



COMPARISON OF INTRAVENOUS NALBUPHINE AND FENTANYL ON ATTENUATION OF PRESSOR RESPONSE DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

Anaesthesiology

Dr Indira

Department Of Anaesthesiology, SMS Medical College, Jaipur

Dr Mamta Khandelwal

Associate Professor, Department Of Anaesthesiology, SMS Medical College, Jaipur

Dr Usha Bafna

Senior Professor, Department Of Anaesthesiology, SMS Medical College, Jaipur

Dr Fareed Ahmed

Senior Professor, Department Of Anaesthesiology, SMS Medical College, Jaipur

ABSTRACT

Background and Aim- Sympathetic response evoked by laryngoscopy and endotracheal intubation is ephemeral but results in marked increase in blood pressure and heart rate. Various drugs and methods have been tried to obtund this response. To obtain ideal drugs, studies still continue. We compared the efficacy of nalbuphine and fentanyl to attenuate the pressor response during laryngoscopy and intubation.

Method- Total 90 patients of ASA grade I & II scheduled for elective surgery under general anaesthesia, were randomized into two groups. Group A received nalbuphine 0.2 mg /kg IV and group B received fentanyl 2 µg/kg IV 5 minutes before intubation. Heart rate and blood pressure (SBP, DBP & MAP) were recorded before administration of study drug, just before intubation and then 1,3,5,10,15 minutes after intubation.

Statistical analysis- All the qualitative data were analysed with chi square test and all the quantitative data were analysed with unpaired student t-test.

Results- Rise of mean HR immediately after intubation was less in group B as compared to group A ($P < 0.05$). Heart rate changed from 92.24 ± 10.78 to 99.51 ± 10.63 bpm ($+2.25\%$) in group B and in group A it was 96.02 ± 13.81 to 106.42 ± 11.44 bpm ($+8.07\%$). One minute post intubation rise of blood pressure (SBP, DBP and MAP) was also less in group B as compared to group A ($P < 0.05$).

Conclusion- Fentanyl appears to be better than Nalbuphine for control of haemodynamic response to laryngoscopy and intubation.

KEYWORDS

Fentanyl, Nalbuphine, hemodynamic changes and endotracheal intubation.

Introduction

The pressor response to laryngoscopy and endotracheal intubation has been described by Reid and Brace in 1940.¹ Tracheal intubation causes a reflex increase in sympathetic activity that may result in hypertension, tachycardia, and arrhythmia. A change in plasma catecholamine concentrations also has been demonstrated to be a part of the stress response. This autonomic changes are variable, transitory, unpredictable and well tolerated in ASA I & II patients, but it may be detrimental in patients with pre-existing hypertension, Cardiac disease, and cerebral pathologies.^{2,3}

Various non-pharmacological methods like smooth & gentle intubation with a shorter duration of laryngoscopy, insertion of LMA in place of endotracheal intubation has been tried.⁴

In pharmacological methods a numbers of drugs have been used. These includes lidocaine spray, IV lignocaine and Opioids, Propanolol, isosorbide dinitrate, Calcium channel blockers, Esmolol, fentanyl, Magnesium sulphate, clonidine, Gabapentin, and dexmedetomidine.^{5,16}

None of the above approaches or agents has been proved to be ideal so the need for an ideal agent to obtund the stress responses to laryngoscopy & intubation is still continuing.

Fentanyl was first synthesized in 1960 and found to be significantly more potent than commonly used opioids such as morphine. Fentanyl has proved ideal for control of the short lived haemodynamic sequelae, associated with laryngoscopy and intubation. Fentanyl brings haemodynamic stability during perioperative period by its action on cardiovascular and autonomic regulatory areas.¹⁷

Nalbuphine is a semi-synthetic opioid agonist-antagonist analgesic of the phenanthrene series. Nalbuphine, unlike other agonist-antagonist opioids eg. pentazocine or butorphanol, does not increase systemic blood pressure, pulmonary artery blood pressure, heart rate, or arterial filling pressure.

We have done this study to compare the effects of fentanyl and nalbuphine on haemodynamic responses to endotracheal intubation to find a better drug in this respect.

Subject and Methods

After approval from the institutional ethical committee 90 patients with study eligibility of ASA grade I and II, aged 20–55 years, weighing 40 to 70 kg, posted for elective surgery under general anaesthesia were selected and randomly allocated into two groups (A & B) by using 'Chit in box' technique.

