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Original Research Article

COMPARATIVE STUDY OF EFFECTS OF PROPOFOL WITH KETAMINE AND PROPOFOL WITH BUTORPHANOL FOR TOTAL INTRAVENOUS ANAESTHESIA IN SHORT SURGICAL PROCEDURES

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Abstract

Background: Total Intravenous Anaesthesia (TIVA) is a technique in which induction and maintenance of anaesthesia is achieved with Intravenous(IV) drug alone avoiding volatile agents. In this process the patient either breaths spontaneously or bag mask ventilation combined with oxygen. Aims and Objectives are to compare the effects of Propofol-Ketamine and Propofol-Butorphanol for TIVA in short surgical procedures in terms of their Hemodynamic stability, Postoperative sedation, Pain on injection with Propofol and Postoperative nausea and vomiting(PONV). **Materials and Methods:** The study was conducted in the Anaesthesiology department, at the tertiary care hospital for a period of 12 months. 60 patients aged between 18 years to 60 years of ASA Class 1 and 2, scheduled for elective surgery of duration of less than one hour were included in the study. Group K-Received Ketamine 1mg/kg+ Propofol 1.5mg/kg, Group B-Received Butorphanol 20microgram/kg + Propofol 1.5mg/kg.In both groups anaesthesia was maintained with Propofol 9mg/kg/hr via infusion pump. Haemodynamic parameters Heart Rate(HR), Systolic Blood Pressure(SBP), Diastolic Blood Pressure(DBP) were monitored as baseline, induction and in post induction period after 10,20,30,40 minutes. Pain on injection of Propofol, Postoperative nausea and vomiting also recorded. **Result:** The SBP and DBP fell in both groups of patients after induction. SBP and DBP differed significantly during various intervals in patients who belonged to group B. such a significant difference was not found in group K. pain on injection with Propofol was not attenuated by Butorophanol pretreatment rather than Ketamine. Postoperative sedation was more in group B(Propofol-Butorphanol) than in group K(Propofol-Ketamine). Both the groups were found to be comparable in terms of postoperative nausea and vomiting. **Conclusion:** Propofol-Ketamine (Group K) combination has been found to be more effective than the other group of patients who belonged to Group B in terms of stability of the haemodynamic parameters as well as sedation was lesser after surgery.

INTRODUCTION

Total intravenous anaesthesia (TIVA) is a technique in which induction and maintenance of anaesthesia is achieved with intravenous drugs alone; avoiding both volatile agents and nitrous oxide. In this process the patients breathe spontaneously or are artificially ventilated with oxygen.[1] Propofol is a newer inravenous anaesthetic agent, having favourable pharmacokinetic profile. It has high clearance rate and rapid decline in blood concentration, making it eminently suitable for infusion. Ketamine, water soluble intravenous anaesthetic, belongs to phencyclidine group with hypnotic, analgesic, amnesic properties and also costeffective.[2] The most common adjuvant is an opioid analgesic for complete anaesthesia. Propofol produces a reduction in both cardiac index and mean arterial pressure, in contrast

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ketamine increase the same.[3] Butorphanol a synthetic opioid is used along with Propofol to provide analgesia. but is associated with adverse effects like cardiodepressant action, dizziness and sedation.[4] Hence we compare two drug regimens, i.e, Propofol-Ketamine and Propofol-Butorphanol for TIVA technique in patients undergoing short surgical procedures.

Aim: To compare the combination of Propofol-Ketamine with Propofol-Butorphanol for total intravenous anaesthesia.

Objectives

1. To compare haemodynamic stability.
2. To study the effect of abolishing pain on injection with Propofol.
3. Postoperative sedation and Postoperative nausea and vomiting between two groups.

MATERIALS AND METHODS

The study was done in government general hospital, ongole over a period of 18 months. The study was undertaken after obtaining ethical committee clearance and informed consent from all patients. Source of data: 60 patients belonging to ASA class I and II. Randomly allocated into two groups. Group K: 30 patients received Propofol-Ketamine combination. Group B: patients received Propofol-Butophanol combination.

Inclusion Criteria

Adult patients of either sex aged between 18-60 years posted for elective short surgical procedures belonging to ASA Class I and II.

Exclusion Criteria

ASA grade III and IV, patient refusal, patients with cardiovascular, respiratory, hepatic, renal disorders, hypersensitive to drugs, bleeding disorders.

Statistcs: The results obtained in the study are analysed using Microsoft Excel and SPSS 20 software. The present study results between the two groups was compared statistically using Chi square test and Student 't' test.

RESULTS

Age distribution in study groups: In this study, patients between age group of 18-60 year of both sexes were included. The age distribution in K group was 39.83+- 10.75 years and in B group was 39.33+-10.67 years. When the two groups were compared, it was found to be statistically insignificant.

