Original Research Article

A clinical study to compare the clinical efficacy of propofol alone with propofol ketamine combination during ambulatory anesthesia

Smita Bharti[1], Prashant[2*], Ajay Kumar[3]

[1]Senior Resident, Department Of Anesthesia And Critical Care, Patna Medical College And Hospital, Patna, Bihar, India
[2]Senior Resident, Department Of Anesthesia And Critical Care, Patna Medical College And Hospital, Patna, Bihar, India
[3]Assistant Professor, Department Of Anesthesia And Critical Care, Patna Medical College And Hospital, Patna, Bihar, India

Received: 04-08-2021 / Revised: 07-09-2021 / Accepted: 20-10-2021

Abstract

Aim: The present study was conducted to compare the clinical efficacy of propofol alone with propofol ketamine combination during ambulatory anesthesia. **Materials and Method:** Hospital Based study conducted on 80 patients belonging to ASAI & II, aged between 20-40 yrs, 40 in each group was taken. Group P: Propofol alone Group PK: Propofol ketamine combination. Induction doses, pulse rate, oxygen saturation, systolic, diastolic blood pressure, mean arterial pressure and complication if anywere recorded. **Result:** Induction dose of propofol was decreased in propofol-ketamine combination group. Mean basal systolic blood pressure of propofol alone group was 118.4+/9.36 and in propofol-ketamine group was 117.9+/-8.77 which were statistically comparable. None of the patients experienced emergence delirium in our study. **Conclusion:** Propofol ketamine combination provides better haemodynamic stability as compared to propofol.

Keywords: propofol, ketamine, total intravenous anaesthesia, ambulatory (TIVA)

Introduction

Use of anesthesia with the aim to admit and discharge the patients on the present day of the surgical procedure is called as ambulatory anesthesia.

Total intravenous anesthesia is a technique in which induction and maintenance of anesthesia is achieved with intravenous drugs alone, thus avoiding both volatile agents and nitrous oxide.

Propofol (2, 6, di-isopropyl phenol) is the most recent intravenous anaesthetic to be introduced into clinical practice and is being widely used due to its hemodynamic property. Propofol is a non-opioid, non-barbiturate, sedative hypnotic agent. It possesses anti emetic effect & reliably produces sedation. Because of its clear headedrecovery nature it is preferred in ambulatory surgeries. Side effects include dose related cardiovascular & respiratory depression, bradycardia and hypotension. It also lacks analgesic property.

Ketamine is phencyclidine derivative & known to produce analgesia & amnesia. It causes minimal respiratory depression and does not cause myocardial depression. However ketamine when used as a sole agent for procedural sedation & analgesia results in occurrence of emergence reactions, which are associated with dreaming, delirium and illusions. In few cases laryngospasm and airway obstruction has also been noted.

This study is designed to compare propofol alone with propofol and ketamine for TIVA in ambulatory anesthesia.

*Correspondence
Dr. Prashant
Senior Resident, Department of Anesthesia And Critical Care, Patna Medical College and Hospital, Patna, Bihar, India.
E-mail: drprashant003@gmail.com

Material and Methods

This prospective randomized study was conducted at Department of Anesthesia and Critical Care, at Patna Medical College and Hospital, Patna. The study was approved by the institutional research and ethical committee. The study was conducted between July 2019 and March 2020. An informed and written consent was taken from the participating subjects prior to the commencement of the study.

The study was conducted on 80 patients, aged 20 to 40 yrs of ASA grade I and ASA grade II, scheduled for ambulatory anesthesia i.e. incision and drainage of abscesses, closed reduction of fracture upper limb. The patients were randomly allocated in two different groups (40 of each) i.e. propofol alone (Group P) and combination of propofol & ketamine (Group PK) andfollowing things are to be recorded i.e

1. Haemodynamics, intra operatively.
2. Induction requiremts, of propofol and ketamine.
3. Time of recovery from induction.
4. Incidence of post-operative Complications.
5. Duration of pain relief post operatively.

Patients with ASA grade III, IV & V and patients below 20 yrs of age and above 40 yrs of age, unwilling Pt, history of allergy to drugs were excluded from the study. Mode of selection was randomized double blind.

18 G Cannula, Drugs, Disposable Plastic Syringes and (SpO2, PR. NIBP) anesthesia machine, Resuscitation Equipment's (stand by).

All pt were kept fasting for at least 6 hrs prior to anesthesia. Preoperative base line heart rate, BP, respiratory rate SpO2 were recorded.

