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Original Research Paper

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COMPARISON OF PROPOFOL-NALBUPHINE AND PROPOFOL –FENTANYL COMBINATIONS IN TOTAL INTRAVENOUS ANAESTHESIA

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ABSTRACT

Introduction: Use of Total Intravenous Anaesthesia (TIVA) has increased in recent past. It has become method of choice in Day Care Surgery practice. G.A. with inhalational agents requires specific vaporizers for different inhalational agents. These vaporisers require costly periodic maintenance and calibration.

Material And Methods: Total 100 patients between age of 30 and 65 years belonging to ASA grade I and II under- going surgery up to 90 min duration were included. The patients were divided into two groups each of 50 patients. Patients in group A received Nalbuphine 0.2mg/Kg body weight IV and patients in group B received Inj. Fentanyl 2 g/Kg body weight IV, 5 min before induction.

Patients were induced with Propofol 2mg/ kg body weight and Inj. Vecuronium 0.1mg/kg body weight. All patients were intubated. Maintenance of Anaesthesia was done with Propofol infusion. Patients were ventilated with controlled ventilation, breathing circuit attached to circle absorber. Vital parameters were monitored. Residual neuro-muscular paralysis was reversed with Inj. Neostigmine and Inj. Glycopyrolate intravenously.

Results: Initially reduction was observed in pulse rate and blood pressure in both groups followed by elevation. Rise from basic level was similar in both groups. Subsequent rise was more in Fentanyl group throughout the procedure while it came down to near base level in Nalbuphine group. At the end of procedure elevation of SBP and DBP was seen more in Fentanyl group. The First rescue analgesic requirement was earlier in Fentanyl group. Nausea, Shivering, Respiratory Depression and Sedation were more in Fentanyl group in postoperative period.

Conclusion: Nalbuphine provided comparatively better hemodynamic stability and excellent post operative analgesia. Nausea, vomiting and sedation were less with Nalbuphine. The induction was found to be smooth in both groups. Recovery from anaesthesia was early in Nalbuphine group.

KEYWORDS : Propofol, Nalbuphine, Fentanyl, Total Intravenous Anaesthesia

INTRODUCTION

Use of TIVA has increased in recent past due to smooth induction, stable operating conditions, easiness in control of anaesthesia, smooth recovery, comparatively lower cost than G.A with inhalational agents and no pollution of O.T. area. Availability of better newer drugs with minimum cardiac depressant effects, lesser Nausea and Vomiting in post operative period (PONV), easiness to control anaesthesia and smooth recovery has made TIVA method of choice for induction and maintenance of anaesthesia.

Before advent of TIVA, all surgical procedures were being performed under GA with inhalational anaesthetic agents. Specific vaporizers are required for different inhalational agents; they require periodic costly calibration and maintenance. Release of exhaled anaesthetic gases produce pollution of O.T. environment.

Purpose of this study was to compare hemodynamic response and analgesic effect of two drug combinations using (1) Propofol--Nalbuphine and (2) Propofol- Fentanyl in induction for TIVA. Maintenance, recovery characteristics and side effects were also studied.

MATERIAL AND METHODS

Total 100 adult patients between age of 30 and 65 years belonging to ASA I and II of either sex under-going surgical procedures lasting up to 90 min duration were included in the study. The patients were divided into two groups of 50 patients each. Patients taken for procedure at odd serial no. 1, 3, 5..... of 100 patients, received Nalbuphine 0.2mg/Kg body weight I/V (Group A) and patients taken for surgery at even serial no. 2,4,6..... of 100 patients received Inj. Fentanyl 2μg/Kg body weight I/V (Group B), 5 min before induction.

Patients with previous history of hypersensitivity to any of study drugs, allergy to egg or fat, on long term Phenothiazines and MAO Inhibitors treatment, anticipated difficult intubation, patients with significant systemic diseases like cardiovascular, renal, hepatic diseases, thyroid disease , neurological disorders, H/O Bronchial asthma and other respiratory diseases, H/O seizure disorders, H/O opium addiction, Alcohol abuse, recent H/O head injury, pregnant women and patients who did not give consent were excluded One capsule of Omeprazole 20 mgs and one tablet of Alprazolam 0.25 mg were given at 10.00 PM in previous night of procedure.

All patients were pre-loaded with Lactated Ringer's solution (15 ml/kg Body weight). ECG, pulse oximetery probe and NIBP cuff were attached when patient came in O.T. Vital parameters like heart rate, SpO2 and NIBP were recorded as base line.

Patient were induced with Propofol 2 mg/ kg body weight and Inj. Vecuronium 0.1 mg/kg followed by bag mask ventilation with O2 and N2O for 3 minutes. All patients were intubated with appropriate size endo-tracheal tube.

Vital parameters were recorded at time of induction, 1,3,5 min and at 5 min intervals for initial 20 min of induction and then at every 10 min intervals till completion of surgery.

