ORIGINAL ARTICLE

Comparison of Haemodynamic Stability at Co-Induction of Propofol-Pethidine and Propofol-Nalbuphin

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ABSTRACT

Aim: To compare frequency of haemodynamic stability of Nalbuphine-Propofol and Pethidine-Propofol combination at induction of general anesthesia to patients undergoing elective surgeries.
Methodology: It was a randomized controlled trial study. Age 20–50 years from both genders. ASA I & II: Patients falling in ASA category I & II. Patients for elective abdominal surgeries under general anaesthesia. Out of 200 patients, 100 patients were enrolled in each group of combination i.e. Propofol-Pethidine and Propofol-Nalbuphine.
Place and duration of study: This study was conducted in the Department of Anaesthesiology and Intensive Care Unit at Shaikh Zayed Hospital, Lahore from 01-12-2011 to 31-05-2012
Results: Age, weight, gender and ASA status were found to be insignificant. The trend of heart rate increased in Pethidine group and decreased in Nalbuphine group within three minutes with significant p <0.001. Systolic blood pressure decreased in both groups within the study time with significant p <0.001. 82% of patients from Pethidine group while 74% in Nalbuphine group had heart rate within 20% of the baseline (p <0.001) at 1 minute. At 2 minutes 67% and 49% patients in Pethidine and Nalbuphine group respectively, fell within 20% of the baseline (p <0.001). Similarly at 3 minutes 72% and 43% of patients in both groups respectively had stable heart rate (p <0.001). While monitoring systolic blood pressure, 74% in Pethidine group and 34% in Nalbuphine group fell within 20% of the baseline at 1 minute. At 2 minutes it reduced to 27% and 12% respectively in both groups (p 0.012).
Conclusion: It is concluded that either combination Pethidine-Propofol or Nalbuphine-Propofol can be used as induction agent but Pethidine-Propofol is a better choice and provides better haemodynamic stability and better analgesia, recovery profile and postoperative pain relief.
Keywords: Hemodynamic stability, Nalbuphine-Propofol, Pethidine-Propofol, Heart rate and Systolic BP.

INTRODUCTION

The development of intravenous anesthetics has been an important component of anesthetic management for over seventy years. The first sedative barbiturate was synthesized in 1903 by Emil Fischer (1852-1919) of Berlin[1]. Propofol is the most frequently used intravenous anesthetic today. It has achieved widespread use since its introduction, because of its rapid induction, rapid recovery profile inspite of side effects such as hypotension and bradycardia and others[2,3]. When combined with the analgesic agents like opioids, Propofol provides all the components of satisfactory induction agent of general anaesthesia.[4]Induction with propofol has also some untoward effects. These include pain on injection, myoclonus, apnea and rarely thrombophlebitis. However decrease in the systemic blood pressure associated with induction of anaesthesia with propofol is its most significant side effect[5].

Side effects of Propofol like bradycardia or hypotension can be overcome by the co-induction of Propofol with the sympathetic drugs such as Ketamine, Epinephrine or Ephedrine combinations or more precisely Phenylephrine which is a synthetic non catecholeamine stimulates only alpha 1 adrenoreceptors[5,6]. Sympathetic response to laryngoscopy and intubation can be obtunded with Propofol in combination with opioids. Although studies have shown that both Pethidine and Nalbuphine reduce the ionotropic response to airway instrumentation at the time of induction[7] but Pethidine being having anticholinergic activity, causes tachycardia, which overcome the bradycardia caused by Propofol induction, when combined with Propofol and maintains haemodynamic variables within 20% of the base line.[8] On the other hand, Nalbuphine has the ability to suppress the sympathetic responses during laryngoscopy in combination with Propofol attenuating unwanted cardiovascular overactivity[9,10].

Nalbuphine is a semi-synthetic opioid agonist-antagonist analgesic of the phenanthrene series. It is chemically related to the widely used opioid antagonists, naloxone and naltrexone and the potent opioid analgesic, oxymorphone. It is a potent analgesic. Its analgesic potency is essentially equivalent to that of morphine on a milligram basis. Its onset of action occurs within 2 to 3 minutes after intravenous administration and in less than 15 minutes following subcutaneous or intramuscular injection. The plasma half-life of nalbuphine is 5 hours and in clinical studies the duration of analgesic activity has been reported to range from 3 to 6 hours[11].

