

Propofol Ketamine versus Propofol Fentanyl for Day Care Surgeries Comparison of Postoperative Recovery

HIRANAND¹, GOTAM KUMAR², RAVI KUMAR³, MUBARAK SHAH⁴, MUHAMMAD MOBASHIR-UL-HAQUE⁵, UDESH KUMAR⁶¹Senior Registrar, Shaheed Mohtarma Benazir Bhutto Institute of Trauma Karachi^{2,3,6}Senior Lecturers, Department of Anaesthesia, Sindh Institute of Urology & Transplantation Karachi⁴Junior Consultant, Department of Anaesthesia, The Kidney Center Karachi⁵Senior Registrar, Department of Anaesthesia, Sindh Infectious Diseases Hospital & Research Centre, KarachiCorrespondence to: Hiranand, Email: heranand75@gmail.com, Cell: 0331-3733027

ABSTRACT

Background: Intravenous anaesthetic should result in early discharge and rapid recovery with minimum side-effects. Propofol is considered gold standard in day care surgeries. Ketamine and fentanyl can also be used but they have several disadvantages including postoperative vomiting and nausea, emergence delirium and prolonged recovery.

Aimed: To compare mean recovery between propofol-ketamine and propofol fentanyl in day care surgeries.

Study Design: Single blinded randomized control study.

Place and Duration of Study: Department of Anaesthesiology, The Indus Hospital Karachi from 1st January to 31st May 2019.

Methodology: Sixty patients (30 in each group) with ASA grade I-II who had undergone elective day care surgery, 20 to 60 years of age of either gender were included at a tertiary care setup. In patients of Arm1, the induction of anesthesia was done with ketamine (1.0 mg/kg body wt) and propofol (1.0 mg/kg body wt.) given in IV line. In patients of Arm2, anesthesia induction was done with fentanyl (2.0 µg/kg body wt.) and propofol (1.5 mg/kg body wt.) given in IV doses. A pre-designed pro forma was used to record information of patients. Dexamethasone 0.1mg/kg body weight was used as antiemetic.

Results: Mean age of the patients at the time of surgery was 34.57±32 years with no significant difference in mean age between Arm-1 and Arm-2 (34.4±11.5 vs 34.7±11.2 respectively, p-value=0.902). Overall Median Modified steward recovery score at 5, 10 and 15 minutes was (Med (IQR): 8(7-9), 9(8-9) and 9(9-9) respectively). Moreover, Analysis shows that there is no significant difference in median Modified steward coma score at 5, 10 and 15 minutes between both Arms.

Conclusion: The mean recovery score is less after propofol-ketamine use in day care surgeries as compared to propofol fentanyl use.

Keywords: Propofol, Ketamine, Recovery time

INTRODUCTION

Intravenous sedation is second most comfortable, effective, and safest technique after inhalation sedation. There are two basic techniques available i.e. combination of different medicines or administration of only 1 medicine which is mainly benzodiazepine.¹ Widely and frequently used sedatives are midazolam, ketamine, propofol and fentanyl.²

Propofol, a widely used drug for induction, often causes local pain on administration in vein.³ Dexmedetomidine an α adrenergic agonist is used to alleviate propofol injection pain.⁴ Benefits of propofol include rapid post-procedure drug clearance, improved patient comfort and rapid recovery/discharge.⁵ Use of propofol usually increases the chances of body irritation, respiratory depression, coughing and anxiety during surgery.⁶

Ketamine, a synthetic phencyclidine derivative, safe and effective sedative agent. Ketamine produces combination of analgesia, amnesia, and sedation with minimal effects on airway and vital reflexes.⁷ Ketamine acts as NMDA receptor antagonist by inhibiting this receptor by reducing mean time and frequency of NMDA receptor channel opening thus preventing central sensitization.⁸ Ketamine also has analgesic effect but enhances the risk of complications including nausea, severe listlessness, hallucination, delirium, delayed recovery and severe muscle spasms.⁹

Fentanyl, which is synthetic opioid, is also widely used as analgesic and anesthetic.¹⁰ Literature has shown that propofol-ketamine is a better⁹ or equally safe and effective¹¹ as propofol-fentanyl for minor surgeries in terms of hemodynamic stability but literature on post-operative complications and recovery profile of both the combinations is scarce.

