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ORIGINAL ARTICLE

Comparative Study Between Propofol-Ketamine and Propofol-Butorphanol for TIVA Technique in Short Surgical Procedures

Shruti Gupta, Rajdeep Kour, Seema Sambyal

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 with bag mask ventilation combined with oxygen. AIMS AND **Objective:** To compare Propofol -Ketamine and Propofol -Butorphanol for TIVA in short surgical procedures in terms of their Hemodynamic stability, Postoperative sedation, Pain on injection with Propofol & Post operative nausea and vomiting. **Material And Methods**: This prospective, comparative study was conducted in 50 patients (18 - 60 years of age), ASA grade I and II, scheduled for elective surgery of duration less than 1hour. Patients were randomly divided into two groups : Group B-P receive inj.Butorphanol 20 ug/ kg + inj.Propofol 1.5 mg/kg and Group K-P receive inj. Ketamine 1mg/kg + inj. Propofol 1.5 mg/kg and Anesthesia was maintained with injection Propofol in the dose of 9mg/kg/hour. **Results:** Demographic data were comparable between two groups. Both groups were comparable in Hemodynamic parameters however in Group-BP there was decrease in mean blood pressure which was statistically insignificant. The incidence of sedation was more in group BP (36%) as compared to group KP (24%) but difference was statistical insignificant. In group BP, the incidence of pain was 4%, where as in group KP it was 36 % and this was statistical significant and the incidence of PONV is comparable in both groups. **Conclusion:** we concluded that both groups were comparable in terms of their Hemodynamic stability, Postoperative sedation and PONV but the Pain on injection with Propofol was significantly less in group BP (p value <0.01)

Key Words

Butorphanol, Ketamine, Propofol, PONV, TIVA, Short Surgical Procedures

Introduction

InTIVA has been attempted since 1934 but its use was hampered by cumulative effect of longer acting drugs, inadequate methods of administration of drugs like with intermittent bolus administration leading to peaks & unstable anaesthetic conditions and fear of intraoperative awareness. But with invention of newer induction agents, opoids and amnestic agents having shorter half life ,with advents of infusion pumps, syringe pumps and target controlled infusions these problems have been declined and TIVA is gaining popularity day by day. [1] With TIVA it is possible to provide truly balanced anaesthesia and better titrate each component to a desired clinical effect. [2]

Propofol , a GABA modulator is a newer intravenous anaesthetic agent, having pharmacokinetic profile that favors administration by continous intravenous infusion.[3] The prompt recovery without residual sedation

Post Graduate Departments of Anaesthesiology & Intensive Care GMC Jammu, J&K India

Correspondence to: Dr Seema Sambyal, Post Graduate Student, Post Graduate Department of Anaesthesiology & Intensive Care, GMC Jammu J&K India

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and low incidence of nausea and vomiting makes propofol particularly well suited to ambulatory anaesthesia techniques .Propofol has emerged as a gold standard for TIVA [4] for short surgical interventions and day care surgeries but has no intrinsic analgesic property therefore it has to be combined with an analgesic. [5]

Pain relief forms an important constituent of balanced anaesthesia. Ketamine and opoids like butorphanol are the popular analgesics in this context. Ketamine , is a potent analgesic which has very high margin of safety, no irritation of the veins, and no negative influence on ventilation and circulation.[6,7] Neither propofol nor ketamine are suitable as sole anaesthetic agents so they may be combined in TIVA technique.[8]

Butorphanol is a agonist-antagonist opoid that resemble pentazocine. The chief advantages of this agent are its potent analgesia, low toxicity and very low potential for abuse. [9] Butorphanol provides good analgesia but is associated with adverse effects like cardiodepressant action, dizziness and sedation. [10]

Virtually all IV anesthetic agents like thiopentone, methohexitone, Etomidate, Morphine etc have been tried for TIVA but they have been abandoned because of their own drawbacks. [11]

Thus, in this study we compared two drug regimens i.e. Propofol-Ketamine and Propofol-Butorphanol for TIVA technique in patients undergoing short surgical procedures.

Aims & Objective

To compare Propofol -Ketamine and Propofol -Butorphanol for TIVA in short surgical procedures in terms of their Hemodynamic stability, Postoperative sedation, Pain on injection with Propofol & Post operative nausea and vomiting.

Material & Methods

After obtaining approval from hospital ethical committee, the study was conducted in the Department of Anaesthesiology and Intensive care GMC Jammu . 50 patients aged between 16 - 60 years , of both sexes with physical status ASA I and II were randomly selected for elective surgery of duration less than 1 hour. Pre-Anesthetic check up was done a day before surgery which included a detailed history, a thorough physical and systemic examination and relevant investigations. Patient with difficult mask ventilation, psychiatric disorder, cardiac disease and who may require muscle relaxant were excluded from the study.

An informed written consent was taken from each patient and patient was kept fasting for 8 hours before surgery. In the pre-operative room, I/V line secured and pre-medication was given 30 minutes before surgery with injection Midazolam 0.01 mg/kg, injection Glycopyrollate 0.2 mg I/V stat & injection Diclofenac 75mg I/M stat .