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MATERIALS AND METHODS

After the approval from Hospital Ethical Committee, the patients were selected on preoperative counseling visits. Informed consent was taken from all the patients. All the patients i.e. (200 {100 in each group}) were evaluated according to ASA grading and inclusion and exclusion criteria were fulfilled. Patients were divided into two groups randomly and labeled Group N for Nalbuphine and Propofol combination and Group P for Pethidine and Propofol combination. Patient's profile including age, gender and hospital registration number were recorded on the structured proforma. After the patient entered the operation theatre baseline reading of heart rate and systolic blood pressure were taken. Then patients were preoxygenated for 3 minutes. Group N received Nalbuphine 0.2mg/kg of body weight and Propofol 2.5 mg/kg of body weight and Group P received Pethidine 1 mg/kg of body weight and Propofol 2.5mg/kg of body weight. Immediately after that atracurium 0.4 mg/kg of body weight was administered. For 3 minutes after induction, patient were ventilated manually with the help of face mask. Then tracheal intubation was performed. Anaesthesia was maintained at Isoflurane 1% with Nitrous Oxide 50% in Oxygen. The heart rate was recorded at baseline and at 1 minute intervals for 3 minutes after the induction of anesthesia. Haemodynamically stability was labeled to patients whose heart rate and systolic blood pressure fall within 20% of the baseline reading at each reading taken. Patients were hydrated throughout the procedure. Any anxiety was relieved by good counseling before the induction of anaesthesia. All patients were divided into two equal groups of 100 patients each. One group (group P) was given anesthesia with Propofol-Pethidine and the other (group N) with Propofol-Nalbuphine combinations. The two groups were matched for age, weight, gender and ASA status.

RESULTS

The average age for group A was 35±9 years and for group B was 34±8 years (Table 1).The male number of patients was 37 and 38 in each group respectively which was considered same with p 0.884 (Table 2). Similarly there were 78 patients in each groups with ASA status I and 22 patients with ASA status II in each group (Table 3). The average heart rate recorded at base line was 88±13 beats/minute in group P, while 92±12 in group N (Table 4). The average systolic blood pressure recorded at base line was 137±13mmHg in group P which reached to 100±11 at 3 minutes and in group N was 138±15 which reached 93±10mmHg (Table 5).

The difference of heart rate and blood pressure were at a percentage below or above 20% of base line all heart rates and blood pressures at baseline were set at 100 and then the values at 1, 2 and 3 minutes were calculated as percent of baseline for all 200 cases. The average heart rate when set at 100 at baseline reached to 110.88±16.03 at 1 minute, 112.73±16.48 at 2 minutes and 110.73±16.31 at 3 minute in group P. Heart rate recorded in group N was 85.71±10.46 at 1 minute, 81.97±13.16 at 2 minutes and 78.59±14.99 at 3 minutes. The difference between two groups at 1, 2 and 3 minutes were highly significant with p<0.001 (Table 6-7).The average systolic blood pressure set at 100 at baseline reached to83.19±6.42 at 1 minute, 76.51±7.43 at 2 minutes and 72.97±8.17 at 3 minute in group P. Similarly systolic blood pressure recorded in group N was 77.38±6.58, 71.17±7.81and 67.75±8.04 at 1, 2 and 3 minutes respectively. The difference between two groups at 1, 2 and 3 minutes were statistically significant with p<0.001 (Table 8). There were 4 patients for whom heart rate dropped more than 20% from base line and 14 for whom it raised more than 20% in group P. In group N there were 25 patients whom heart rate declined below 20% of the baseline value and 1 case for whom it raised above 20%. At 2 minute the stable cases were 67% and 49% in group P and N respectively. In group P 30% of patients were unstable on the higher side while 3% of the unstable patients had heart rate below the 20% of the baseline value with a highly significant difference (p< 0.001).

Table 1: Age distribution of patients (n=200)

Age (years)	Group P (n=100)		Group N (n=100)	
	No.	%	No.	%
20 – 29	35	35.0	28	28.0
30 – 39	30	30.0	39	39.0
40 – 50	35	35.0	33	33.0
Total	100	100.0	100	100.0
Mean±SD	34.54±8.57		34.17±8.08	

Table 2: Gender distribution of patients

Age (years)	Male		Female	
	No.	%	No.	%
20 – 29	33	44.0	30	24.0
30 – 39	22	29.0	47	38.0
40 – 50	20	27.0	48	38.0
Total	**75**	**100.0**	**125**	**100.0**
Mean±SD	32.43±8.54		35.51±7.98	

Male to female ratio: 0.60:1

Table 3: Distribution of patients according to ASAI and ASAII

Age (years)	ASA I (n=156)		ASA II (n=44)	
	No.	%	No.	%
20 – 29	62	40.0	1	2.0
30 – 39	60	38.0	9	20.0
40 – 50	34	22.0	34	77.0
Total	**156**	**100.0**	**44**	**100.0**
Mean±SD	**32.22±7.7**		**41.93±5.61**	

When cutoff of 20% used at 1 minute to see if the patient was considered stable or not, it was observed that as per change in systolic blood pressure, there were 74% cases stable in group P and 34% in group N. There were 26% patients for whom systolic blood pressure dropped more than 20% from base line in group P and 66% in group N. The difference between the groups was highly significant with p<0.001. At 2 minute the stable cases reduced to 27% and 12% in group P and N respectively. 78% and 88% patients in group P and N respectively dropped systolic blood pressure below 20% of the baseline value with a highly significant difference (p0.012). Similarly at 3 minutes stable cases were17% and 6% in two groups respectively. Out of unstable patients 83% and 94% in group P and N respectively reduced their pressures below 20% of the baseline value (p 0.027). Haemodynamic stability at 1 minute was noted to be 66% and 25% in group P and N respectively. It was reduced drastically to 17% and 5% at 2 minutes.

