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Comparison of Propofol- Ketamine Combination with Propofol- Butorphanol Combination for Total Intravenous Anesthesia on Short Surgical Procedures

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Abstract
AIM & BACKGROUND: *Total intravenous anaesthesia is the use of intravenous agents for induction and maintenance of anaesthesia. This study compares propofol- ketamine with propofol-butorphanol for short surgical procedures in terms of hemodynamic, respiratory stability, postoperative sedation, nausea/vomiting and pain relief after injecting propofol.*
METHODS: *A randomized double blinded study conducted in 60 patients belonging to ASA I &II, aged between 25- 50 years. Patients were divided into two groups: Group K Propofol- Ketamine combination(n=30) and Group B Propofol- Butorphanol combination(n=30). The baseline values for heart rate, mean arterial pressure and SPO2 recorded and every five minutes after induction for half an hour.****RESULTS:*** *MAP in Butorphanol group at 5, 10, 15, 20, 25, and 30 minutes after induction was significantly lesser but heart rate after induction was significantly greater than the Ketamine group with p value < 0.05. Pain after propofol injection was greater in Ketamine group with a significant p value of 0.006. No statistical significance for sedation and PONV among the groups.*
CONCLUSION *:Propofol- Ketamine combination provided better hemodynamic and respiratory stability; however pain after injecting propofol was lesser with Propofol-Butorphanol combination.*
Keywords: *Total intravenous anaesthesia, propofol- ketamine, propofol- butorphanol, hemodynamic stability, respiratory stability, sedation*

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I. Introduction

Total intravenous anesthesia is a technique of general anesthesia using a combination of intravenous agents only in the absence of inhalational agents.The patient either breaths spontaneously or are artificially ventilated with oxygen[1]. Total intravenous anaesthesia overcomes some of the disadvantages of traditionalinhalation anesthesia, like:

1. Rapid induction
2. Good plane of surgical stage of anaesthesia
3. Speedy and complete recovery with decreased post operative nausea and vomiting
4. It avoids risk of malignant hyperthermia syndrome and environmental hazards unlike inhalational agents[2]

Due to the invention of newer induction agents, opioids and amnestic agents with shorter half life and advents of infusion pumps , syringe pumps and target controlled infusions, TIVA is gaining popularity day by day[3]

Propofol- a newer intravenous anaesthetic agent with favorable pharmacokinetic profile has emerged as a gold-standard for TIVA[4,5] for short surgical procedures and day care surgery. Propofol is a GABA receptor modulator. Since it has a high clearance rate and rapid decline in blood concentration, it is suitable for infusion.When propofol infusion is discontinued there is rapid recovery from anaesthetic state.

Pain relief forms an important constituent of balanced anaesthesia[1]. The main drawback of propofol is lack of analgesia, so it has to be combined with an analgesic like Ketamine or Opioids like Butorphanol.

Ketamine -a phencyclidine derivative produces “dissociative anesthesia”. It is a N-METHYL-D-ASPARTATE receptor antagonist, which induces : analgesia, amnesia, and unconsciousness. Because of this, Ketamine is closest to being a "complete" anesthetic.

Butorphanol tartrate – a synthetic opioid. Predominantly a Kappa receptor agonistand Mu opioid receptor antagonist. It is 3 times more potent than morphine with a shorted duration of action(0.5-3 hours). The chief advantages of this agent are: its potent analgesia, low toxicity and very low potential for abuse[6,7].

In this study,we have compared two drug regimens, i.e. Propofol-ketamine and propofol-butorphanol for TIVA technique in patients undergoing short surgical procedures.

II. Material And Methods

This was a comparative prospective double blinded study conducted from September 2020 to October 2020 in the Department of Anesthesiology, Rangaraya medical college teaching hospital, Kakinada.After ethical committee approval 60 patients undergoing elective short surgical procedures (less than 1 hour) were selected.

Inclusion criteria:

1. patients of either sex,
2. patient belonging to ASA grade I and II,
3. age between 25-50 years,
4. patient planned for elective surgery undergoing various short surgical procedures.

