

# Comparison of Attenuation of Hemodynamic Response to Laryngoscopy with Nalbuphine versus Fentanyl in Patients undergoing Laparoscopic Cholecystectomy

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## ABSTRACT

**Aim:** To compare the hemodynamic response in laryngoscopy with fentanyl versus nalbuphine in patients undergoing laparoscopic cholecystectomy.

**Study Design:** Randomized controlled trial.

**Place and Duration of Study:** Department of Anesthesiology, Surgical Intensive Care and Pain management, Dow University of Health and Science, Dr. Ruth K.M. PFAU, Civil Hospital Karachi from 17<sup>th</sup> July 2020 to 16<sup>th</sup> January 2021.

**Methodology:** Sixty patients between the age of 20-60 years of both genders falling under ASA Class-I and II undergoing laparoscopic cholecystectomy for cholelithiasis which were randomly allocated into two treatment groups. Patients in Group A received fentanyl while Group B was given nalbuphine before endotracheal intubation. Outcome variables were mean heart rate and mean diastolic and systolic blood pressure measured 15 minutes after intubation.

**Results:** The mean age was 41.7±11.9 years. There were 21 (35.0%) male and 39 (65.0%) female patients. Mean body mass index was 25.5±2.6 kg/m<sup>2</sup>. Thirty five (58.3%) patients belonged to ASA Class-I while 25 (41.7%) patients belonged to ASA class-II. There was no statistically significant difference between fentanyl and nalbuphine in terms of mean heart rate 15 minutes after intubation (87.37±3.30 vs. 86.33±4.23 bpm; p-value=0.296). However, the mean diastolic (73.23±3.77 vs 81.40±4.79 mmHg; p<0.001) and systolic (117.30±4.21 vs 121.53±4.75 mmHg) hypotension was observed in fentanyl group as compared to nalbuphine group.

**Conclusion:** Intravenous fentanyl infusion significantly attenuated the hemodynamic response to tracheal intubation in terms of significantly lower mean diastolic and systolic blood pressure as compared to conventional practice of nalbuphine which is desirable in patients undergoing general anesthesia.

**Keywords:** Endotracheal intubation, Hemodynamic response, Fentanyl, Nalbuphine

## INTRODUCTION

Laryngoscopy is associated with a triggered circulatory response caused by the irritation in respiratory tract which results in elevated blood pressure and heart rate.<sup>1,2</sup> Laparoscopic cholecystectomy is the common surgical procedure which is used for the removal of gall bladder. Hemodynamic perturbations associated with pneumoperitoneum during laparoscopic cholecystectomy may cause serious health hazard to the patient.<sup>3</sup> Attenuation of these hemodynamic responses during laryngoscopy and laparoscopic cholecystectomy has been one of the most desired goals in conducting smooth anesthesia. Premedication are generally given to the patients prior to surgery.

Various medicines are administered for this purpose including fentanyl and nalbuphine. Fentanyl proved to be effective against airway stimulation by suppressing pressor response. A large number of advantages are associated such as fast and short duration of action, cardiovascular stability and reduced burden of respiratory depression. Nalbuphine is also helps in the stimulation of airway passage. It also shows similar hemodynamic effects like fentanyl.<sup>4-10</sup> Fentanyl citrate is effective in blunting the pressure response to laryngoscopy and intubation with different potency with different dose titration.<sup>11</sup> The various studies have been conducted regarding the effect of both agents on attenuation of hemodynamic responses during laryngoscopy and debate is still continuing on effectiveness of both agents in this regard.<sup>1-11</sup>

Sharma et al<sup>12</sup> observed significant difference in the hemodynamic response after 15 minute in nalbuphine and fentanyl group patients in terms of mean heart rate (82.93±3.6 bpm vs 80.03±6.8 bpm; p<0.05), mean systolic blood pressure (118.53±5.1 mmHg vs 124.67±2.6 mmHg; p<0.05), mean diastolic blood pressure (79.17±4.7 mmHg vs 77.80±11.32 mmHg; p<0.05) following intubation.

Prasad et al<sup>10</sup> didn't observe significant difference in the hemodynamic response after 15 minute in nalbuphine and fentanyl group patients, mean heart rate (86.11±3.78 bpm vs. 88.12±2.32 bpm; p=0.38), mean systolic blood pressure (129.1±4.87 mmHg vs. 117.10±4.11 mmHg; p=0.38) and mean diastolic blood

pressure (78.12±15.11 mmHg vs 77.80±11.32 mmHg; p=0.77) in India. In another similar study involving Indian population, Buchh et al<sup>13</sup> also reported similar significantly lower mean systolic blood pressure (124.42±1.03 mmHg vs. 118.34±6.1 mmHg; p=0.035) after 15 minutes of intubation in patients with nalbuphine and fentanyl.

