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Original Research Article

Comparison of Nalbuphine and Fentanyl on Hemodynamic Response in Patients Undergoing Laparoscopic Surgeries under General Anaesthesia

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Conflict of interest: Nil

Abstract

Introduction: To prevent hemodynamic response to laryngoscopy, intubation and pneumoperitoneum various drugs are used. Opioids are commonly used in premedication, being a good analgesic, to support analgesia during surgery and to provide pain relief in immediate postoperative period. Among opioids, Fentanyl and Nalbuphine effectively control the hemodynamic stress response associated with laparoscopic surgeries in the present study, we compared the hemodynamic parameters of Fentanyl and Nalbuphine during laryngoscopy and endotracheal intubation for induction of general anesthesia.

Materials & Methods: In this study total 50 patients undergoing laparoscopic surgeries were randomly divided into two groups. Total 25 patients of **Group N** received Inj. Nalbuphine 0.2mg/kg diluted in 10 ml NS injected slowly before induction. Another 25 patients of **Group F** received Inj. Fentanyl 2µg/kg diluted in 10 ml NS injected slowly before induction. The pulse rate, blood pressure, ECG, oxygen saturation and respiratory rate were noted at 0 minute, thereafter every 5 minutes for the initial 15 minutes, then every 10 minutes till 2 hrs and then every 2 hourly up to 16 hours in post-operative period.

Result: Intraoperative HR and SBP stability was better in group N compare to group F ($p<0.0001$). Post extubation SBP changes were not statistically significant. Fentanyl is better than Nalbuphine in attenuating the rise in DBP after laryngoscopy and intubation but Nalbuphine is more efficacious in control of DBP during intraoperative period than Fentanyl.

Conclusion: The hemodynamic stress response to laryngoscopy and endotracheal intubation was less with Fentanyl as compared to Nalbuphine. However, Nalbuphine provides better hemodynamic stability than Fentanyl intraoperatively.

Keywords: Fentanyl, Hemodynamic stress, Intubation, Laryngoscopy, Nalbuphine.

Introduction

Direct laryngoscopy and tracheal intubation is an invasive procedure which leads to stress response resulting from increase in sympathetic and sympathoadrenal activity, as evidenced by increased plasma catecholamine concentrations and activation of α and β adrenoreceptors leading to tachycardia and hypertension. This increase in blood pressure and heart rate are transitory, variable and unpredictable. Although most patients can tolerate these transient effects without any significant consequences, but this could be detrimental in susceptible individuals causing arrhythmias, left ventricular failure, myocardial ischemia, increased bleeding, raised intracranial and intraocular pressure and cerebrovascular haemorrhage in them. [1]

Opioids specifically have been found to be useful in attenuation of this cardiovascular response, but may cause respiratory depression and rigidity or may prolong the recovery time. Fentanyl is a synthetic pure μ-receptor agonist replacing morphine and pethidine because of shorter time to peak analgesic effect, larger safety margin, minimal respiratory depression at analgesic doses and rapid termination of effect after small bolus doses, and relative cardiovascular stability. [2] Nalbuphine is an opioid agonist-antagonist used as analgesic. Its analgesic potency is equivalent to of morphine on a milligram basis. [3] It binds to μ, kappa, and delta receptors. Nalbuphine may partially reverse or block opioid-induced respiratory depression from the μ-agonist analgesic. Nalbuphine, unlike other agonist–antagonist opioids, for example, pentazocine or butorphanol, does not increase systemic blood pressure, pulmonary artery blood pressure, heart rate (HR), or arterial filling pressure. For this reason, Nalbuphine may be useful to provide sedation and analgesia in patients with heart disease, for example, during cardiac catheterization. [4,5] In the present study, we compared the hemodynamic parameters of Fentanyl and Nalbuphine during laryngoscopy and endotracheal intubation for induction of general anesthesia.

Materials & Methods

Study area & Study population: This Randomized controlled study was conducted among 50 patients undergoing laparoscopic surgeries in civil hospital Ahmedabad after obtaining approval from institutional ethics committee and written informed consent.