Exclusion criteria :

1. patient belonging to ASA III and ASA IV,
2. patient with anticipated difficult intubation and difficult mask ventilation,
3. patient with comorbid medical conditions,
4. history of drug hypersensitivity, drug abuse and
5. unwilling patients

The patients were admitted to the hospital a day before the surgery. They underwent a thorough pre-anaesthetic checkup. Fasting guidelines followed. After shifting the patient to the operation theatre Standard ASA monitors were connected and premedicated with Midazolam 2 mg and glycopyrrolate 0.2 mg intravenously. These patients were randomly assigned to one of the two groups in a double blinded manner for induction viz;

1. GROUP B: inj. Butorphanol 20µgm/kg + inj. Propofol 1.5mg/kg
2. GROUP K: inj. Ketamine 1 mg/kg + inj. Propofol 1.5mg/kg

Pain on injection with propofol was noted in the form of vocal response, arm withdrawal or tears on eye suggesting pain. The hemodynamics parameters including blood pressure, heart rate, SPO2 were noted again and then after each 5 minutes of interval till 30 minutes. Anaesthesia maintained with propofol in the dose of 9mg/kg/hr via syringe pump infusion till the end of surgical procedure and spontaneous respiration was maintained with 100% oxygen via facemask and bains circuit assistance. Incidence of hypotension or hypertension, changes in electrocardiogram and other complications during operation were noted and appropriate action was taken. Incidence of postoperative nausea and vomiting (PONV) was noted. PONV treated with ondensetron 4-8 mg when needed.

Sedation was assessed in postoperative period using MODIFIED RAMSAY SEDATION SCORE.

SCORE	LEVEL OF SEDATION
1	Anxious, agitated, restless or both
2	Co operated, oriented and tranquil
3	Responds to commands only
4	Exhibits brisk response to tactile stimuli or loud auditory stimulus
5	Exhibits brisk response to tactile stimuli or loud auditory stimulus
6	Exhibits no response

STATISTICAL ANALYSIS

The data was entered in the Microsoft excel sheet and statistically analyzed using SPSS SOFTWARE Version 16.0. Paired sample t- test was used to compare the means between the two groups. p-value less than 0.05 was considered significant.

III. Results

Demographic profiles and ASA grading of the patients scheduled for study were comparable(Table 1)

Parameters	Group B	Group K	P value
Age	36.45±3.20	37.23±2.05	0.65
Sex	Male 20 Female 10	Male 17 Female 13	0.728
Weight	52.86±2.72	53.23±2.21	0.204

Duration of surgery	25±8.0	24±8.2	1

Table 1: Demographic trends

There was significant difference in heart rate between both the groups from 10 minutes to 30 minutes(Table 2, Figure 1)

	Group B		Group K			
Heartrate	Mean	SD	Mean	SD	P value	Inference
Baseline	70.23	8.92	69.26	8.83	0.673	NS
Premedication	74.63	9.46	72.33	7.48	0.3005	NS
Induction	77.84	11.62	75.80	9.23	0.4545	NS
5 min	80.62	13.54	75.82	9.11	0.1126	NS
10 min	83.16	12.68	74.63	8.23	0.003	S
15 min	80.21	11.37	74.42	8.48	0.0292	S
20 min	82.30	12.01	74.26	9.58	0.005	S
25 min	78.84	12.48	70.96	7.11	0.003	S
30 min	78.42	10.58	70.64	6.92	0.001	S

Table 2: Intergroup comparison of changes in Heart rate
(S- significant NS- nonsignificant)

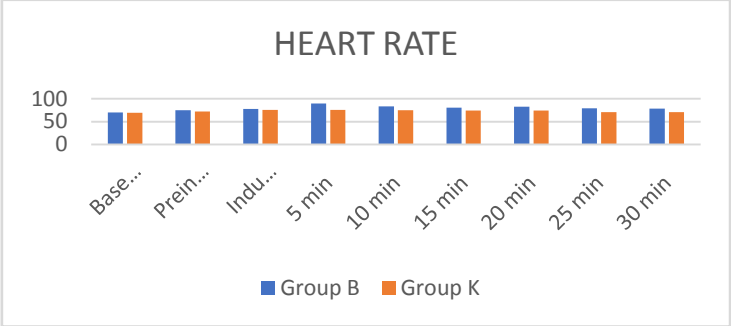

Figure 1: Intergroup comparison of changes in Heart rate

There was significant difference in mean arterial pressure between both the groups from 10 minutes to 30 minutes(Table 3, Figure 2)