In the operating room , monitors were attached to the patient and baseline parameters HR, NIBP, SPO2 were recorded and the patients were randomly divided in 2 groups :

***Group B P** : Inj.Butorphanol 20 ug/kg + inj.Propofol 1.5 mg/kg.*

***Group K P** : Inj. Ketamine 1mg/kg + inj. Propofol 1.5 mg/kg.*

Firstly, we give bolus of injection Butorphanol 20ug/kg IV slowly over 1minute in Group B P and injection Ketamine 1mg/kg IV in Group K P then Propofol was given in a dose of 1.5 mg/kg IV slowly and Pain on injection with Propofol was noted in both Groups in the form of vocal response, facial grimace, arm withdrawal or tears on eye suggesting pain. Anesthesia was maintained with injection Propofol in the dose of 9mg/kg/hour via infusion pumps till end of surgical procedure and spontaneous respiration was maintained 100 % O2 via facemask and bain-circuit assistance when needed. All hemodynamic parameters BP, HR, SPO2 were noted at the time of induction and then after every 5 minutes interval till 30 minutes. Anaesthesia drugs were stopped 5 minutes before end of surgery.

The incidence of hypotension, changes in ECG and other complications during operation were noted and appropriate action was taken. Sedation was assessed in post-operative period using Modified Ramsay Sedation Score. Incidence of post operative nausea and vomiting (PONV) was noted and treated with injection Ondansetron 0 .1mg/kg IV when needed.

Results

Stastistical analysis of data hence obtained was entered in Microsoft Excel 2016 and the analysis was done in SPSS v 16.0. The outcomes were presented as numbers and percentages for categorical variables and mean ± SD for continuous variables. Chi square test was used to test the association between the outcomes and the independent variables .

The statistical significance for quantitative variables was calculated by comparing means and p value of <0.05 was considered as statistically significant unless specified otherwise. The Demographic profile of both the groups with respect to Sex ,Age, Weight and ASA

Table 1. Showing The Demographic Profile of Patients

	GROUP 1 (BP) (TOTAL =25)	GROUP 2(KP) (TOTAL =25)
Male	14(56%)	12(48%)
Female	11(44%)	13(52%)
ASA I	19(76%)	19(76%)
ASA II	6(24%)	6(24%)
Age (Yrs)	35.48 ±10.441	35.40 ±9.609
Weight (Kgs)	62.20 ±6.970	61.44 ±4.164

Table 2. Intergroup Comparison of Mean Arterial Blood Pressure

Mean BP (Minutes)	GROUP 1(BP) MEAN	S.D	GROUP (2KP) MEAN	S.D	p value	Inference
Baseline	83.64	7.697	82.12	10.084	2.537	NS
5	86.40	7.500	78.88	9.867	2.479	NS
10	84.32	6.375	76.80	9.587	2.303	NS
15	82.08	7.118	76.84	9.232	2.331	NS
20	80.68	6.081	75.88	8.604	2.107	NS
25	80.77	5.822	75.04	8.188	2.099	NS
30	80.64	5.583	76.00	7.031	2.369	NS
40	82.60	3.286	72.40	1.673	1.649	NS

Table 3. Intergroup Comparison of Heart Rate

H.R (Minutes)	GROUP 1(BP) MEAN	S.D	GROUP 2(KP) MEAN	S.D	p value	Inference
Baseline	80.36	9.716	77.96	9.800	2.760	NS
5	84.12	9.167	80.08	8.866	2.578	NS
10	83.48	7.252	81.08	9.305	2.359	NS
15	80.24	7.568	79.80	8.898	2.336	NS
20	79.60	7.388	79.28	8.605	2.268	NS
25	80.05	6.701	78.72	7.679	2.116	NS
30	79.79	7.170	77.93	7.787	2.786	NS
40	82.00	7.842	80.33	3.512	4.905	NS

Table 4. Intergroup Comparison of Spo2.

SPO_2 (Minutes)	GROUP 1(BP) MEAN	S.D	GROUP 2(KP) MEAN	S.D	p value	Inference
Baseline	98.16	.688	97.96	0.889	0.225	NS
5	98.84	.374	98.16	0.800	0.177	NS
10	98.71	.464	98.12	0.833	0.194	NS
15	98.68	.476	98.44	0.651	0.161	NS
20	98.68	.557	98.68	0.557	0.157	NS
25	98.70	.470	98.76	0.436	0.135	NS
30	98.67	.617	98.73	0.458	0.198	NS
40	98.60	.548	99.00	0.000	0.327	NS

status were comparable. There was no statistically significant difference in MAP between two groups. There was no statistically significant difference in HR between two groups. There was no statistically significant difference in SPO2 between two groups. The incidence of Post operative sedation was 36% in group BP and 24 % in Group KP which was statistically non significant. The incidence of Pain on injection was 4% in group BP and 36% in Group KP which was statistically significant p-value <0.01. There was no statistically significant

Table 5. Intergroup Comparison of Post-Operative Sedation(Pos)

POS	GROUP 1(BP)		GROUP(2KP)		TOTAL		p value	Inference.
	N	%age	n	%age	N	%age		
Present	9	36%	6	24%	15	30%		
Absent	16	64%	19	76%	35	70%		
Total	25	100%	25	100%	50	100%	1.00	NS

Table 6. Intergroup Comparison on Pain On Injection (Poi).