Method of Randomization: Patients included in the study were randomized by using random number tables into two study groups with equal patients in both of the study group. **Group N:** 25 patients received Inj. Nalbuphine 0.2mg/kg diluted in 10 ml NS injected slowly before induction. **Group F:** 25 patients received Inj. Fentanyl 2μg/kg diluted in 10 ml NS injected slowly before induction.

Inclusion Criteria a) Patients in the age group of 15-60 years of age b) Having ASA (American Society of Anaesthesiologists) grade I & II. c) Patient who gave informed written consent to be included in the study.

Exclusion Criteria: a) Those with clinically significant cardiovascular, respiratory, hepatic, renal, neurologic, psychiatric or metabolic disease. b) Pregnant women c) Morbid obesity d) Those with a history of alcohol and drug abuse.

Methods

All patients were pre-medicated with Inj. Glycopyrrolate 0.004 mg/kg IV and Inj. Ondansetron 0.15 mg/kg IV. The patient was pre oxygenated for 3 mins using 100% oxygen with bain's circuit. Group N received Inj. Nalbuphine 0.2mg/kg diluted in 10 ml NS injected slowly before

induction. Group F received Inj. Fentanyl 2µg/kg diluted in 10 ml NS injected slowly before induction. Induction of anaesthesia was carried out using Inj. Thiopentone sodium 5-7 mg/kg and Inj. Scoline 2 mg/kg. Intubation was carried out using an appropriate size ET tube. Anaesthesia was maintained using oxygen, 1-2 % Sevoflurane and Inj. Vecuronium Bromide 0.08mg/kg IV. Patients were watched for any complication during intraoperative period. After satisfied criteria for extubation, thorough oral and endotracheal suction was done and patients were extubated. Post operatively, all patients were observed for pain score, sedation score, side effects, requirement of rescue analgesic, aldrete score. The pulse rate, blood pressure, ECG, oxygen saturation (SpO2) and respiratory rate were noted at 0 minute, thereafter every 5 minutes for the initial 15 minutes, then every 10 minutes till 2 hrs and then every 2 hourly up to 16 hours in post-operative period.

Statistical analysis: Data was entered and analyzed in Micro soft excel 2010. Categorical variables were presented with frequency and percentage and continuous variables were presented with mean and standard deviation (SD). Categorical variables were compared using the Chi-square test; continuous variables were compared using unpaired t-test.

Result

This study was conducted on 50 patients of ASA grade I and II undergoing elective laparoscopic surgery under general anaesthesia. Group N received Inj Nalbuphine 0.2mg/kg iv before induction and Group F received Inj. Fentanyl 2µg/kg iv before induction. Both the groups were comparable in terms of age, gender, weight and ASA grade, which was statistically insignificant ($p>0.05$) between two groups. Duration of surgery and anaesthesia were similar in both groups.

Table 1: Baseline characteristics of participants

Characteristics	Group N	Group F	p value
Age (years)	42.92 ± 9.07	45.84 ± 9.61	0.27
Gender			
– Male	12 (48.0%)	14 (56.0%)	0.77
– Female	13 (52.0%)	11 (44.0%)	
Weight (kg)	53.92±6.99	54.12±6.28	0.92
ASA			
– I	9 (36%)	7 (28.0%)	0.76
– II	16 (64%)	18 (72.0%)	
Duration of surgery (minutes)	124 ± 34	120 ± 31	0.66
Duration of anaesthesia (minutes)	160 ± 29	156 ± 24	0.59

Group F and Group N reported rise in HR from baseline in immediate post intubation period. In both group HR was increased at 1 min and more increased in group N compare to group F. Difference was statistically significant between two groups. HR touched baseline early in group N followed by Group F. Intraoperative HR stability was better in group N compare to group F till 90 mins and statistically significant till 90 mins ($p<0.0001$) in both groups. In both groups, HR was increased immediately after extubation which was significant ($p=0.0012$).