	Group B		Group K			
MAP	Mean	SD	Mean	SD	P Value	Inference
Baseline	90.01	6.52	82.63	8.52	0.252	NS
Premedication	84.64	7.82	85.52	9.22	0.691	NS
Induction	84.63	7.03	90.10	5.89	0.001	S
5 min	82.54	7.64	88.90	6.10	0.007	S
10 min	82.26	8.16	88.50	6.88	0.002	S
15 min	82.22	7.54	88.42	6.32	0.001	S
20 min	80.02	7.16	85.23	6.10	0.003	S
25 min	78.20	6.30	84.20	5.25	0.002	S
30 min	76.03	7.11	82.53	5.71	0.004	S

Table 3: Intergroup comparison of changes in Mean arterial pressure

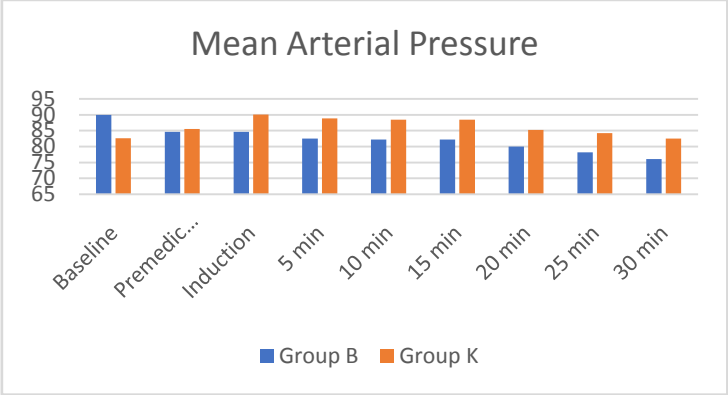

Figure 2: Intergroup comparison of changes in Mean arterial pressure

There was significant difference in oxygen saturation between both the groups during induction upto 30 minutes(Table 4, Figure 3)

	Group B		Group K			
SPO2	Mean	SD	Mean	SD	P value	Inference
Baseline	99.86	0.56	99.62	0.62	0.121	NS
Premedication	99.83	0.32	99.84	0.32	0.9041	NS
Induction	99.40	0.76	99.82	0.30	0.006	S
5 min	99.46	0.78	99.82	0.30	0.021	S
10 min	99.42	0.72	99.78	0.28	0.013	S
15 min	99.46	0.78	99.78	0.28	0.038	S
20 min	99.43	0.73	99.90	0.30	0.001	S
25 min	99.44	0.76	99.90	0.30	0.003	S
30 min	99.43	0.73	99.94	0.26	0.0007	S

Table 4: Intergroup comparison of changes in SPO2

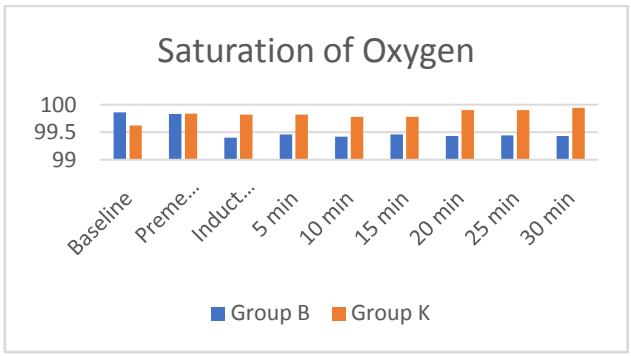

Figure 3: Intergroup comparison of changes in SPO2

Pain on injection with propofol was significantly low in the butorphanol group (Table 5, Figure 4)