One of the primary concerns of anaesthetics is to use economical anaesthetic drugs that have, stable hemodynamic, quicker recovery and less post-operative complications. Ketamine is less expensive than fentanyl and is easily accessible in Pakistan. Studies have shown that ketamine in combination with propofol has equally or more stable hemodynamic than propofol-fentanyl but very few research have been done to study the effect of these two drug combinations on recovery profile and the results

of these studies are contradictory. So, if we can find that propofol-ketamine have quick recovery than we can use this combination as an alternative to propofol-fentanyl in our setting. This will help reduce health care cost in our hospital. Therefore, we aimed to do a single blinded study to compare mean recovery between propofol-ketamine and propofol fentanyl in day care surgeries.

MATERIALS AND METHODS

This single blinded randomised control trial study was conducted in a tertiary care setup at Karachi, Pakistan from 1st January 2019 to 31st May 2019. The protocol was approved by the Interactive Research and Development (IRD) ERC # IRD-IRB-2018-04-011. Non-probability consecutive sampling technique was used, sample was calculated assuming P-K Sample size Modified Steward recovery Scoring system; 11.42±4¹⁰ and 5.50±3.14¹² with 80% power and 5% α , 60 participants were enrolled (30 per group). We included the patients undergoing elective day care surgery both gender's with ASA grade I or II. We excluded the patients who had previous history of; allergy to any drug, patients on beta blockers, jaundice or hypertension and pregnant women or surgery time >1 hour. All patients and/or legal representatives were informed about objectives and written informed consent was taken from all patients.

All eligible patients were randomly assigned into two study arms, arm 1: Propofol-ketamine and arm 2: Propofol-fentanyl by envelope method (SNOSE PROTOCOL i.e. they were sequentially numbered, opaque sealed envelopes.).¹² The principal investigator opened the envelope to determine if the patient is assigned to Arm 1 (propofol-ketamine) OR Arm 2 (propofol-fentanyl). In both groups, injection of midazolam (0.08 mg/kg, max 5 mg) was administered 2 min before anaesthesia induction. In patients of Arm 1, the induction of anaesthesia was done with ketamine (1.0 mg/kg body wt) and propofol (1.0 mg/kg body wt.) given in IV line. In patients of Arm2, anaesthesia induction was done with fentanyl (2.0 µg/kg body wt.) and propofol (1.5 mg/kg body wt.) given in IV doses. After induction, appropriate laryngeal mask airway was inserted in both groups. Anaesthetic drug administration was stopped 5-7 min earlier. A dedicated nurse who collected the data

post-operatively was blinded to the anesthetic technique used for each patient. A pre-designed pro forma was used to record information of patients like age, gender, height, weight, BMI, ASA grade, arm, type of surgery, time anesthetic drugs given, time anesthetic drugs stopped, surgery start time, surgery end time, date of surgery, modified steward recovery Scoring system at 5, 10, 15 minutes. Dexamethasone 0.1mg/kg body weight was used as antiemetic.

All the data was entered and analyzed using SPSS version 21.0. Normality test was checked by using Shapiro Kolmogorov. Frequency and percentage were computed for all the qualitative variables like gender, ASA grade and type of surgery. Independent sample t-test was applied to assess significant difference in modified steward score between both arms. Effect modifiers were controlled through stratification of age, gender, BMI, duration of anesthetic drugs and duration of surgery. P-value \leq was taken as significant.

RESULTS

Thirty (50%) were in Arm-1 (Propofol-Ketamine) and 30(50%) were in Arm-2 (Propofol-Fentanyl). Mean age of the patients at the time of surgery was 34.57 ± 32 years with no significant difference in mean age between Arm-1 and Arm-2 (34.4 ± 11.5 vs 34.7 ± 11.2 respectively, p-value=0.902 (Tables 1). Percentage of patients according to different variables is shown in Table 2.

Overall Median Modified steward recovery Scoring system at 5, 10 and 15 minutes was (Med (IQR): 8(7-9), 9(8-9) and 9(9-9) respectively). Moreover, Analysis shows that there is no significant difference in median Modified steward recovery score at 5, 10 and 15 minutes between both Arms (Table 3).