1. **Intra Operative Period:** After securing 18 G cannula and connecting to NIBP, pulse oximeter and ECG monitor, patients were premeditated 15 to 20 mint prior to induction with Injection Glycopyrulate 0.2mg.
2. Injection ondansetron 4mg.
3. Injection fentanyl 1microgram per kg.

4. Injection midazolam 1mg.

The anaesthesia machine was kept ready along with oxygen delivery system, emergency resuscitation equipment's and emergency drugs.

In a double blind manner pt. were randomly assigned to one of the two group's i.e.

Group P: 40 pt. received propofol slowly till the point of induction.

Group PK: 40 pt. received ketamine 0.5mg per kg IVslowly followed by propofol IV till the point of induction.

Baseline Blood Pressure, Pulse rate, respiratory rate, SpO2 were recorded.

Then the anaesthesia was maintained with propofol bolus 10mg IV in propofol group, Propofol ketamine bolus 10+10mg IV in propofol-ketamine group based on requirements-namely-spontaneous moments, tachycardia, high blood pressure, increase in respiratory rate, appearance of tears. Spontaneous respiration was maintained with 100% O2 with mask and bain's circuit.

Blood Pressure, ECG Changes, Respiratory rate, basal pulse rate and saturation were noted followed by every 5 minutes recording till the end of the procedure. Post operatively duration of pain relief was also noted.

For nausea and vomiting inj ondansetron 100-150 microgram per kg IV was given. The time for first analgesic demand was noted. The regular analgesics were administered for the remaining 24hrs for pain relief to the pt.

Hypertension defined as >140/90 mm of hg Hypotension defined as < 90/50 mm of hg Hypoventilation defined as respiratory rate <8/minute Desaturation defined as SPO2 <93%

All the parameters were monitored very keenly.

Statistical analysis

The Student T-Test was used to assess the statistical significance of paired date a p value of <0.05 was considered significant.

Results

Demographic profiles of the patients scheduled for study were comparable.

Table 1: Intergroup comparision of changes in systolic blood pressure

Mean Systolic BP	Propofol		Propofol-Ketamine		T stat	P - Value	Inference
	Mean	SD	Mean	SD			
At 0 MIN	118.4	9.36	117.9	8.77	0.22	>0.05	NS
At 5 MIN	96.3	7.35	120.6	8.28	-13.89	<0.001	HS
At 10 MIN	99.7	6.68	122.9	8.14	-13.96	<0.001	HS
At 15 MIN	103.8	7.03	117.9	7.99	-8.43	<0.001	HS
At 20 MIN	108.9	5.64	123.3	7.93	-9.33	<0.001	HS
At 25 MIN	110.1	5.35	121.4	7.95	-7.46	<0.001	HS
At 30 MIN	110.9	5.45	122.6	6.99	-8.31	<0.001	HS

NS-Nothing significant, HS-Highly significant

Table 2: Intergroup comparision of changes in Diastolic blood pressure

Mean Diastolic BP	Propofol		Propofol-Ketamine		T stat	P - Value	Inference
	Mean	SD	Mean	SD			
At 0 MIN	75.1	6.14	72.9	6.67	1.53	>0.05	NS
At 5 MIN	60.9	3.54	74.0	6.84	-10.76	<0.001	HS
At10 MIN	63.4	3.77	72.4	6.50	-7.61	<0.001	HS
At15 MIN	66.3	4.68	72.5	7.19	-4.53	<0.001	HS
At20 MIN	70.6	3.08	73.9	6.84	-2.74	<0.05	HS
At25 MIN	67.9	5.07	72.9	6.39	-3.84	<0.001	HS
At30 MIN	68.1	4.93	75.3	6.83	-5.44	<0.001	HS

NS-Nothing significant, HS-Highly significant

Table 3: Intergroup comparision of changes in pulse rate

Mean PR	Propofol		Propofol-Ketamine		T stat	P Value	Inference
	Mean	SD	Mean	SD			
AT0 MIN	79.3	5.86	77.6	4.78	1.42	>0.05	NS
AT5 MIN	72.9	5.24	77.6	4.99	-4.06	<0.001	HS
AT10MIN	72.2	4.87	77.5	5.10	-4.71	<0.001	HS
AT15MIN	72.3	5.42	78.9	5.73	-5.33	<0.001	HS
AT20MIN	72.3	5.16	77.4	5.29	-4.37	<0.001	HS
AT25MIN	72.7	4.89	80.0	6.04	-5.98	<0.001	HS
AT30MIN	73.1	4.92	78.6	5.49	-4.68	<0.001	HS