Patient with major organ dysfunction (hypertension, cerebrovascular disease, ischemic heart disease, arrhythmias, shock), on medications (like hypnotics, narcotic analgesics, α_2 agonists, calcium channel blockers, β blockers) and with reactive airway diseases, having known allergy to anaesthetic agents used in study, with anticipated difficult intubation and in whom intubation was done after more than 1 attempt or more than 30 seconds were excluded from the study.

Pre-anaesthetic checkup was done in all patients as per institutional protocol. Written informed consent was taken for performance of general anaesthesia after complete explanation about the study protocol.

On arrival in the operation theatre, fasting status, written informed consent and PAC were checked. Routine non-invasive monitors attached and baseline parameters were recorded. Intravenous line established and Ringer Lactate was started. Patients were premedicated with inj. ranitidine 50mg, Glycopyrrolate 0.2mg and ondansetron 4 mg intravenously. Data were collected 5 minutes after premedication. Study drugs Nalbuphine (0.2mg/kg IV) or Fentanyl (2mcg/kg IV) were diluted with normal saline to make a total volume of 10 ml and injected IV slowly over 1 minute.

Patients were pre-oxygenated with 100 % O₂ for three minutes. Induction was done with inj. Thiopentone sodium 5mg/kg iv followed by inj. Vecuronium 0.1 mg/kg iv and ventilated with 100% oxygen for 3 minutes. Data were collected just before intubation. Direct laryngoscopy and intubation was done with appropriate size endotracheal tube.

Data were collected at 1, 3, 5, 10 and 15 minutes after intubation. Then surgery was allowed to commence after 15 minutes of intubation & anaesthesia was maintained with 60% Nitrous Oxide and 40% Oxygen, 1% isoflurane and inj. vecuronium 1 mg i.v. SOS. At the end of the surgery patients were reversed with Inj. Neostigmine (0.05

mg/kg i.v.) and Inj. Glycopyrrolate (0.008mg /kg i.v.) & Extubation was done after patient fulfilling the criteria of extubation. Patient was shifted to recovery room .In recovery room patients were observed for sedation score and any postoperative complications.

Statistical Analysis

All the data were entered on M.S.Office Excel and analyzed statistically using SPSS Statistical software (ver.18.0.0) and XL Stat. All the qualitative data were analysed with chi square test and all the quantitative data were analysed with comparison of mean + SD and unpaired student t-test. The levels of significance and α - error were kept 95% and 5 % respectively for all statistical analyses. Statistically significance showed when p value <0.05

Results

Both groups were comparable in term of Age, Weight, Sex, ASA physical status and duration of surgery. (Table no.1)

There was decrease in heart rate in both groups just before intubation

but it was more in group B (5.22%) as compare to group A (2.49%). it was not statistically significant. Heart rate was increased in both groups at 1 and 3 min after intubation. Group B showed a better response than group A with a statistically significant difference (p 0.05).In group B, after intubation the mean heart rate came less than the mean baseline value of heart rate after 5min of intubation but in group A it took 10 min. (Table 2)

Table 1: Demographic data

Particulars	Group A	Group B	P value
Age(years) (Mean ±SD)	32.62±10.57	34.76±9.09	0.307
Sex (male:female)	9:36	5:40	0.249
Weight(kg) (Mean ±SD)	52.40±7.32	54.73±6.09	0.103
ASA(I:II)	41:4	42:3	0.697
Duration of surgery(Mean ±SD)	47.8±8.74	47.06±8.66	0.690

Table 2 :Mean Heart Rate at Various Time Intervals

	Group A		% Percentage change from basal value	Group B		P value
	Mean (per min)	SD		Mean (per min)	SD	
Baseline	98.47	18.71		97.32	13.43	0.738 NS
5 minute after premedication	97.59	13.40	-0.89	95.29	13.75	0.424NS
Just before Intubation	96.022	13.816	-2.49	92.24	10.78	0.151 NS
1 minute post intubation	106.42	11.44	8.07	99.51	10.63	0.004S
3 minute post intubation	103.56	11.17	5.17	97.51	10.517	0.01S
5 minute post intubation	99.533	10.826	1.08	95.69	10.86	0.097NS
10 minute post intubation	95.93	11.33	-2.58	93.91	13.874	0.451NS
15 minute post intubation	92.98	10.58	-5.58	89.44	10.87	0.121 NS