Table 1: Age distribution.

Groups	N	MEAN AGE(years)	T value	P value
Group K	30	39.83+-10.75	0.1808	0.8571
Group B	30	39.33+-10.67		

Sex distribution in study groups: In Ketamine group, out of 30 patients, 14(46.7%) were females and 16(53.3%) were male patients. In Butorphanol group, out of 30 patients 15(50%0)were females and 15(50%) were male patients. There was no statistically significant difference between the two groups.

Table 2: Sex distribution

Sex	Group K		Group B		Chi square value	P value
	Number	%	Number	%		
Female	14	46.7	15	50	0.065	0.398
Male	16	53.3	15	50		
Total	30	100	30	100		

Change in heart rate at various intervals: Baseline HR in Ketamine group was 76.03+-4.991 and in Butorphanol group was 74.10+-4.99, both the groups were compared statistically. On arrival in Ketamine group the mean HR was 77.10+-4.860 and in Butorphanol group it was 79.13+-7.71. Both the groups were compared statistically. Mean HR at induction in Ketamine group was 78.11+-4.720 and in Butorphanol group it was 73.00+-8.12, the differences were significant statistically (P<0.05). At 10minutes mean HR in Ketamine group was 77.00+-4.801 and in Butorphanol group it was 71.01+-6.95. Difference in both the groups was statistically significant. The mean HR at 20minutes in Ketamine group was 78.58+-7.956 and in Butorphanol group was 71.02+-4.46; there was a significant difference when compared. At 30minutes, the mean HR in Ketamine group was 78.71+-5.925 and in Butorphanol group, it was 69.56+-3.94. The difference was statistically significant. At 40minutes the mean HR in Ketamine group was 81.30+-8.031 and in Butorphanol group it was 70.20+-5.31 this difference was highly significant. P value <0.05 significant (S), >0.05 nonsignificant(NS).

Table 3: Heart rate comparision

Heart rate	Group K		Group B		T value	P value
	Mean	SD	Mean	SD		
Baseline	76.03	4.991	74.10	4.99	1.496	NS

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Arrival	77.10	4.860	79.13	7.71	1.221	NS
Induction	78.11	4.720	73.00	8.12	2.979	S
10minutes	77.00	4.801	71.01	6.95	3.884	S
20minutes	78.58	7.956	71.02	4.46	4.539	S
30minutes	78.71	5.925	69.56	3.94	7.043	S
40minutes	81.30	8.031	70.20	5.31	6.314	S

Change in systolic blood pressure at various intervals in two groups: The basal SBP in Ketamine group was 131.8 ± 14.188 mm of Hg and in Butorphanol group was 134.67 ± 13.903 mm of Hg. Both the groups were comparable statistically. On arrival, SBP in Ketamine group was 133.0 ± 14.426 mm of Hg and in Butorphanol group was 139.42 ± 11.837 mm of Hg. Both the groups were comparable statistically. SBP at induction in Ketamine group was 134.93 ± 13.580 and in Butorphanol group was 120.82 ± 13.685 mm of Hg. The difference in SBP in two groups was statistically highly significant. SBP at 10 minutes in Ketamine group was 132.36 ± 11.691 mm of Hg and in Butorphanol group it was 116.70 ± 23.468 mm of Hg. The difference in SBP in two groups was statistically highly significant. SBP at 20 minutes in Ketamine group was 134.20 ± 12.510 mm of Hg and in Butorphanol group was 121.90 ± 11.382 of mm of Hg. The difference in SBP in two groups was statistically highly significant. SBP at 30 minutes in Ketamine group was 132.30 ± 11.798 and in Butorphanol group was 120.76 ± 17.917. The difference in SBP in two groups was statistically highly significant. SBP at 40 min in Ketamine group was 133.00 ± 11.140 mm of Hg and in Butorphanol group was 125.60 ± 14.630 mm of Hg. The difference in SBP in two groups was statistically highly significant.

Table 4: SBP comparision

SBP	Group K		Group B		T value	P value
	Mean	SD	Mean	SD		
Baseline	131.80	14.188	134.67	13.903	0.791	NS
Arrival	133.00	14.426	139.42	11.837	1.884	NS
Induction	134.93	13.580	120.82	13.685	4.008	S
10minutes	132.36	11.691	116.70	23.468	3.271	S
20minutes	134.20	12.510	121.90	11.382	3.983	S
30minutes	132.30	11.798	120.76	17.917	2.946	S
40minutes	133.00	11.140	125.60	14.630	2.204	S