Maintenance of Anaesthesia was done with I/V infusion of Propofol at rate of 10 mg/kg body weight/hour for first 10 min, 08mg/kg body weight/hour for next 10 min and 06 mg/Kg body weight/hour for remaining duration. Inj. Vecuronium 0.015 mg/Kg Body weight was given every 20 to 40 min. All patients

were ventilated with O2 and N2O, controlled ventilation and breathing circuit attached to circle absorber. Supplemental dose of 25 mg of Propofol was planned to be given during surgical procedure if required.

For fluid resuscitation during operation I.V. Ringer Lactated fluid was given. This was calculated as per following criteria: First 10 kg of body weight 4ml /kg, second 10 kg of body weight 2ml/kg, remaining body weight 1 ml/kg body weight. 50% of this was infused in first hour and remaining 50% in second hour. Residual neuro-muscular block was reversed with Inj. Neostigmine 0.05mg/kg body weight and Inj. Glycopyrolate 0.008mg/kg body Wt. intravenously at the end of surgery.

Patients were observed in post operative period for vital parameters, untoward symptoms and signs like respiratory depression, pruritus, nausea, vomiting, sedation and shivering.

RESULT

Both groups were comparable in demographic characteristics in respect of age, weight, male-female gender ratio and duration of surgery. The pulse rate and blood pressure showed slight reduction after receiving drugs. They showed elevation at the time of induction in both groups. This initial rise in heart rate and B.P. from basic rate was almost similar in both groups. Rise was found subsequently throughout the procedure also in both groups and was observed more in Fentanyl group than in Nalbuphine group. Pulse rate increased up to 20% from base level in Fentanyl group and up to 10% in Nalbuphine group. This rise returned to near base level in Nalbuphine group. Elevation of SBP and DBP was observed again at the end of procedure. It was more in Fentanyl than in Nalbuphine group.

The induction was smooth in both groups.

No patient required supplemental dose of Propofol during surgery in both group. The requirement of rescue analgesic was earlier in Fentanyl than in Nalbuphine group (100.36 Minutes Vs 135.60 Minutes after initial dose). Nausea, Shivering and Respiratory Depression (fall in SpO2 below 90% with room air) in post operative recovery was observed more in Fentanyl group. In Fentanyl group 10% patients were found to have sedation, while no patient in Nalbuphine group showed signs of sedation. Recovery from anaesthesia was early and smooth in Nalbuphine group.

Table 1 Demographic Characteristics

	Group A (Nalbuphine)		Group B(Fentanyl)	
Age (Yrs)	Mean	SD	Mean	SD
	45.93	15.68	42.7	17.06
Weight (Kg)	61.27	9.9	63.37	13.36
Duration of procedure (min)	85	12.52	82	13.68
Gender M/F (%)	20/80		16/84	

Table 2 Percentage Change Of Pulse Rate At Different Stages Of Anaesthesia

	Group A (Nalbuphine)	Group B (Fentanyl)
Before Induction	5	5
During Induction	10	20
1 min After intubation	8	20
3 min after induction	5	10
5 min after induction	5	10
10 min after induction	5	08
15 min after induction	7	12
20 min after induction	5	15
30 min after induction	08	15
40 min after induction	08	16
50 min after induction	6	15
60 min after induction	7	15
70 min after induction	7	14
80 min after induction	8	15
90 min after induction	8	16

Table 3 Changes In Mean Systolic Blood Pressure (SBP)

Time	Group A (Nalbuphine)		Group B (Fentanyl)	
	Mean (mm of Hg)	% change from base line	Mean (mm of Hg)	% change from base line
Base line	118.10		123.53	
3 Min after drug	110.05	6.81	115.50	6.50
During Laryngoscopy & Intubation	125.84	6.56	128.58	4.08
1 Min after intubation	123.43	4.5	129.45	4.8
3 Min after intubation	122.83	4.01	127.52	4.04
5 Min after intubation	123.10	4.24	129.02	4.45
10 Min after intubation	122.35	3.6	129.89	5.15
15 Min after intubation	123.41	4.5	130.32	5.5
20 Min after intubation	119.96	1.58	131.12	6.15
30 Min after intubation	119.81	1.45	131.63	6.56
40 Min after intubation	121.12	2.56	136.45	10.46
50 Min after intubation	120.46	2.83	136.38	10.28
60 Min after intubation	119.60	1.8	132.36	7.06
70 Min after intubation	121.50	4.08	134.12	8.47
80 Min after intubation	122.48	5.01	132.6	7.25
90 Min after intubation	122.60	5.4	134.76	8.98

Table 4 Changes In Mean Diastolic Blood Pressure (DBP)

Time	Group A (Nalbuphine)		Group B (Fentanyl)	
	Mean (mm of Hg)	% change from base line	Mean (mm of Hg)	% change from base line
Base line	78.0		**76.0**	
3 Min after intubation	72.7	6.80	80.94	6.50
During Laryngoscopy & intubation	82.96	6.36	79.86	5.08
1 Min after intubation	81.43	4.4	79.95	5.2
3 Min after intubation	81.23	4.15	79.60	4.74
5 Min after intubation	81.32	4.14	79.34	4.40
10 Min after intubation	80.96	3.8	79.87	5.10
15 Min after intubation	81.70	4.75	80.21	5.55
20 Min after intubation	79.03	1.38	80.59	6.05
30 Min after intubation	79.20	1.55	80.22	5.56
40 Min after intubation	79.95	2.50	80.90	6.46
50 Min after intubation	80.60	3.33	81.56	7.28
60 Min after intubation	80.55	3.26	80.78	6.26
70 Min after intubation	80.90	3.71	80.88	6.39
80 Min after intubation	79.90	2.43	80.46	5.84
90 Min after intubation	80.94	3.76	81.24	6.86