Table 3 :Mean SBP at Various Time Interval

	Group A		% Percentage change from basal value	Group B		P value
	Mean (mmHg)	SD		Mean (mmHg)	SD	
Baseline	127.78	9.18		129.20	10.42	0.493 NS
5 minute after premedication	119.64	9.04	-6.37	122.33	7.19	0.121 NS
Just before Intubation	106.89	12.68	-16.35	106.73	10.85	0.950 NS
1 minute post intubation	128.73	12.26	0.74	123.64	11.49	0.045 S
3 minute post intubation	114.87	11.90	-10.10	113.82	6.35	0.604 NS
5 minute post intubation	108.93	10.88	-14.75	106.60	7.33	0.235 NS
10 minute post intubation	105.11	11.56	-17.74	102.93	7.05	0.283 NS
15 minute post intubation	104.8	8.72	-17.98	102.20	7.50	0.133 NS

There was no significant difference between the baseline values of SBP in both groups. Group B showed a better response than group A with a statistical significant difference at 1 min after intubation (P <0.05). At 3,5,10 and 15 min post intubation, the statistical difference was non-significant but group B was found better than group A. (Table 3)

Just before intubation the mean DBP fell to 70.02± 12.13mmHg and 69.60± 8.41mmHg from baseline in group A & B respectively (P>0.05). In both groups mean DBP was increased from baseline at immediate after intubation. It was 11.45% in group A and 1.4 % in group B and the result was found to be statistically significant (P<0.05).

Preoperatively, there was a decrease in MAP in both groups after 5 min of administration of study drug. After intubation, group B showed a better response than group A with a statistical significant difference at 1 min after intubation (P <0.05). At 3,5,10 and 15 min post intubation, the statistical difference was non- significant but group B showed better response than group A. (Figure 1)

There was no episode of hypotension and bradycardia in any case in group B but in group A it was found in 2.22% of patients. Nausea and vomiting was more in group A than group B. Respiratory depression

was more in group B (6.66%) as compared to group A (2.22%). (Figure 2)

Figure 1. Change in MAP(mmHg) in two groups

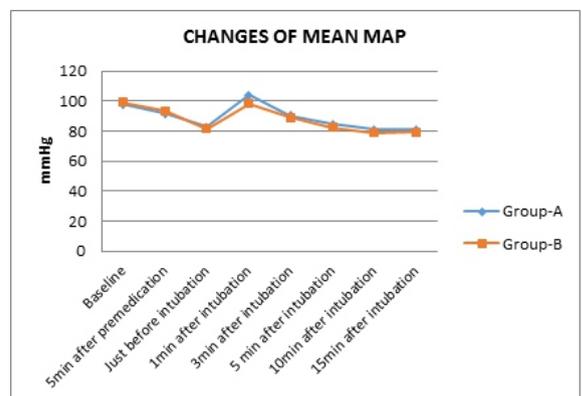
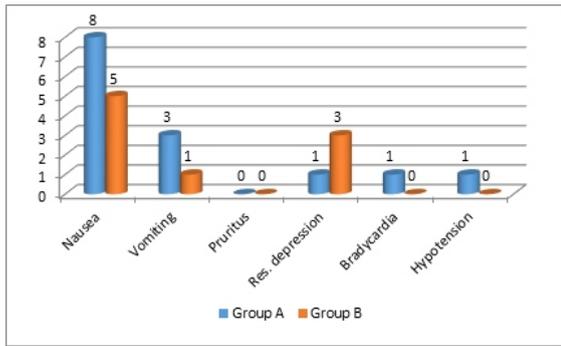


Figure 2: Side Effects



22 patients in group A and 30 patients in group B have sedation score 1. There were 21 & 15 patients, with sedation score of 2 in group A & B respectively. Only two patients in group A have sedation score 3, but there was no case in group B of sedation score 3. Patients with sedation score 4 were not found in any of the two group. (Table 4)

Table 4: Sedation Score

	Group A (1/2/3/4)	Group B (1/2/3/4)	P value
Sedation Score	22/21/2/0	30/15/0/0	0.06
Mean ±SD	1.55±0.58	1.33±0.47	

Discussion

Laryngoscopy and intubation are two most consistent manoeuvres that lead to significant increase in blood pressure and heart rate. To obtund these adverse effects by various pharmacological and non- pharmacological methods is main concern of anaesthesiologist.