In the light of this evidence, administration of nalbuphine and fentanyl can thus attenuate the hemodynamic response to existing suggestion contains controversy where Sharma et al<sup>12</sup> reported insignificant difference in mean heart rate (82.93±3.6 bpm vs. 80.03±6.8 bpm; p<0.05), mean systolic blood pressure (118.53±5.1 mmHg vs 124.67±2.6 mmHg; p<0.05) after 15 minutes of intubation in patients as compared to nalbuphine and fentanyl respectively in India. Prasad et al<sup>10</sup> observed insignificant difference in mean heart rate (86.11±3.78 bpm vs 88.12±2.32 bpm; p=0.38), mean systolic blood pressure (129.1±4.87 mmHg vs. 117.10±4.11 mmHg; p=0.38) and mean diastolic blood pressure (78.12±15.11 mmHg vs 77.80±11.32 mmHg; p=0.77) among such patients in India. Due to this conflict in existing research evidence and lack of local such published material the purpose of the current study is to repeat this trial and further confirm the results. If the results of the present study show attenuation of hemodynamic response following nalbuphine versus fentanyl in patients undergoing laparoscopic cholecystectomy, it will enable better anesthetic care of such cases in future practice.

## MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Anesthesiology, Surgical Intensive Care and Pain management, Dow University of Health and Science, Dr. Ruth K.M. PFAU, Civil Hospital Karachi from 17<sup>th</sup> July 2020 to 16<sup>th</sup> January 2021 and 60 cases were enrolled. Patients willing to give written informed consent, either gender (male/female) aged between 20-60 years undergoing laparoscopic cholecystectomy and ASA physical status I and II were included. Patients with cardiac disease (ejection fraction <50% on echocardiography), hypertensive patients (BP more than 140/90 mmHg on more than 2 occasions at least 4

hours apart), diabetics (fasting blood sugar  $\geq 110$  mg/dl), obese (BMI  $\geq 30$  kg/m<sup>2</sup>) and peripheral vascular disease were excluded. Patients were divided into two groups and named as group F and group N on the basis of anesthesia administration fentanyl and nalbuphine respectively. Fentanyl was given in 2 $\mu$ g/kg IV and nalbuphine was given in 0.2mg/kg IV. These two drugs were diluted with ml distilled water. Investigators were unbiased so these things not involved in outcome assessment. Data collectors or outcome assessors were also blinded from group allocation throughout the study. After 3 minutes of administration and oxygenation, induction was done with injection Propofol 1-2.5mg/kg I.V till the loss of verbal response and Injection succinylcholine 1-1.5 mg/kg IV. Intubation and laryngoscopy was done after 1 minute and 30 seconds of succinylcholine administration. Anesthesia was maintained with 1% isoflurane O<sub>2</sub>-air. Injection Atracurium 0.5mg/kg was used for muscle relaxation. Heart rate, blood pressure, oxygen saturation were monitored continuously and recorded before giving the study drug, after giving the study drug, at intubation then after at 1, 3, 5, 10 and 15 minutes post-intubation. Final outcome was taken at 15 minutes post-intubation. All the collected data was entered and analyzed through SPSS-17. Independent sample t-test has been applied to compare the mean heart rate, mean systolic blood pressure and mean diastolic blood pressure between the two groups taking p-value  $\leq 0.05$  as significant.

## RESULTS

Both the study groups can be compared in terms of mean BMI, mean age, and distribution of various subgroups based on gender, ASA status, age and BMI [Table 9 1]. The heart rate 15 minutes after intubation ranged from 80 bpm to 93 bpm with a mean of 86.85 $\pm$ 3.80 bpm. The diastolic blood pressure ranged from 68 mmHg to 88 mmHg with a mean of 77.32 $\pm$ 5.93 mmHg while the systolic blood pressure ranged from 111 mmHg to 130 mmHg with a mean of 119.42 $\pm$ 4.94 mmHg. No significant difference between nalbuphine and fentanyl in terms of mean heart rate 15 minutes after intubation (87.37 $\pm$ 3.30 vs. 86.33 $\pm$ 4.23 bpm;  $p=0.296$ ), however, the mean diastolic (73.23 $\pm$ 3.77 vs. 81.40 $\pm$ 4.79 mmHg;  $p$ -value  $<0.001$ ) and systolic (117.30 $\pm$ 4.21 vs. 121.53 $\pm$ 4.75 mmHg) hypotension was observed in nalbuphine group as compared to fentanyl group (Table 2).