Table 4: Comparison of heart rate between two groups of patients

Heart rate	Base line	1 minute	2 minutes	3 minutes
Pethidine-Propofol	87.74±12.65	96.12±12.03	97.79± 13.05	96.16± 13.79
Nalbuphine-Propofol	92.43±11.68	78.79±10.92	75.43± 13.47	72.32± 15.07
t. value	2.725	10.67	11.93	11.67
p. value	0.007	0.000	0.000	0.000

Table 5: Comparison of systolic blood pressures between two groups of patients

Systolic Blood pressure	Base line	1minute	2 minute	3 minute
Pethidine-Propofol	137.33±13.34	113.87±10.81	104.66±10.87	99.74±11.11
Nalbuphine-Propofol	138.15±14.88	106.36±10.09	97.61±9.63	92.93±10.27
t. value	-0.410	5.08	4.85	4.51
p. value	0.682	0.000***	0.000***	0.000***

Table 6: Comparison of haemodynamic stability in both groups of patients

	Stability		Total	P value
	Unstable	Stable		
Pethidine-Propofol	90	10	100	0.005
Nalbuphine-Propofol	99	1	100	
Total	**189**	**11**	**200**	

Table 7: Comparison of heart rate in both groups from base line to 3 minutes of patients

Heart Rate	Base line	1 minute	2 minutes	3 minutes
P	87.74±12.65	96.12±12.03***	97.79±13.05***	96.16±13.79***
N	92.43±11.68	78.79±10.92***	75.43±13.47***	72.32±15.07***
Total	90.09±12.37	87.46±14.38*	86.61±17.34**	84.24±18.72***

Table 8: Comparison of systolic blood pressure in both groups from base line to 3 minutes of patients

Systolic blood pressure	Base line	1 minute	2 minutes	3 minutes
P	137.33±13.34	113.87±10.81***	104.66±10.87***	99.74±11.11***
N	138.15±14.88	106.36±10.09***	97.61±9.63****	92.93±10.27***
Total	137.74±14.10	110.12±11.09***	101.14±10.83***	96.34±11.20***

DISCUSSION

The induction of general anesthesia with propofol has been associated with decrease in blood pressure[12,13]. Decreased blood pressure is due to inhibition of myocardial contractility, a decrease in peripheral resistance and sympathetic inhibition.[14]Propofol also causes a lowering of the heart rate secondary to the vagotonic effects.[12] Some studies have also reported severe bradycardia, complete atrioventricular block and cardiac arrest.[15]By Safavi and his colleague, pethidine was compared with sufentanil to attenuate cardiovascular responses to laryngoscopy. It was concluded that in pethidine group there was a significant elevation in heart rate at two and three minutes after induction and before intubation but systolic blood pressure remained unchanged[8].

Khan and his team compared hemodynamic responses of fentanil and nalbuphine and found that nalbuphine group exhibited a decrease of less than 15% of systolic blood pressure after induction. Heart rate showed a slight elevation compared to baseline.[16] Siddiqui and his team compared nalbuphine with tramadol at the induction and declared that in nalbuphine group heart rate raised above 20% of the baseline while systolic blood pressure remained within 20% of the baseline value.[17]

Haemodynamic stability after induction of general anesthesia was observed in this study, when two combinations of drugs i.e. propofol-pethidine and propofol-nalbuphine were used. Pethidine having structural resemblance to atropine manifests anticholinergic effects such as increased heart rate, which is well observed in my study in pethidine group. The probable reason of decreased heart rate in nalbuphine group could be the suppression of the sympathetic response of propofol and nalbuphine. The anticholinergic activity of the pethidine overcomes the negative ionotropic effects of propofol, this could be the reason why heart rate of most of the patients in pethidine group remained within 20% of the baseline. Stability of systolic blood pressure showed a significant variation in both groups, more with nalbuphine. The fall in systemic pressure following induction appears to be due to both vasodilatation and myocardial depression. Haemodynamic stability was noted in patients whose heart rate and systolic blood pressure both remained within 20% of the baseline value. It was found that in both groups it reduced drastically with each minute but in nalbuphine group this reduction was seen in extreme[18].

In both groups stable population significantly decreased from baseline with each minute. Even though arterial pressure was significantly decreased from baseline, this decrease was transient as after three minutes, intubation and laryngoscopy elevated systolic blood pressure as well as heart rate above baseline in both groups. It is therefore concluded that at induction of anesthesia, whatever combination may be used with propofol, there will be a large population of patients experiencing hypotension. But patients receiving pethidine showed comparative hemodynamic stability in all three minutes because of the vagolytic effect.

CONCLUSION

Pethidine due to its anticholinergic activity maintained the heart rate at all three minutes. Hypotension was also to less extent and in lesser population of patients as compared to nalbuphine. It is hence concluded that both combinations, propofol-pethidine and propofol-nalbuphine preserved hemodynamic stability but administration of propofol in combination with pethidine was comparatively better to maintain hemodynamic stability at induction.

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