Yushi et al¹⁸ and chung et al¹⁹ found that Fentanyl in 2µg/kg dose, obtunds the hemodynamic response to laryngoscopy and endotracheal intubation. Large dose of fentanyl (6µg/kg) completely abolish haemodynamic response, but with undesirable side effects so we used 2µg/kg fentanyl in our study. Chawda et al²⁰ observed that nalbuphine in dose of 0.2mg/kg given five minutes before laryngoscopy obtunded the stress response to endotracheal intubation .

Sharma N et al²¹ found that after study drug administration, mean HR decreased by 3% in fentanyl group from basal value as compared to (3.6%) in nalbuphine group. In our study we also observed slightly decreased heart rate in both

In present study both group showed rise in HR after intubation group A showed more rise in HR (8.07%) from baseline then in group B (2.25%). This effect was may be due to stimulation of vagal centre by fentanyl. Nalbuphine itself causes some tachycardia. Our study demonstrated that fentanyl controls heart rate better than nalbuphine.

Our result is strengthened by the studies done by FA Khan et al²², Bhandari et al²³ and Sharma et al²¹

In our study, there was decrease in mean SBP by (6.37%) in group A and (5.32%) in group B after study drug administration which was not statistically significant .Similar results were found in study done by Bhandari R et al²³ they also found a fall in mean SBP in fentanyl and nalbuphine group from baseline value . Sharma N et al²¹ also observed fall in mean SBP (5.4%) in fentanyl group and (2.4%) in nalbuphine group.

In our study, at one minutes after intubation in group A SBP increased (0.74%) from basal value but in group B there was fall in SBP (4.30%) from basal value which was statistical significant (p<0.05). We found fentanyl better as compared to nalbuphine.

Our result supported by Sharma N et al.²¹ in which nalbuphine group had significant rise in SBP(14.9%) after intubation as compared to fentanyl group(4.8%).

In our study there was a decrease in mean DBP in group A by (5.77%) and in group B by (5.33%) after study drug administration. Similar effect of study drugs had been observed by Sharma N et al²¹ and Bhandari et al²³ .

In present study, at 1 min after intubation the mean DBP in group A was increased by 11.45% from baseline but in group B, it increased only 1.4%. The result was found statistically significant (p<0.05).Our results are supported by Sharma N et al²¹ in their study they found (3.4% rise in fentanyl group and 8.5% in nalbuphine group). Study by FA Khan²² also showed 13% increased in nalbuphine group versus 3% in fentanyl group.

In our study after endotracheal intubation, mean MAP in group A was increased by (6.61%) and in group B it was decreased by 0.76 %). This was statistically significant (p<0.05). Thereafter, mean MAP came below base line in both the groups till 15 min Our results are similar to the results observed by Khan et al²² , they found that mean MAP increased by 1% in fentanyl group and 12% in nalbuphine group. B Kay et al²⁴ found a rise in mean MAP in nalbuphine group and in fentanyl group they observed a fall in mean MAP .Thus our study demonstrated that control of MAP after laryngoscopy and intubation was better in Fentanyl group than in Nalbuphine group.

In our study patients of group A had more nausea and vomiting as compared to group B. One patient in the nalbuphine group and three in the fentanyl group showed respiratory depression. Only one patient in nalbuphine group had bradycardia and hypotension. . No significant difference was observed between the groups.

In contrast to our study, Bhandari S et al²² found postoperative nausea, vomiting in 2 (5%) patients in Fentanyl group and 1 patient (2.5%) in Nalbuphine group. In the Fentanyl group, 9 (22.5%) patient had bradycardia while only one patient (2.5%) in Nalbuphine group had bradycardia.

Post- extubation sedation score was recorded in all patients. In analysis, the value was statistically insignificant (p>0.05).

Conclusion

It is concluded from our study that fentanyl controls the haemodynamic response to laryngoscopy and endotracheal intubation much better as compared to nalbuphine.

