.	Fentanyl	30	92.01	9.09	<b>0.02</b>
	Nalbuphine	30	87.17	6.02	
10 min.	Fentanyl	30	90.60	9.35	<b>0.10</b>
	Nalbuphine	30	86.92	7.65	
15 min.	Fentanyl	30	91.23	8.45	<b>0.00</b>
	Nalbuphine	30	85.34	6.76	

Baseline mean arterial pressure was comparable between both groups (p=0.49). However during intubation and subsequently till 15 minutes

following intubation, MAP in patients on Nalbuphine remained lower than Fentanyl group and was statistically significant (p<0.05).

**Table 5** Comparison of adverse effects of drugs

Side Effects	Group		Total	p- value
	Fentanyl	Nalbuphine		
Nausea/ Vomiting	0 0.0%	2 6.7%	0 0.0%	<b>0.49</b>
Hypotension	0 0.0%	0 0.0%	0 0.0%	NA
Pruritus	2 6.7%	0 0.0%	2 3.3%	<b>0.49</b>
Bradycardia	0	0	0	NA

	0.0%	0.0%	0.0%	
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Minimal adverse events were observed during the procedure in both groups including nausea/vomiting (2 cases in Nalbuphine) and pruritus (2 cases in Fentanyl). None of the cases had episode of hypotension or bradycardia.

Both groups were also compared for SpO<sub>2</sub> (p-0.53) and respiratory rate (p-0.89) but were statistically insignificant.

### Discussion

Laryngoscopy and intubation are two most consistent manoeuvres that lead to significant increase in blood pressure by 36% to 45%. and heart rate by 20% to 45%. These changes are maximum immediately after intubation and last for 5-10 minutes. Susceptible patients are prone for myocardial ischemia, increased intracranial pressure, left ventricular dysfunction, hypertensive crisis, cardiac dysrhythmias and myocardial necrosis. Various methods and drugs have been tried to blunt these response with their own limitations.<sup>[7,8]</sup>

Nalbuphine is a cardiostable, potent analgesic with minimum side effects in the dose of 0.2-0.4 mg /kg and its action start within 2-3 minutes<sup>[9]</sup>. Fentanyl is commonly used for intraoperative analgesia as well as sole supplementary agent for induction of anaesthesia. Nalbuphine is a cardiostable, potent analgesic with minimum side effects in the dose of 0.2-0.4 mg /kg and its action start within 2-3 minutes<sup>[9]</sup>.

Adachi YU et al<sup>[10]</sup> used Fentanyl 2µg/kg to obtund the response to fiberoptic endotracheal intubation and found no significant change in haemodynamics with or without Fentanyl.

Sharma et al<sup>[9]</sup> observed increase in heart rate in both Nalbuphine and Fentanyl group post administration and Intubation. In his study maximum rise in HR of 12.5% was seen with Fentanyl during intubation, but 5.9% lower HR 15 min after intubation. Whereas with Nalbuphine maximum increase in HR was 13.1% during intubation and 7% lower than basal value 15 min

after intubation.

In our study, the mean HR was slightly increased in both groups after drug administration (Fentanyl: from 87.07 to 87.8 beats/ min; Nalbuphine: from 84.67 to 85.23beats/ min) which increased further during intubation, from 87.8 to 89.4 beats/ min in Fentanyl group and from 85.23 to 86.07beats/ min in Nalbuphine. However post-intubation, heart rate was gradually decreased in both groups and reached below pre-intubation levels (86.7beats/ min in Fentanyl and 83.07beats/ min in Nalbuphine).

Indira et al.<sup>[11]</sup> observed more rise in heart rate with Nalbuphine as compared to Fentanyl. This effect may be due to stimulation of vagal centre by Fentanyl. Nalbuphine itself causes some tachycardia.

Mean baseline systolic blood pressure and mean arterial pressure was comparable between both groups (p-0.49). However during intubation and subsequently till 15 minutes follow up duration, SBP and MAP in patients on Nalbuphine remained lower than Fentanyl group. Similarly mean Baseline diastolic blood pressure was comparable between both groups (p-0.49). During Intubation and subsequently till 1 minute, DBP in patients on Nalbuphine was lower than Fentanyl group, though it was statistically not significant. After 1 min, post intubation, diastolic blood pressure was comparable among both groups. Prasad H et al.<sup>[12]</sup>, observed no difference between Nalbuphine and Fentanyl groups. The studies concluded that Nalbuphine is one of the better choices for relieving stress to laryngoscopy and intubation, maintaining good hemodynamics intraoperatively and providing pain relief in immediate postoperative period.

Respiratory rate changes in patients remained comparable between both study drugs (p>0.05) before and after intubation. The mean SpO<sub>2</sub> was maintained above 95% levels and was comparable between both study drugs (p>0.05). No ECG changes were observed like arrhythmias and ST-T

changes in our study.

Minimal adverse events were observed in both groups including nausea/ vomiting (2 cases in Nalbuphine) and pruritus (2 cases in Fentanyl).

Chung et al. <sup>[13]</sup> observed that pure  $\mu$  agonists can cause complications such as respiratory depression which can be dangerous in the recovery room. On the other hand, Nalbuphine which is an agonist-antagonist causes less respiratory depression by activating the supraspinal and spinal  $\kappa$  receptors. This makes Nalbuphine quite useful in providing analgesia in mild to moderate postoperative pain. However in present study no major adverse reactions like hypotension or bradycardia were observed in any of the patients.

Present study observed better hemodynamic stability with Nalbuphine, however contrary findings were also observed in few other studies. We thus recommend further studies in this direction with larger sample size, to sketch out a role for each of these two drugs; Nalbuphine and Fentanyl, in attenuation of the laryngoscopic response.

### Conclusion

After comparison of IV Nalbuphine Vs IV Fentanyl in attenuating pressor response during endotracheal intubation it can be concluded that both the drugs show almost equal rise in heart rate at intubation, but increase in both SBP and DBP was more with Fentanyl than Nalbuphine.

Hence Nalbuphine can be preferred to controls the pressor response to laryngoscopy and intubation with no significant adverse effects.

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