Change in diastolic blood pressure at various intervals in two groups: The baseline DBP in Ketamine group was 83.20 ± 7.029 and in Butorphanol group was 80.57 ± 5.984. Both the groups were comparable statistically. DBP on arrival in Ketamine group was 82.74 ± 6.363 mm of Hg and in Butorphanol group was 82.35 ± 6.410 mm of Hg. Both the groups were comparable statistically. On induction DBP in Ketamine group was 81.76 ± 6.597 mm of Hg and in Butorphanol group was 69.83 ± 7.510 mm of Hg. The difference was statistically significant. DBP at 10 minutes in Ketamine group was 79.39 ± 5.912 and in Butorphanol group was 69.03 ± 5.990 mm of Hg. The difference in DBP was statistically highly significant. DBP at 20 min in Ketamine group was 81.13 ± 6.847 and in Butorphanol group was 71.62 ± 5.240 mm of Hg. The difference in two groups was significant statistically. DBP at 30 min in Ketamine group was 79.41 ± 6.406 mm of Hg and in Butorphanol was 74.42 ± 12.1520mm of Hg. The difference was not significant statistically. DBP at 40 min interval in Ketamine group was 78.64 ± 5.332 and in Butorphanol group was 73.07 ± 6.640 and it was statistically significant.

Table 5: DBP comparision

DBP	Group K		Group B		T value	P value
	MEAN	SD	MEAN	SD		
BASELINE	83.20	7.029	80.57	5.984	1.560	NS
ARRIVAL	82.74	6.363	82.35	6.410	0.237	NS
INDUCTION	81.76	6.597	69.83	7.510	6.537	S
10 minutes	79.39	5.912	69.03	5.990	7.260	S
20 minutes	81.13	6.847	71.62	5.240	6.041	S
30 minutes	79.41	6.406	74.42	12.150	1.989	NS
40 minutes	78.64	5.332	73.07	6.640	3.582	S

Comparision of pain on injection with Propofol in two groups: In group K, out of 30 , 17 experienced pain on injection with Propofol (56.7%). In group B, only 7 experienced pain on injection with Propofol (23.3%). There was a statistically significant difference between the two groups.

Table 6: Pain comparision

Pain	Group K		Group B		Chisquare	P Value
	Number	%	Number	%		
Absent	13	43.3	23	76.7	6.944	0.008

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Present	17	56.7	7	23.3		
Total	30	100.0	30	100.0		

Comparision of Postoperative sedation in two groups: In group K, out of 30 patients studied, 11 (36.7%) had postoperative sedation, whereas in Group B 17 (56.7%) had postoperative sedation. Though there was no statistically significant difference on comparison among two groups, it can be clearly inferred that prevalence of sedation was high in group B.

Table 7: Postoperative sedation

	Group K		Group B		Chi square	P value
	Number	%	Number	%		
Absent	19	63.3	13	43.3	1.674	0.098
Present	11	36.7	17	56.7		
Total	30	100	30	100		

Incidence of PONV in two groups: In group K, out of 30 subjects studied, 6 subjects complained of PONV in post-operative period (20%). In group B, 8 subjects complained of PONV (26.7%). The two groups (23.3%) when compared, the incidence of PONV was not significant statistically.

Table 8: PONV

PONV	Group K		Group B		Chi square	P value
	Number	%	Number	%		
Absent	24	80	22	73.3	0.093	0.3807
Present	6	20	8	26.7		
Total	30	100	30	100		

DISCUSSION

We studied two drug regimen; group K- Ketamine+Propofol and group B - Butorphanol+Propofol for TIVA tachnique. In present study, from baseline to postinduction 40minutes, the haemodynamics did not change significantly in both the groups.

In our study with Group K there was no statistically significant change in Heart rate, Systolic blood pressure, Diastolic blood pressure during postinduction and maintenance of anaesthesia throughout the procedure when compared to group B. A similar study was done by Dunihoo and co-workers5 using Propofol-Ketamine on cardiovascular response and wakeup time. They showed that this combination maintained better haemodynamic stability and there was no significant change in heart rate and arterial blood pressure through out the procedure.[6]

In another study Croizer and co-workers,[7] compared the effect of TIVA with Ketamine-Propofol on haemodynamic, endocrine and metabolic stress response with Alfentanyl-Propofol. Anaesthesia was induced with 2mg/kg Ketamine or 0.05mg/kg Alfentanyl, followed by 1mg/kg Propofol. Anaesthesia was maintained with Propofol infusion at an initial rate of 15mg/kg/hr which was reduced to 5mg/kg/hr after 30 minutes. They found that the combination of Propofol-Ketamine was haemodynamically stable through out the surgery in comparision with Propofol-Alfentanyl.

In the present study in Group B basal, post induction and intraoperative haemodynamic variables like heart rate, systolic blood pressure and diastolic blood pressure were monitored. We found that there was statistically decrease in heart rate after induction and during maintenance phase of anaesthesia. A significant decrease in systolic blood pressure and diastolic blood pressure were also observed after induction and during maintenance of anaesthesia with Propofol-Butorphanol.