Table 1: Descriptive statistics of different variables

Variable	No.	%
Gender		
Male	22	36.7
Female	38	63.3
Age (years)	34.57 ± 32	
ASA status		
ASA I	44	73.3
ASA II	16	26.7
BMI (kg/m ²)		

Table 3: Comparison of mean recovery between propofol-ketamine and propofol fentanyl in day care surgeries

Variable	Arm A [P-K]; n=30			Arm B [P-F]; n=30			P value
	Mean \pm SD	Median (IQR)	Min-Max	Mean \pm SD	Median (IQR)	Min-Max	
Modified Steward coma score at 5 min	7.6 \pm 1.4	8 (7-9)	3-9	7.6 \pm 1.1	7 (7-9)	6-9	0.656†
Modified Steward coma score at 10 min	8.6 \pm 0.6	9 (8-9)	7-9	8.6 \pm 0.8	9 (9-9)	6-9	0.231†
Modified Steward coma score at 15 min	8.9 \pm 0.4	9 (9-9)	7-9	9 \pm 0	9 (9-9)	9-9	0.301†
Age (years)	34.4 ± 11.5	31 (23-44)	20-60	34.7 ± 11.2	35 (25-42)	20-59	0.902
BMI (kg/m ²)	24.8 ± 5.7	23.7(20.7-29.2)	16-38.9	26.3 ± 5.5	26 (22.5-27.3)	19.5-46.7	0.318†
Duration of surgery (minutes)	37.2 ± 12.5	40 (25-50)	10-53	37.7 ± 10.4	40 (30-50)	20-60	0.874*
Duration of anesthesia drug given (min)	37.3 ± 12.6	40 (25-50)	15-55	37.5 ± 10.4	40 (30-45)	15-60	0.945*

*P>0.05 Independeng T-test, †Mann-Whitney U test

In our study overall median modified steward recovery score at 5, 10 and 15 minutes was (Med (IQR): 8(7-9), 9(8-9) and 9(9-9) respectively). Moreover, analysis shows that there is no significant difference in median modified steward coma score at 5, 10 and 15 minutes between propofol-ketamine and propofol fentanyl. Results of several studies also proved that, combination of ketofol and ketamine is safe and effective. Use of combination of these two drugs lessens the chances of side effects and enhances the probability of recovery.¹⁵ Combination of propofol and ketamine is same as that of propofol and fentanyl combination and cause dose reduction in dose.^{16,17} Clinical studies proved that mixture of PK and PF is safe to use but ketofol increases the chances of side-effects.¹⁸

In a study on 60 participants, mixture of PK is more-healthier and safer substitution as compared to PF.¹⁹ Another study which is performed over 100 participants in 2016, proved efficacy of mixture drug, PK and PF through comparison. PF mixture leads to decline

Median (IQR)	25.4 (22-28.1)	
Min-Max	16-46.7	
Arm group		
Arm A [P-K]	30	50.0
Arm B [P-F]	30	50.0
Duration of surgery (minutes)	37.45 ± 40	
Duration of anaesthesia drug given (minutes)	37.38 ± 40	
Modified Steward coma score		
At 5 minutes		
Median (IQR)	8 (7-9)	
Min-Max	3-9	
At 10 minutes		
Median (IQR)	9 (8-9)	
Min-Max	6-9	
At 15 minutes		
Median (IQR)	9 (9-9)	
Min-Max	7-9	

DISCUSSION

An ideal IV anaesthesia should be good enough to provide early discharge, fast recovery and minimum side effects. Propofol is considered as gold standard in surgeries. Ketamine and fentanyl are also anaesthetics but have few disadvantages as well including emergence delirium, emergence delirium and postoperative vomiting and nausea. Due to these problems, ketamine with combination of propofol proved a better alternative. It enhances the tolerability and efficacy in contrast to propofol-fentanyl.¹³ It prove to be a better combination because it had superior airway maintenance and hemodynamic stability.¹⁴

Table 2: Percentage of patients according to different variables

Variable	Study Arm		P value
	Arm A [P-K]	Arm B [P-F]	
Gender			
Male	20 (66.7%)	18 (60%)	0.793†
Female	10 (33.3%)	12 (40%)	
ASA grade			
I	22 (73.3%)	22 (73.3%)	0.774†
II	8 (26.7%)	8 (26.7%)	

†Pearson Chi Square test

in pulse numbers in contrast to ketofol whereas, PK shows more hemodynamic stability. Both drugs show quick and safe anesthetic effect with less side effects.²⁰

CONCLUSION

The mean recovery is less after propofol-ketamine use in day care surgeries as compared to propofol fentanyl use. So, we recommend that propofol-ketamine combination should be used routinely in our general practice for day care surgeries for quick recovery which will make our patients more comfortable during recovery phase.