POI	GROUP 1(BP)		GROUP2(KP)		TOTAL		p value	Inference.
	N	% age	n	%age	N	%age		
Present	1	4%	9	36%	10	20%		
Absent	24	96%	16	64%	40	80%		
Total	25	100%	25	100%	50	100%	0.01	**Significant**

Table 7. Intergroup Comparison of Post Operative Nausea And Vomiting(PONV).

PONV	GROUP 1(BP)		GROUP 2(KP)		TOTAL		p value	Inference.
	N	%age	N	%age	N	%age		
Present	2	8%	0	0%	10	20%		
Absent	23	92%	25	100sss%	40	80%		
Total	25	100%	25	100%	50	100%	0.49	NS

difference in PONV between two groups. (*Table-1-7*)

Discussion

Total intravenous anaesthesia has been a subject of interest for all anaesthesiologists, as this is the one of the best way to avoid operation theatre pollution. The availability of rapid and short acting sedative hypnotics, analgesics and muscle relaxants has refocused the attention on complete anaesthesia by intravenous route. The advent of continuous infusion system has made administering TIVA all the more popular and convenient.

But even today, we are still without any one intravenous drug that can alone provide all the requirements of anaesthesia (i.e. unconsciousness, analgesia and muscle relaxation). Hence there is need to administer several different agents to produce the desired results. With this background, this study was conceptualized to compare two drug regimen; Propofol-Ketamine,(Group - KP) and Propofol-Butorphanol,(Group - BP) for TIVA technique.We studied 50 patients, age between 16-60 years with ASA-I and II undergoing elective surgery of duration less than 1hour. Patients were randomly divided in 2 groups: Group B P: Inj. Butorphanol 20 ug/kg + Inj. Propofol 1.5 mg/kg. Group K P: Inj. Ketamine 1mg/kg + inj. Propofol 1.5 mg/kg. There was no statistically significant difference among the two groups in terms of Age, Sex, Weight and ASA status.

In our study with Group - KP, there was no statistically significant change in heart rate, mean blood pressure throughout the procedure but with Group-BP there was decrease in mean blood pressure. However, the results were statistically insignificant when the two groups were compared. The result of our study was similar to the study done by Mayer and coworkers[8] where they compared the haemodynamic and analgesic effect of Propofol-Ketamine with Propofol-Fentanyl. They found distinct decrease in mean arterial blood pressure and heart rate after induction and maintenance of anaesthesia with Propofol-Fentanyl group whereas with Propofol -Ketamine group the hemodynamics were stable .This may be due to antagonistic properties of Propofol (decrease in BP) and Ketamine (increase in BP). Another study done by Croize *et al* [4] using Propofol-Ketamine on cardiovascular response and wake up time. They showed that this combination maintained better haemodynamic stability and there was no significant change in heart rate and arterial blood pressure throughout the surgery in comparison with Propofol -Alfentanil.

The incidence of sedation was more in group BP (36%) as compare to group KP (24%) but difference is statistical insignificant. Similar study was done by P Venkateswarlu *et al* [11] which had no significant difference in sedation while comparing Propofol-Butorphanol and Propofol-Ketamine groups but the prevalence of sedation was higher with Propofol-Butorphanol group .

Mortero R *et al* [12] , showed the effect of Ketamine and Propofol in terms of respiration, postoperative mood, perception and cognition and concluded that a 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. Similar results were reported by Haranein and EI [13] who showed combination of Propofol-Ketamine has better sedation quality than that of Propofol-Fentanyl.Another study done by 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 2 groups studied, group BP abolish the pain on injection with Propofol as compared to group KP. In group BP, the incidence of pain was 4%, where as in group KP it was 36 % and this is statistical significant . This is consistent with the study done by Agarwal *et al* [14] where they found that simple and effective method of attenuating Propofol induced pain is with pretreatment by Butorphanol. One major disadvantages 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 BP was 8% where as in group KP no patient has incidence of PONV similar results ere observed in study done by Sudhmala P *et al* [15] where incidence of nausea was more in Propofol-fentanyl group than Propofol-Ketamine group but the difference was statistically insignificant as in our study. Regmi NK et al [1] and Aasim SA *et al* [16] were also came to the same conclusion showing no difference in incidence of PONV between Butorphanol and Fentanyl when used as pre-induction agent.

Conclusion

The present study showed that both the groups Propofol-Butrphanol (BP) and Propofol-Ketamine (KP) combination has the advantage of offering better hemodynamic stability and Postoperative recovery in terms of sedation and can be used for TIVA in short surgical procedures. However, Propofol-Butorphanol (BP) group has an advantage over Propofol-Ketamine (KP) group in terms of attenuating pain on injection which was stastistically significant.

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Conflicts of Interest

There are no conflicts of interest.

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