References

- Reid LC and Brace DE: Irritation of the respiratory tract and its reflex effect upon the heart. Surg Gynaec&obst 1940;70: 157-62.
- Edwards ND, Alford AM, Dobson PM, Peacock JE, Reilly CS. Myocardial ischaemia during tracheal intubation and extubation. Br J Anaesth 1994;73:537-9.
- Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anesthesiology 1977;47:524-5
- Karl et al-Insertion of LMA in place of endotracheal intubation to attenuate the cardiovascular response. IJA,1999;43:30-35.
- Stoelting RK and Peterson C: Circulatory changes during direct laryngoscopy and tracheal intubation: influence of duration of laryngoscopy with or without prior lidocaine. Anaesthesiology 1977; 47: 381.
- Dahlgren N and Messeter K: Treatment of stress response to laryngoscopy and intubation with Fentanyl. Anaesthesia 1981 Nov;36(11):1022-6.
- Curran J, Crowley M and Sullivan GO: Droperidol and endotracheal intubation: Attenuation of pressure response to laryngoscopy and intubation. Anaesthesia, 1980; 35: 290-294.
- McCammon RL, Hilgenberg JC and Stoelting RK: Effect of propranolol on circulatory responses to induction of diazepam- Nitrous oxide anesthesia and to endotracheal intubation. Anesth Analg. 1981 Aug;60(8):579-83.
- Elkayam, Uri and Wilbert S Aronow: Glyceryl trinitrate (Nitroglycerine) ointment and isosorbide dinitrate: review of their pharmacological properties and therapeutic use. Drugs 1982; 23: 165.
- Cardiovascular effects of Esmolol in anaesthetized humans. Anaesth Analg. 1985;64:327.
- Ebert DO, John P, Pearson JD, Gelman S, Harris C and Bradley EL: Circulatory responses to laryngoscopy: The comparative effects of placebo, Fentanyl and esmolol. Can. J. Anaesth. 1989; 36: 301-6.
- Puri GD, Marudhachalam KS, Chari Pramila and Suri RK: The effect of Magnesium sulphate on haemodynamics and its efficacy in attenuating the response to endotracheal intubation in patients with coronary artery disease. Anesth Analg 1998;87:808-11.
- Gopinath R, Thota S. Nifedipine to attenuate cardiovascular responses to endotracheal intubation. J Anaesth Clin Pharmacology. 1989;5:99.
- Zalunardo MP, Zollinger A, Spahn DR, Seifert B, Radjaipour M, Gautschi K, Pasch T. Effect of intravenous and oral clonidine on hemodynamic and plasma catecholamine response due to endotracheal intubation. J Clin Anesth 1997; 9: 143-7.,
- Bafna U, Goyal VK, Garg A. A comparison of different doses of gabapentin to attenuate the haemodynamic response to laryngoscopy and tracheal intubation in normotensive patients. J Anaesthesiol Clin Pharmacol 2011;27:43-6.
- Yavasoaoglu B, Kaya FN, Baykara M, et al. A comparison of esmolol and dexmedetomidine for attenuation of intraocular pressure and haemodynamic responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol. 2008;25:517--9..
- Gurulingappa, Md Asif Aleem, M.N. Awati, Adarsh S. Attenuation of Cardiovascular Responses to Direct Laryngoscopy and Intubation. Journal of Clinical and Diagnostic Research. 2012 December, Vol-6(10): 1749-1752
- Yushi U, Maiko S, Hideyuki H. Fentanyl attenuates the haemodynamic response to endotracheal intubation more than the response to laryngoscopy. Anesth Analg. 2002;95:233-7.
- Chung KS, A comparison of fentanyl K Mikawa, K Nishina et al. Comparison of Nicardipine, Diltiazem and Verapamil for controlling cardiovascular responses to tracheal intubation. Br J Anaesth 1996;76(2): 221-226.

20. Chawda PM, Pareek MK, Mehta KD. Effect of nalbuphine on haemodynamic response to orotracheal intubation. *J Anaesthesiol Clin Pharmacol* 2010; 26(4):458-460.
21. Sharma N, Parikh H; A comparative study of hemodynamic responses to intubation: fentanyl versus nalbuphine. *GUJARAT MEDICAL JOURNAL / AUGUST-2014 Vol. 69 No. 2*
22. Rajlaxmi B., Shivani R., Amit T., Anumeha J, Nimisha M, Anshul S, Shomik. "Attenuation of Haemodynamic Response to Endotracheal Intubation with Nalbuphine and Fentanyl: A Comparative Study". *Journal of Evolution of Medical and Dental Sciences* 2015; Vol. 4, Issue 64, August 10; Page: 11172-11181, DOI: 10.14260/jemds/2015/1609.
23. Khan FA, Hameedullah. Comparison of fentanyl and nalbuphine in TIVA. *JPMA* 2002; 52:459.
24. Kay B, Healy TE., Blocking the circulatory responses to tracheal intubation. A comparison of fentanyl and nalbuphine. *Anaesthesia* 1985;40:960-3.