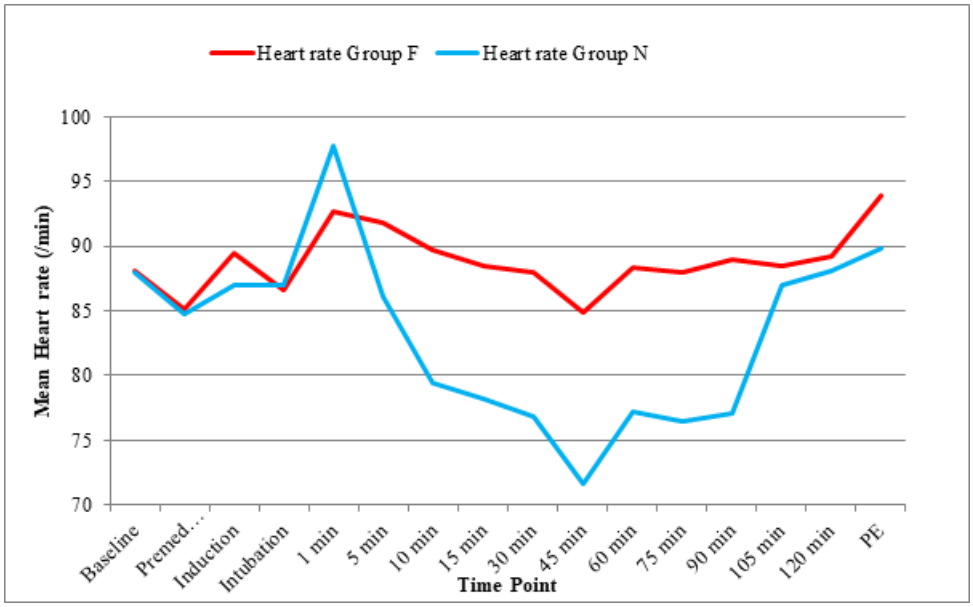

Figure 1: Comparison of heart rate in both the groups

Group F and Group N showed rise of SBP at 1 min post intubation and 5 min post intubation. Group F showed better SBP stability as compared to Group N at immediate post intubation period. SBP came back near to baseline in group F at 15 mins and in group N at 10 mins. Intraoperatively, SBP changes were significant between both groups till 90 min (p=0.0031), after that SBP changes were not significant. Intraoperatively, group N showed better SBP stability compare to group F.

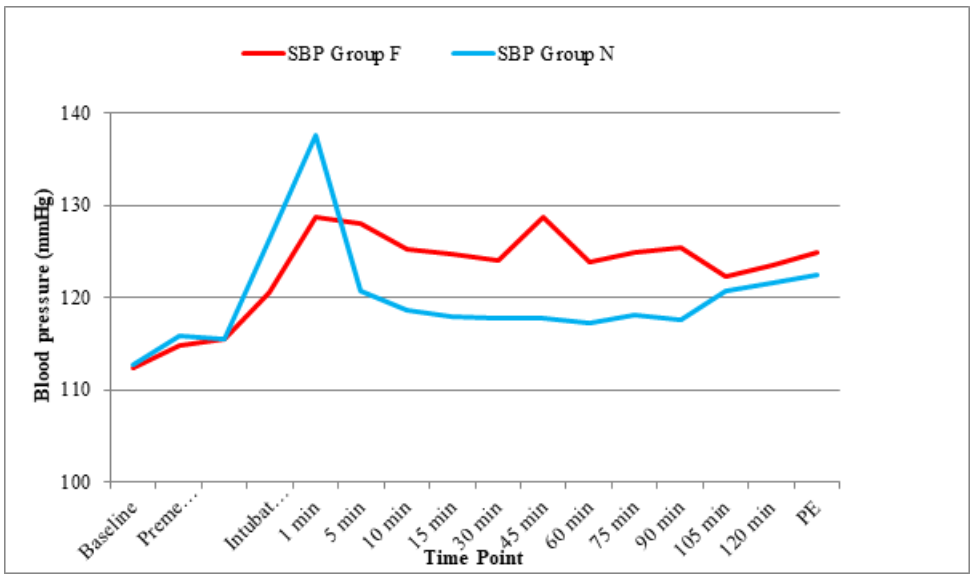

Figure 2: Comparison of SBP in both the groups

Fentanyl was better than Nalbuphine in attenuating the rise in DBP after laryngoscopy and intubation but we observed that Nalbuphine was more efficacious in control of DBP during intraoperative period than Fentanyl. Fentanyl provided better control of MAP than Nalbuphine during intubation, while intraoperative period Nalbuphine provided better control of MAP than Fentanyl which was statistically significant.