	Group B		Group K		Total			
POI	n	%	n	%	n	%	P value	Inference
Absent	20	66%	15	50%	35	60%	0.006	Significant
Present	10	35%	15	50%	25	40%		
Total	30	100%	30	100%	60	100%		

Table 5: Intergroup comparison of pain on injection with Propofol

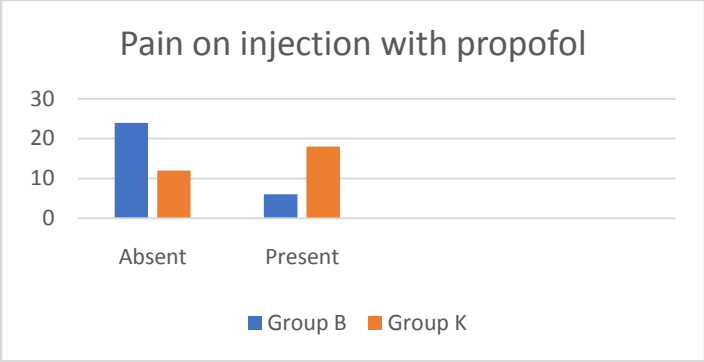

Figure 4: Intergroup comparison of pain on injection with Propofol

IV. Discussion

The ideal characteristics of the drugs to be used for TIVA include:

1. the plasma concentrations of the drugs has to be reached quickly and
2. the plasma concentration to be maintained over a period of time to produce the desired effect.
3. they should have rapid clearance rate and
4. little delay between change in infusion rates, plasma levels and pharmacological actions.

Propofol is a commonly used induction agent in day care procedures. When propofol is used as a sole agent a larger dose is needed and may be associated with hemodynamic and respiratory effects like hypotension, bradycardia, apnoea or hypoventilation. To decrease the above mentioned adverse effects, Ketamine, and opioids like Butorphanol, may be combined.Ketamine and Butorphanol when combined with propofol increase blood pressure, heart rate, cardiac index and simultaneously decrease the amount of propofol needed[6]

In our study, in ketamine group, there was statistically significant changes inheart rate, mean arterial pressure), and SPO2 during post induction and maintenance of anaesthesia throughout the procedure when compared to butorphanol group.

In a study by Regmi NK Et al[1], they compared propofol-ketamine with propofol-butorphanol combination. They concluded that propofol-ketamine combination produced better hemodynamic stability than the butorphanol combination.

Furuya a, et al. in their study investigated for arterial pressure changes during induction of anaesthesia with propofol by adding intravenous ketamine[8].They concluded that administration of ketamine before induction with propofol preserved haemodynamic stability in terms of blood pressure and heart rate compared with induction with propofol alone .

A similar study conducted by NALINI K B, and et al. Compared propofol and ketamine versus propofol and fentanyl in terms of hemodynamic stability and analgesia. They concluded that the combination of ketamine and propofol is a safe and possibly superior alternative to propofol – fentanyl combination, in terms of hemodynamic stability .

In our study, Propofol-Butorphanol group had statistically significant decrease in SPO2 after induction and during maintenance phase of anaesthesiain comparison to Propofol-ketamine group,

Aasim SA, Syamasundara RB, Zubair[9] SI conducted a similar study on 50 patients, they concluded that propofol–ketamine group had better haemodynamic stability without respiratory depression.

In our studypain on injection with propofol was lesser inbutorphanol group when compared to the ketamine group. Incidence of pain was 20% in Butorphanol group, where as in ketamine group it was 60%.This is consistent with a study done by Agarwal and coworkers[10], where they found that the effective method of abolishing propofol induced pain is with pretreatment by butorphanol.

There was no statistical significant difference in PONV and sedation among the two groups.

V. Conclusion

In our study we concluded that Propofol-ketamine (Group K) combination has the advantage of offering better hemodynamic and respiratory stability. Attenuation of pain on injection is the only added advantage of propofol–butorphanol (Group B) combination whereas postoperative recovery in terms of sedation and PONV is similar among them.

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