A study was conducted by Mayer and coworkers where they compared the haemodynamic and analgesic effect of Propofol-Ketamine with Propofol-Fentanyl an opioid similar to Butorphanol. They found that distinct decrease in mean arterial blood pressure and heart rate after induction and maintenance of anaesthesia with Propofol-Fentanyl were seen.[8]

Aasim SA et al. also stated that hemodynamic stability was better in patients in the Propofol – Ketamine group.[9]

Saha and coworkers conducted a randomised double blind study to evaluate the efficiency of combination of Propofol-Ketamine and Propofol-Fentanyl in 60 patients undergoing minor surgery.[10] They showed that significant decrease in heart rate after induction and maintenance of anaesthesia with Propofol and Fentanyl. A significant decrease in systolic blood pressure was also observed.

Propofol a modern intravenous hypnotic produces a reduction in both cardiac index(C.I) and mean arterial pressure (MAP). ketamine a potent analgesic in contrast causes an increase in mean arterial blood pressure and cardiac index. The aim of present study was to investigate whether the combination of Propofol-Ketamine or Propofol-Butorphanol can give better haemodynamic stability during induction and maintenance of anaesthesia. We concluded that, the single dose of Ketamine during induction of anaesthesia was enough to neutralize the cardiodepressant effect of Propofol. During the maintenance of anaesthesia there was better haemodynamic stability in Ketamine group than in Butorphanol group. Butorphanol intensified the fall

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in arterial blood pressure after Propofol induction and patients in this group were more sedated.

A difference in incidence of sedation in two groups was noted. In Ketamine group the incidence was 36.7% where as in Butorphanol group the incidence was 56.7%.

A study conducted by Sheppard,[11] showed the effect of Ketamine and Propofol in terms of respiration, postoperative mood, perception and cognition. They concluded that, the mixture of Propofol and Ketamine provided haemodynamic stability during anaesthesia and produced a positive mood state during recovery period without side effect. The combination also appeared to prompt early recovery of cognitive function.

This may be due to the fact that Propofol inhibits NMDA receptors in hippocampus neurons, which may have contributed to the positive effect on mood. Sedative effects of Propofol are partially antagonized by arousal effect of Ketamine.[11]

A comparision of recovery in patients receiving Fentanyl and Butorphanol was done by Wetchler and coworkers and they concluded that Butophanol has longer recovery period. Similar results were given by Agarwal A et al.[12,13]

Pain on injection with Propofol is attenuated by various methods like injection of Propofol in carrier fluid, large vein and use of antiemetics, analgesics and anaesthetic drugs.

Of the two groups studied, Butorphanol group enabled to abolish the pain on injection with Propofol. Incidence of pain was 23.3% in group B, where as in Ketamine group it was 56.7%.

This is consistent with study done by Agarwal and coworkers, where they found that simple and effective method of attenuating Propofol induced pain is with pretreatment by Butorphanol.

One more disadvantage of TIVA is PONV, which is the rate limiting factor in patient discharged from postoperative ward. In our study, the incidence of PONV in group K was 20.0% where as in group B it was 23.3%. the difference between the two groups was statistically insignificant.

These results are similar to a study by Wetchler and group,[12] where they found that there was no difference in incidence of PONV between Butorphanol and Fentanyl when used as pre-induction agent. Regmi et al, study results were in accordance with the present study findings.[14]

Summary: Maintaining haemodynamic stability, reducing pain on injection with propofol and preventing PONV in TIVA technique is a contentious subject and there is no perfect method to reduce it. We studied 60 patients of either sex aged 18-60 years of ASA-I and ASA-II grade, undergoing short surgical procedures less than 60 minutes. They were randomly allocated into two groups, group K, receiving Propofol-Ketamine and group B, receiving Propofol-Butorphanol. Both the groups were induced with Propofol 1.5mg/kg IV and maintained with Propofol 9mg/kg/hr IV.

Observations made were: in both the groups, upon induction there was fall in both systolic and diastolic blood pressure. There was significant difference in both systolic and diastolic blood pressure upon arrival, induction and at various intervals of surgery in group B. such a significant difference was not found in group K.

Pain on injection with Propofol was attenuated by Butorphanol pretreatment rather than Ketamine.

Post-operative sedation was more in group B (Propofol-Butophanol) than in group K (Propofol-Ketamine) PONV- there was no statistically significant difference between the two groups.

CONCLUSION

We found that Propofol-Ketamine (group K) combination has the advantage of offering better haemodynamic stability and postoperative recovery in terms of sedation. Attenuation of pain on injection was the only added advantage of Propofol-Butorphanol (group B) combination. There was no difference in the incidence of PONV with both drugs.

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