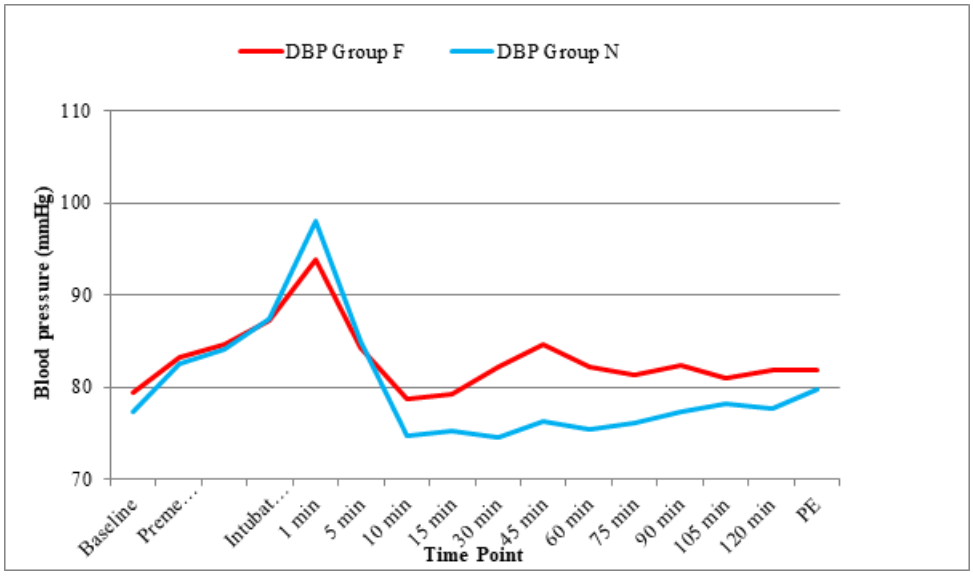

Figure 3: Comparison of DBP in both the groups

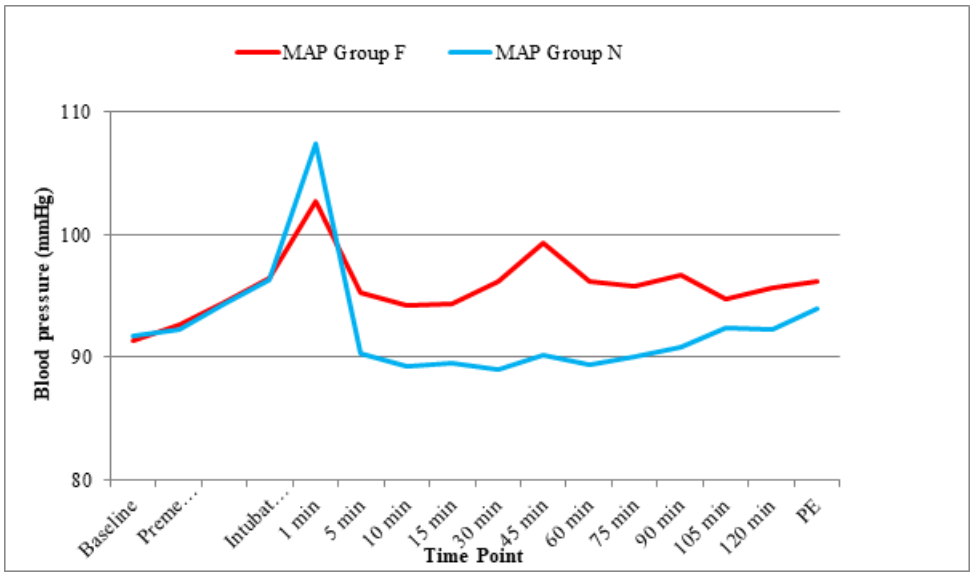

Figure 4: Comparison of MAP in both the groups

Discussion

Studies have shown that narcotics such as Fentanyl [6] and Nalbuphine [7,8] are effective in blunting pressor response to laryngoscopy and endotracheal intubation. Narcotics are used as sole or supplementary agents for the induction of anesthesia. The aim of the present study was to compare hemodynamic parameters of two groups. In Present study, age, weight, the duration of surgery were comparable between both which was comparable with other studies.