NS-Nothing significant, HS-Highly significant

Table 4: Intergroup comparision of changes in Mean arterial pressure

Mean Arterial Presure	Propofol		Propofol-ketamine		T stat	P - Value	Inference
	Mean	SD	Mean	SD			
At 0 MIN	89.5	6.94	87.3	5.74	1.48	>0.05	NS
At 5 MIN	72.6	4.09	89.5	5.39	-15.73	<0.001	S
At 10 MIN	75.4	4.14	89.2	5.17	-13.14	<0.001	S
At 15 MIN	78.8	4.99	87.6	6.03	-7.11	<0.001	S
At 20 MIN	83.3	3.45	90.3	5.86	-6.46	<0.001	S
At 25 MIN	81.9	4.46	89.1	5.33	-6.48	<0.001	S
At 30 MIN	82.3	4.34	91.1	5.67	-7.73	<0.001	S

NS-Nothing significant, HS-Highly significant, S-Significant

Table 5: Intergroup comparision of changes in mean oxygen saturation

Mean oxygen saturation	Propofol		Propofol-Ketamine		T stat	P - Value	Inference
	Mean	SD	Mean	SD			
At 0 MIN	99.8	0.67	99.5	0.96	1.22	>0.05	NS
At 5 MIN	99.6	0.81	98.6	1.52	3.68	<0.001	HS
At10 MIN	99.8	0.61	99.8	0.67	0.35	>0.05	NS
At15 MIN	99.8	0.61	99.8	0.81	0.35	>0.05	NS
At20 MIN	99.9	0.53	99.8	0.61	0.39	>0.05	NS
At25 MIN	100.0	0.53	99.9	0.53	0.28	>0.05	NS
At30 MIN	99.8	0.67	99.5	0.90	1.69	>0.05	NS

NS-Nothing significant, HS-Highly significant

Table 6: Intergroup comparision of changes in mean respiratory rate

Mean RespiratoryRate	Propofol		Propofol-Ketamine		T stat	P - Value	Inference
	Mean	SD	Mean	SD			
At 0 MIN	16.3	1.19	15.8	2.07	1.35	>0.05	NS
At 5 MIN	16.75	1.96	14.5	1.74	5.43	<0.001	HS
At 10 MIN	16.7	1.32	15.45	1.19	4.43	<0.001	HS
At 15 MIN	16.45	1.47	15.35	1.31	3.54	<0.001	HS
At 20 MIN	16.15	1.05	16.35	1.78	-0.77	>0.05	NS
At 25 MIN	16.5	1.47	16.25	1.58	0.87	>0.05	NS
At 30 MIN	16.3	1.07	16.2	1.47	0.43	>0.05	NS

NS-Nothing significant, HS-Highly significant

Table 7: Induction dose requirements of propofol in both groups

	Induction dose (Mean+/-SD)mg/kg	P value
Propofol group	2.02+/-0.16	<0.001
Propofol-Ketamine group	1.62+/-0.1	

Table 8: Time to recover from induction doses in study groups

	Mean		P Value	Inference
	Propofol (MIN)	Propofol-Ketamine(MIN)		
Time of recovery from induction dose	2.63	9.80	<0.001	HS

NS-Nothing significant, HS-Highly significant NS-Nothing significant, HS- Highly significant

Table 9: Duration of pain relief postoperatively/time taken for firstanalgesic demand

	Propofol	Propofol-Ketamine
Time for first analgesic demand (MIN)	8.6 +/- 1.89	48.5 +/- 7.61

Discussion

The total intravenous anaesthesia has been a subject of interest for all anaesthesiologists, as this is the best route to avoid operation theatre pollution.

With the invention of continous infusion system TIVA gained popularity but even today, we are still without any one IV drugs that can alone provide all the requirements of anaesthesia (i.e unconsciousness, analgesia and muscle relaxation). Hence there is need to administer several different agent to produce the desired results.

Ketamine when used in subanaesthetic dose reduces the dose of propofol required for induction. This is known as co-induction. It provides haemodynamic stability.

IN 2001 kaushik saha *et al* too found a statistically significant decrease in the induction dose of propofol in combination with ketamine, in comparision to fentanyl. In our study also, induction dose of propofol was decreased in propofol-ketamine combination group.