Table 5

First Analgesic dose requirement time after initial dose (VAS based)		
Group A	(Nalbuphine)	135.60 Minutes
Group B	(Fentanyl)	100.36 Minutes

Table 6 Supplemental Dose Requirement And Untoward Symptoms..

	Group A (Nalbuphine)	Group B (Fentanyl)
Supplemental dose of Propofol during operation.	0	0
Pruritis	0%	10%
Nausea in post operative recovery room.	6%	30%

Respiratory Depression (fall in SpO2 below 90% without O2 in post operative period.)	0%	5%
Shivering	10%	18%
Sedation	0 %	10%

Table 7 Recovery From Anaesthesia

Parameter	Group B (Nalbuphine)		Group B (Fentanyl)	
	Mean	SD	Mean	SD
Time of opening of eyes on verbal command from end of TIVA (Min)	8.39	3.0	11.46	3.8
Time duration of orientation from end of TIVA (Min)	19.39	5.7	23.77	7.8

DISCUSSION

Rise in heart rate and blood pressure are routinely observed during laryngoscopy and intubation due to steep rise in serum catecholamine levels [1, 2]. Various pharmacological agents have been used as adjuvants for blunting these effects [3, 4]. Ultra short acting beta-blocker (Esmolol) and opioids have been tried for blunting cardiovascular changes induced by tracheal intubation [5].

Most serious side effect associated with use of opioids is respiratory depression. Nalbuphine is chemically related to Naloxone. It has ceiling effect of respiratory depression. It is also said to cause less nausea and vomiting compared to Morphine, Pethidine and Pentazocine.[6]. It is cost effective with established safety features. Its comparable analgesic potential to Morphine was demonstrated in the study done by Joseph Yanulevich [7] in 1983.

Nalbuphine also has potential to reverse morphine induced respiratory depression. Hence Nalbuphine is considered to have higher safety profile in comparison to opioids. Analgesic potency of Nalbuphine is equivalent to that of Morphine on milligram basis up to dosage of approximately 30 mg. Mark W. Guniona [8] rationales use of mixed agonist—antagonist Nalbuphine in opioid based analgesia in his study.

Zeng Z. et al [9] concluded that Nalbuphne provides better safety than Morphine in their meta-analysis of randomized controlled trials for comparison of analgesic effect and safety of Nalbuphine with Morphine. The side effects like pruritus and respiratory depression are less.

It has been observed by Khan F. A et al that Nalbuphine provides cardiovascular stability and causes less nausea vomiting in TIVA technique. [10, 11]

Fentanyl was introduced in 1960's when Morphine and Pethidine were being used for analgesia during surgeries. Fentanyl's shorter duration of action, lesser respiratory depression and cardiac stability made it standard analgesic replacing Morphine and Pethidine in post operative period [12]. Muhammed Ahsan[13] compared Nalbuphine with placebo and observed that placebo group showed enhanced haemodynamic response in comparison to Nalbuphine group. Khan [14] compared Nalbuphine with Fentanyl and documented 25% rise in heart rate after intubation in the Nalbuphine group in comparison to Fentanyl group. There was no rise in MAP after endotracheal intubation in his study He noticed comparable incidence of nausea and vomiting with both drugs. Duration of analgesia was shorter in Fentanyl than Nalbuphine group (37 minutes vs. 62 minutes). The time required for first analgesic dose was shorter in Fentanyl group than in Nalbuphine group in our study also. Rise in heart rate and incidence of nausea were more in Fentanyl group in immediate post operative period in our study.

Weiss et al (15) studied Fentanyl and Nalbuphine in Coronary Artery Bypass Surgery, all patients were given Nalbuphine during and after intubation. Only one patient received Fentanyl and this patient required Nitroglycerine to control MAP. N Sharma [16] had compared haemodynamic response of Nalbuphine with Fentanyl and showed no significant increase in SBP, DBP and HR.

Mikita J. Chaudhari [17] compared efficacy of Nalbuphine and Clonidine in preventing hemodynamic response to laryngoscopy and intubation. The results obtained were similar.

Few cases in Fentanyl group showed sedation, pruritus and shivering in our study.

CONCLUSION

We conclude that Nalbuphine gives better haemodynamic stability; it provides excellent post operative analgesia therefore reduces requirement of analgesic in post operative period in comparison to Fentanyl. It produces less respiratory depression, less nausea, less shivering in post operative recovery period. Nalbuphine is potent analgesic for use in peri-operative period. These features make Nalbuphine ideal analgesic in TIVA.

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