HR

In our study, HR comparison in baseline in Group-F (88.16±5.84) and Group-N (87.92±5.67) were not significant. Changes in HR after giving the study drugs were also not significant between Group-F and Group-N .There was increased in heart rate after intubation in both groups from baseline. HR was more increased in group N compare to group F at 1 min intubation. So group F provided better HR stability compare to group N during laryngoscopy and intubation. HR began to return back to baseline after 5 minutes in Group-N and Group-F were statistically significant. Intraoperative

changes in HR were statistically significant between Group-F & Group-N at all-time except at 105 mins, 120 mins. Intraoperative HR stability was better in group N as compared to group F till 90 mins and statistically significant ($p<0.0001$) in both groups. In both groups, HR was increased immediately after extubation which was significant ($p=0.0012$).

Different study results for intubation differs for HR changes during laryngoscopy and intubation. Sharma N. et al. [9] observed rise of HR at laryngoscopy & intubation (13%) and 5 mins after intubation maximum rise in HR (12.5%) remained higher than the baseline. Bhandari et al. [10] concluded Fentanyl provides a better hemodynamic condition for laryngoscopy and endotracheal intubation. In the study of Khanadav et al., [11] at induction (0 min), there was decrease in HR in Fentanyl and Nalbuphine group. Increase in HR from the base-line was recorded highest as 12.97% and 12.84% at 1 min after intubation in the Fentanyl and Nalbuphine groups, respectively. However, the variation was statistically non significant ($P = 0.748$). Thereafter, HR showed a gradual decrease in both the groups over the next 5 min, almost returning to baseline at 10 min after intubation. The results were not significantly different between the two groups. Bhandari et al. [10] stated that mean HR after intubation showed significantly increased value of 88 ± 11.45 beats/min in Fentanyl group and 102.68 ± 16.04 beats/min in Nalbuphine group and was statistically significant. Khan et al. [12] compared Nalbuphine with Fentanyl after endotracheal intubation and documented 25% rise in HR after intubation in the Nalbuphine group when compared with Fentanyl group.

SBP

In our study, SBP rise in group N was 14% during intubation and remained higher after that. Group F and Group N showed rise of SBP at 1 min and 5 min post intubation. Group F showed better SBP stability as compared to Group N at immediate post intubation period. At 5 mins after intubation, SBP in Group-N (120.8±6.48) and in Group-F (128±8.46) were higher than baseline value. SBP returned to baseline in group F at 15 mins and in group N at 10 mins. Intraoperatively SBP changes were significant between both groups till 90 min ($p=0.0031$), after that SBP changes were not significant. Intraoperatively group N showed better SBP stability compare to group F. Post extubation SBP changes were not statistically significant. In the study of Prasad HK et al [13], significant rise in SBP was found at 1 min post intubation period and 5 min after intubation SBP was lower than baseline value in both groups. Sharma K. et al.[9], significant rise in SBP from baseline was found at 1 min post intubation period returned to baseline at 5 mins with nalbuphine. Bhandari et al. [10] observed significant attenuation of the hemodynamic changes (SBP) in patients of Nalbuphine group as compared to patients of Fentanyl group. In contrast to our study, Khanaday et al. [11] reported better hemodynamic stability with Fentanyl compared to nalbuphine. The mean SBP shows a significant variation at the time of induction, being higher in Fentanyl group (119.52 ± 9.18 vs. 114.96 ± 9.63). At 1 min after intubation, there was a significant rise in the mean SBP in Group N compared to Group F (133.72 ± 8.90 vs. 126.10 ± 8.91). Subsequently, mean SBP revealed a downward trend in both groups, but continued to be significantly higher in Nalbuphine group till 10 min after intubation.

DBP

In our study, significant rise in DBP from baseline was found in immediate post intubation period. Group F and Group N showed rise of DBP at 1 min post intubation and this rise was more in Group

N as compared to Group F. DBP returned to baseline at 10 mins in both groups. Group N showed better DBP stability as compared to Group F intraoperatively. Post extubation DBP changes were not statistically significant. Therefore, Fentanyl is better than Nalbuphine in attenuating the rise in DBP after laryngoscopy and intubation but we observed that Nalbuphine is more efficacious in control of DBP during intraoperative period than Fentanyl.