Similar to the study of Briggs and co-workers, our study was also found the mean induction dose requirement of propofol in propofol alone group was 2.02+/0.16 mg/kg. And in propofol-ketamine group mean induction dose of propofol was 1.6+/- 0.10 mg/kg. which was statistically significant.

In the study done by Shiba goel MD, Neerja Bhardwaj MD in 2008 only 5% of patients in groups PK and PM showed >20% fall in SBP compared to 89% in group P(P<0.005). More children in groups PK and PM had acceptable conditions for LM insertion compared to group P(P<0.05). The time to achieve Steward Score of 6 was longer in groups PK and PM compared to group P(<0.005). In children, the combination of propofol with ketamine or midazolam produces stable hemodynamics and improved LM insertion conditions but is associated with delayed recovery.

Hence the present study was undertaken to study the effectiveness of ketamine as co-induction agent with propofol in comparision to propofol alone.

In 2014 a study was done by Fernando Martinez- Taboada and Elizabeth, A leece to compare anaesthetic induction in 70 healthy dogs using propofol or ketofol (apropofol-ketamine mixture), following premedication. either propofol (10mg/ml) of ketofol (9mg propofol and 9mg ketamine/ml) was titrated intravenously until laryngoscopy and tracheal intubation were possible. Induction mixture volume (mean±SD) was lower for ketofol (0.2±0.1 ml kg) than propofol (0.4±0.1 ml/kg)(p<0.001). PR increased following ketofol (by 35±20 beats minute) but not consistenly following propofol (4±16 beats minute)(p<0.001). Ketofol administration was associated with a higher mean arterial blood pressure (MAP) (82±10 mmhg) than propofol (77±11)(p=0.05). Ketofol use resulted in a greater decrease in FR-1 (median range): Ketofol-32 (-158 to 0) propofol -24(-187 to 2) breaths minute (p<0.001) sedation was similar between groups. Tracheal intubation and induction qualities were better with ketofolthan propofol (p=0.04 and 0.02 respectively).

In 2010 a study done by Fernando SF Cruz Adriano B Carregaro

Alceu G Raiser, Marina Zimmerman, Rafael Lukarsewski and Renata PB Steffen to evaluate TIVA with propofol (P) alone or in combination with ketamine (PK) in rabbits undergoing surgery found that ketamine potentiates propofol-induced anesthesia in rabbits, providing better maintenance of heart rate.

In 2008 a Study done by M. Koch, D. De Backer, J.L. Vincent, L. Barvais, D. Hennart and D. Schmartz to know the effects of propofol on human microcirculation found that the 15 pt had a mean (range) age of 35(25-41) yr. During the assessment of the microcirculation, the mean calculated propofol effect-site concentration was 6.5 micrograms. / Ml (range 4.5-10 micrograms/ml). There were no significant changes in heart rate or SpO2, but body temperature decreased during anesthesia and the arterial pressure decreased at the endof the intervention.

In 1991 a study was done by Guit and co-workers (A comparision of combination of propofol-fentanyl and propofol with ketamine in 18 patients who underwent non-cardiac surgery) to who concluded that propofol ketamine combination resulted in hemodynamically stable anaesthesia without the need for additional analgesics. Postoperative behavior was normal in all patients and none of the patients reported dreaming during or after operation. Propofol seems to be effective in eliminating side effects of a subanaesthetic dose of ketamine in humans.

Similar to the above studies our study also had decrease in mean heart rate, mean systolic blood pressure, mean diastolic pressure, mean arterial pressure in propofol group when compared to propofol ketamine combination group. i.e. Mean basal systolic blood pressure of propofol alone group was 118.4+/9.36 and in propofol-ketamine group was 117.9+/-8.77 which were statistically comparable.

Decrease in mean systolic blood pressure was seen inpropofol alone group, where maximum fall was noted at 5 minutes after induction (96.3+/-7.35) which was highly significant when compared to propofol-ketamine combination group throughout 30 minutes of observation.

Similar fall of mean diastolic blood pressure was observed in propofol alone group from basal mean diastolic blood pressure (75.1+/6.14) maximum drop was observed at 5 minutes after induction (60.9+/-3.54) statistically significant difference was present between two groups throughout the 30 minutes observation.

Similar decrease in mean arterial pressure was noted in propofol alone group when compared to propofol- ketamine group, which was statistically significant.