Table 1: Comparison of baseline characteristics of the both groups (n=60)

Characteristics	Fentanyl (n=30)	Nalbuphine (n=30)	P value
Age (years)	41.5 $\pm$ 12.5	41.8 $\pm$ 11.6	0.923
20-39	14 (46.7%)	13 (43.3%)	0.795
40-60	16 (53.3%)	17 (56.7%)	
Gender			
Male	11 (36.7%)	10 (33.3%)	0.787
Female	19 (63.3%)	20 (66.7%)	
BMI (Kg/m <sup>2</sup> )	25.5 $\pm$ 2.4	25.4 $\pm$ 2.9	0.946
20-25	14 (46.7%)	15 (50.0%)	0.796
25-30	16 (53.3%)	15 (50.0%)	
ASA status			
Class I	17 (56.7%)	18 (60.0%)	0.793
Class II	13 (43.3%)	12 (40.0%)	

Table 2: Comparison of hemodynamic response to intubation in the both groups (n=60)

Hemodynamic Response	Fentanyl (n=30)	Nalbuphine (n=30)	P value
Heart rate (bpm)	87.37 $\pm$ 3.30	86.33 $\pm$ 4.23	0.296
Diastolic blood pressure (mmHg)	73.23 $\pm$ 3.77	81.40 $\pm$ 4.79	$<0.001$
Systolic blood pressure (mmHg)	117.30 $\pm$ 4.21	121.53 $\pm$ 4.75	0.001

## DISCUSSION

Respiratory response was triggered in tracheal intubation and laryngoscopy in process of general anesthesia. These sometime

cause high risk of mortality in patients.<sup>1-3</sup> A number of drugs have been formulated and varying improvements in laryngoscopic hardware and technique have been developed to attenuate this hemodynamic response to intubation with varying degree of success.<sup>3,4</sup>

Laparoscopy gives many advantages to surgeons and revolutionized the medical science. This procedure has been performed under general anesthesia.<sup>11</sup> Pathophysiological changes including the alteration of cardiorespiratory function occur after carbon dioxide pneumoperitoneum and extremes of patient positioning.<sup>1,2,11</sup> These changes add up to the sequential effects of endotracheal intubation during anesthesia to produce a characteristic hemodynamic response.<sup>11</sup>

Nalbuphine is a routine drug administered during induction of anesthesia to counteract this hemodynamic response.<sup>1,5</sup> Sharma and Parikh<sup>12</sup> showed that fentanyl show better results in case of lowering heart rate than nalbuphine. However, different results were also reported in different literature.<sup>10,12,13</sup>

Female predominance was observed in present study. Bhurt et al<sup>14</sup> also show similar results. Another study was also reported the similar findings as reported by Faizi et al.<sup>15</sup> Pal et al<sup>16</sup> conducted study in Agha Khan Hospital also show similar results.

In the present study, there was no considerable difference observed between both groups in terms of mean heart rate 15 minutes after intubation (87.37 $\pm$ 3.30 vs 86.33 $\pm$ 4.23 bpm;  $p=0.296$ ). However, the mean diastolic (73.23 $\pm$ 3.77 vs 81.40 $\pm$ 4.79 mmHg;  $p<0.001$ ) and systolic (117.30 $\pm$ 4.21 vs 121.53 $\pm$ 4.75 mmHg) hypotension was observed in nalbuphine group as compared to fentanyl group.

In a similar trial in India, Khanday et al<sup>17</sup> observed insignificant difference in mean heart rate between fentanyl and nalbuphine (85.34 $\pm$ 3.98 vs 84.84 $\pm$ 6.69 bpm;  $p=0.651$ ) following intubation. They too confirmed that fentanyl was superior to nalbuphine in the attenuation of hemodynamic response in terms of significantly lower mean diastolic (80.10 $\pm$ 8.93 vs. 85.06 $\pm$ 7.60 mmHg;  $p=0.004$ ) and systolic (117.78 $\pm$ 8.24 vs 126.72 $\pm$ 9.12 mmHg;  $p<0.001$ ) blood pressure. In another recent Indian study, Makker et al<sup>18</sup> also reported similar significant difference between fentanyl and nalbuphine in terms of mean diastolic (74.30 $\pm$ 6.26 vs 79.46 $\pm$ 6.57 mmHg;  $p=0.001$ ) and systolic (114.17 $\pm$ 12.33 vs 121.57 $\pm$ 6.51 mmHg;  $p=0.001$ ) blood pressure. They too observed insignificant difference in mean heart rate (77.10 $\pm$ 10.28 vs. 77.87 $\pm$ 8.52 bpm;  $p=0.862$ ) after endotracheal intubation in line with the present study.

In the present study, intravenous fentanyl infusion significantly attenuated the hemodynamic response to tracheal intubation in terms of significantly lower mean diastolic and systolic blood pressure as compared to conventional practice of nalbuphine which is desirable in patients undergoing general anesthesia and laparoscopic surgery and is therefore recommended. Side effects were not compared in present study nor did we consider their effect on post-operative patient's analgesia and recovery. A larger multicenter trial addressing these limitations is required to further establish the role of fentanyl in general anesthetic practice. Such a study is highly recommended in future clinical research.

## CONCLUSION

Intravenous fentanyl infusion significantly attenuated the hemodynamic response to tracheal intubation in terms of significantly lower mean diastolic and systolic blood pressure as compared to conventional practice of nalbuphine which is desirable in patients undergoing general anesthesia and is therefore recommended in future practice.

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