Khan et al. [14] has compared Nalbuphine 0.2 mg/kg and Fentanyl 2 µg/kg as total intravenous anaesthesia with propofol infusion in laparoscopic surgery. These drugs were given 5 mins before induction. They found significant increase in DBP (13%) in Nalbuphine group versus 3% in Fentanyl group. In the study of Khanaday et al. [11], there was a non significant decrease in mean DBP in the Fentanyl and Nalbuphine groups at induction. On the other hand, at 1 min after intubation, the mean DBP was increased to 85.86 ± 5.86 mmHg and 90.06 ± 9.52 mmHg in Fentanyl and Nalbuphine groups, respectively, and the variation was found to be statistically significant ($p = 0.009$).. A progressive fall of DBP till 10 min, was seen to be more in Fentanyl group compared to Nalbuphine group with statistically significant difference. The results of Park et al. [15] found significant increase DBP after intubation in patients receiving Fentanyl 1 µg/kg given 15 min before intubation. DBP increased to 40% above baseline in fentanyl group 30 s after intubation. The inadequate effect of Fentanyl to attenuate the hemodynamic response in this study may be related to the lower dose used and longer-than-optimal time lag from administration to laryngoscopy. In the study of Channaiah et al. [16], greatest attenuation in SBP and DBP was observed at intubation with a significant difference from the control group ($p < 0.001$). There is more consistent decrease in DBP after 1 minof intubation.

MAP

MAP is a derived value and is important in relation to the autoregulatory responses of the heart, brain, and kidneys. In our study, significant rise in MAP from baseline was found in immediate post intubation period. However, Group N showed more rise of MAP at immediate post intubation period compare to Group F ($p=0.0034$). MAP returned to baseline in both groups at 5 mins post intubation period. Intraoperatively MAP stability was better in Group N compare to Group F. In both groups, rise in MAP in immediate post extubation period from baseline value. Fentanyl provides better control of MAP than Nalbuphine during intubation, while intraoperative period Nalbuphine provides better control of MAP than Fentanyl which is statistically significant.

In the study of Khanaday et al. [11], there was a significant fall at induction in MAP from baseline in patients of both Fentanyl and Nalbuphine groups. After 1 min, there was a decrease in MAP in both the groups. However, Fentanyl group exhibited more decrease as compared to Nalbuphine group till 10 min after intubation with a significant difference between Fentanyl and Nalbuphine groups. This study has shown that MAP control after laryngoscopy and intubation is better in Fentanyl group than that in Nalbuphine group. In accordance with our study, Channaiah et al. [16] noted that intergroup MAP yielded significant attenuation in the Fentanyl group for all recorded time periods. Chawda et al. [17] observed significant increase in MAP after intubation in placebo compared to Nalbuphine. Similarly, Ahsan-ul-Haq et al. [7] noticed increase in MAP just after induction in placebo group which was significant whereas Nalbuphine prevented this rise, in contrast to our study where Nalbuphine couldnot attenuate the rise in MAP completely. Bhandari et al. [10]

concluded that control of MAP is better by Nalbuphine than Fentanyl during laryngoscopy and intubation which was statistically significant.

Madhu S et al. [18] included 60 ASA I patients who underwent elective appendectomy were randomised to receive either Nalbuphine 0.1mg/kg or Fentanyl 2µg/kg as analgesics 5 minutes prior to intubation. Nalbuphine and Fentanyl group showed rise in heart rate of 3.81% and 6.03% respectively. Mean arterial pressure was comparable at all time points of observation except at the time of insertion of second port wherein Fentanyl group showed 12.70% increase as compared to 4.54% fall from baseline in Nalbuphine group.

In the study of Managavi V et al. [19], heart rate was better controlled in group N than group F at 1 min, 3 min and 5 mins post extubation and is statistically significant (P value < 0.05). Both groups showed a rise in SBP immediately after intubation. Group N showed a significantly lower SBP in comparison to group F ($p<0.005$). [20] The DBP showed a similar trend. At one, three, and five minutes after intubation, HR, SBP, DBP, and MAP were similar between the groups

Conclusion

The hemodynamic stress response to laryngoscopy and endotracheal intubation in the form of increased heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure were less with Group F as compared to Group N. But Group N provides better hemodynamic stability than Group F intraoperatively.

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