REFERENCES

- Golpayegani MV, Dehghan F, Ansari G, Shayeghi S. Comparison of oral Midazolam-Ketamine and Midazolam-Promethazine as sedative agents in pediatric dentistry. Dent Res J 2012;9(1).
- Heard C, Smith J, Creighton P, Joshi P, Feldman D, Lerman J. A

- comparison of four sedation techniques for pediatric dental surgery. *Paediatr Anaesth*. 2010; 20(10): 924-30.
3. Sumalatha GB, Dodawad RR, Pandarpurkar S, Jajee PR. A comparative study of attenuation of propofol-induced pain by lignocaine, ondansetron, and ramosetron. *Indian J Anaesth* 2016; 60(1): 25-9.
 4. Singh D, Jagannath S, Priye S. Prevention of propofol injection pain: Comparison between lidocaine and ramosetron. *J Anaesthesiol Clin Pharmacol* 2014;30(2): 213.
 5. Thornley P, Al Beshir M, Gregor J, Antoniou A, Khanna N. Efficiency and patient experience with propofol vs conventional sedation: a prospective study. *World J Gastrointest Endosc* 2016;8(4):232-8.
 6. Eshghi A, Mohammadpour M, Kaviani N, Tahririan D, Akhlaghi N. Comparative evaluation of bispectral index system after sedation with midazolam and propofol combined with remifentanyl versus ketamine in uncooperative during dental 82 procedures. *Dent Res J (Isfahan)*. 2016; 13(1):1-6.
 7. Heidari SM, Loghmani P. Assessment of the effects of ketamine-fentanyl combination versus propofol-remifentanyl combination for sedation during endoscopic retrograde cholangiopancreatography. *J Res Med Sci* 2014; 19(9):860-6.
 8. Liu Y, Zheng Y, Gu X, Ma Z. The efficacy of NMDA receptor antagonists for preventing remifentanyl-induced increase in postoperative pain and analgesic requirement: a meta-analysis. *Minerva Anesthesiol* 2012;78(6):653-67.
 9. Goyal R, Singh M, Sharma J. Comparison of ketamine with fentanyl as coinduction in propofol anesthesia for short surgical procedures. *Int J Crit Illn Inj Sci* 2012;2(1): 17.
 10. Guit J, Koning H, Coster M, Niemeijer R, Mackie D. Ketamine as analgesic for total intravenous anaesthesia with propofol. *Anaesthesia* 1991;46(1):24-7.
 11. Bajwa SJS, Bajwa SK, Kaur J. Comparison of two drug combinations in total intravenous anesthesia: Propofol-ketamine and propofol-fentanyl. *Saudi J Anaesth* 2010; 4(2):72.
 12. Doig GS, Simpson F. Randomization and allocation concealment: a practical guide for researchers. *J Crit Care* 2005;20(2):187-91.
 13. Saha K, Saigopal M, Sundar R, Palniappan M, Mathew AC. Comparative evaluation of propofol-ketamine and propofol-fentanyl in minor surgery. *Indian J Anaesth* 2001;45: 100-3.
 14. Vora KS, Prabodhachandran MS, Bhosale GP, Singhal N, Parikh GP, Shah VR. Comparison of admixtures of propofol-thiopentone, propofol-ketamine and propofol in ambulatory surgery. *J Anaesth Clin Pharmacol* 2005;21:413-8.
 15. Stanley TH, Berman L, Green O, Robertson D. Plasma catecholamine and cortisol responses to fentanyl – Oxygen anesthesia for coronary-artery operations. *Anesthesiology* 1980;53:250-3.
 16. Khutia SK, Mandal MC, Das S, Basu SR. Intravenous infusion of ketamine-propofol can be an alternative to intravenous infusion of fentanylpropofol for deep sedation and analgesia in paediatric patients undergoing emergency short surgical procedures. *Indian J Anaesth* 2012;56:145-50
 17. Sharma S, Jaitawat SS, Partani S, Saini R, Sharma N, Gupta S. A randomised controlled trial to compare TIVA infusion of mixture of ketamine propofol (ketofol) and fentanyl-propofol (fentofol) in short orthopaedic surgeries. *IJCA* 2016;3(3):400-16.
 18. Akin A, Guler G, Esmooglu A, Bedirli N, Boyaci A. A comparison of fentanyl-propofol with a ketamine-propofol combination for sedation during endometrial biopsy. *J Clin Anesth* 2005;17:187-90.
 19. Kb N, Cherian A, Balachander H, Kumar C Y. Comparison of propofol and ketamine versus propofol and fentanyl for puerperal sterilization, A randomized clinical trial. *J Clin Diagn Res* 2014;8:GC01-4.
 20. Singh Bajwa SJ, Bajwa SK, Kaur J. Comparison of two drug combinations in total intravenous anesthesia: Propofol-ketamine and propofol-fentanyl. *Saudi J Anaesth* 2010;4:72-9.