There was a significant decrease in mean pulse rate statistically after propofol induction in propofol alone group after successive intervale i.e. 5,10,15,20,25,30 minutes was 72.9+/-5.24, 72.2+/-4.87, 72.3+/-5.42, 72.3+/-5.16, 72.7+/- 4.89, 73.1+/-4.92 respectively, mean basal pulse rate of propofol-ketamine group was 77.6+/-1.42, mean pulse rate at 5,10,15,20,25,30 intervals was 77.6+/-4.78, 77.5+/-5.10, 78.9+/-5.73,77.4+/-5.29, 80.0+/-6.04, 78.6+/-5.49 respectively.

In 2001 Rosendo Mortero *et al* concluded that co-administration of small dose ketamine attenuates propofol induced hypoventilation, produces positive mood effects without perceptual changesafter surgery, and May provided earlier recovery of cognition. Similar to the above study, out study also showed reduction inrespiratory rate in propofol-ketamine combination group at5,10,15 minutes when compared to propofol alone groupwhich was statistically significant for some period (till 15 minutes), after that there was no significant difference between two group. But there was no hypoventilation orapnea.

In 2013 Sherry N. Rizk, Enas M Samir studied sedation, behavior, pain and severity of emergence delirium. Emergence delirium was significantly more frequent in the control group ($p<0.001$), but comparable in ketofol and propofol groups. Ketofol provides a promising new option for controlling emergence agitation with adequate postoperative sedative and analgesic effect, good recovery criteria and hemodynamic stability compared topropofol and control groups in children undergoingadenoidectomy or adeno tonsillectomy.

Similar to above study, emergence delirium was not observed in ketofol group none of the patients experienced emergence delirium in our study.

Conclusion

Our study concluded that propofol ketamine combination (PK) as compared to propofol (P) provides better haemodynamic stability as there is less induction requirements of propofol with less side effects and also the duration of pain relief post operatively was longer. Time to recover from induction dose was prolonged in propofol ketamine group.

References

1. Kaushik Saha, Saigopal M, Rajini Sundar, Palaniappan M, Anil C Mathew. Comparative evaluation of propofol- ketamine and propofol-fentanyl in minor surgery. Indian J Anaesth. 2001; 45(2):100-103.
2. Briggs P, Clarke RST, Dundee JW, Moore J. "Use of di – iso propyl phenol as main agent for short procedures.British Journal of Anaesthesia. 1981; 53:11 97.
3. Shiba Goel MD, Neeraja Bharadwaj MD, Kajal Jain MD. Efficacy of ketamine and midazolam as co-induction agents with propofol for laryngeal mask insertion in children. Pediatric Anesthesia 2008; 18:628-634.
4. Fernando Martinez-Taboada and Elizabeth A Leece. Comparison of propofol with ketofol, a propofol- ketamine admixture, for induction of anaesthesia in healthy dogs. Veterinary Anaesthesia and Analgesia. 2014; 41:575-582.
5. Fernando SF Cruz, Adriano B Carregaro, Alceu G Raiser, Marina Zimmerman, Rafael Lukarsewski and Renata PB Steffen. Total intravenous anesthesia with propofol and S (+)-ketamine in rabbits. Veterinary Anaesthesia and Analgesia. 2010; 37:116-122.
6. Koch M, De Backer D, Vincent JL, Barvais L, Hennart D, Schmartz D. Effects of propofol on human microcirculation. Br J Anaesth. 2008; 101(4):473-8.
7. Guit TBM, Koning HM, Coster ML. Ketamine and analgesia for total intravenous anesthesia with propofol. Anesthesia. 1999; 46:24-27.
8. Rosendo F. Mortero *et al*. The effects of small-dose ketamine on propofol sedation: respiration, post-operative mood, perception, cognition and pain. Anesth. Analg. 2001; 92:1465-9.
9. Knox JWD, Bovill JG, Clarke RSJ, Dundee JW. Clinical studies of induction agents XXXVI: KETAMINE. Br J Anaesth 1970; 42:875.
10. Diwale DB, Moulick NB, Bhatt PN, Matta JS, Bhalla SK. Comparative evaluation of ketamine and ketamine- diazepam in cardiac catheterization. Ind J Anaesth 1983; 31(2):132-139.
11. Schutter J, Stanski DR, White PF. Pharmacodynamicsmodelling of the EEG effect of ketamine in man. Journal of Pharmacokinetic Bio pharm. 1967; 15:241.
12. Sherry N. Rizk, Enas M. Samir. Use of ketofol to control emergence agitation in children undergoing adenotonsillectomy. Egyptian Journal of Anaesthesia. 2014; 30(1), 13-19.

Conflict of Interest: Nil Source of support: Nil