IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 4 Ser.9 (April. 2023), PP 17-22
www.iosrjournals.org

A Comparative Study on Ketamine and Propofol Versus Fentanyl And Propofol For Total Intravenous Anaesthesia In Short Surgical Procedures In A Tertiary Care Hospital

Dr. Siddhartha Das Roy
Junior Resident Department of Anaesthesiology Narayan Medical College and Hospital Sasaram Bihar.
Dr. Ritvik Rajat
Junior Resident Department of Anaesthesiology Narayan Medical College and Hospital Sasaram Bihar.
Dr. Hriday Kumar
Professor Department of Anaesthesiology Narayan Medical College and Hospital Sasaram Bihar.

Abstract
Introduction:
Total intravenous anaesthesia can be an effective alternative to inhalational anaesthesia. Propofol has been considered as a gold-standard for total intravenous anaesthesia (TIVA) for short surgical procedures with its main shortcoming being lack of analgesia, therefore it is always combined with an analgesic. Ketamine and fentanyl are the popular analgesic in this context.
Aim:
To compare the induction characteristics, maintenance of anaesthesia, awakening and recovery characteristics while performing TIVA with either propofol-ketamine or propofol-fentanyl combinations.
Method:
This randomised, single blinded study was conducted, from April 2022 to March 2023, in a tertiary care hospital in Sasaram Bihar. Total of 76 patients of either sex, aged between 18-45 years with a duration of surgery less than 30 mins were equally divided into two groups. Group A received propofol ketamine (1:1), prepared by mixing 4 mL ketamine (50 mg/mL) with 20 mL of 1% Propofol (10 mL/kg), while group B received propofol-fentanyl solution (1:1) was prepared by mixing 4 mL (50 µg/mL) of fentanyl with 20 mL of 1% propofol (10 mg/mL). Induction was done with ketamine 10 mg/ kg + Propofol 1 mg/kg in group A and fentanyl 1.5 µg/kg + Propofol 1.5 mg/kg while maintenance of anaesthesia was achieved with continuous infusion of the prepared solutions for either group respectively at a rate of around 20 mL/hour or more, as per required to maintain the Ramsay Sedation Scale (RSS) score of 6. Intraoperative haemodynamic parameters, including respiratory rates, awakening time, recovery time and the possible the side effects were recorded at regular intervals. Student's t-test was used for quantitative data and Chi-square test for qualitative data. A p-value of less than 0.05 was considered statistically significant.
Result:
Patients of group B developed significantly more incidents of bradycardia (20 in group B and 3 in group A) and hypotension (28 in group B and 2 in group A). Respiratory depression was also significantly more in group B (p-value<0.005). Recovery, VAS score, awakening and other side effects were all compared in the two groups.
Conclusions:
Ketamine and fentanyl with propofol infusion for short surgical procedures are equally safe and efficacious. In both groups stable haemodynamics and good recovery profile were noted.
Keywords: Total Intravenous Anaesthesia; Ketamine; Propofol; Fentanyl.

Date of Submission: 10-04-2023 Date of Acceptance: 23-04-2023

I. INTRODUCTION

Total intravenous anaesthesia (TIVA) is a modified form of general anaesthesia where induction as well as maintenance of anaesthesia is done with intravenous agents alone. TIVA is administered as a combination of hypnotic and analgesic drugs without administration of any inhalation agents[1] . It can be an effective alternative to general endotracheal anaesthesia when rapid recovery from anaesthesia is desired [2]. Drugs used for TIVA should have quick onset, smooth induction, easy maintenance, quick recovery, and minimal side effects. TIVA has many advantages over inhalational anaesthesia[1], such as no operating room pollution, minimal cardiac depression, less neurohumoral response, decreased oxygen consumption, evasion of

distension of air-filled body spaces and provides optimum operating conditions for the surgeon. Disadvantages of TIVA are need for specific equipment such as a target-controlled infusion (TCI) set, syringe pumps or infusion pumps for accurate administration and drugs. TIVA needs optimal drug metabolism in the body for rapid recovery from anaesthesia. Recovery may be delayed in TIVA in patients with hepatic disease. TIVA is administered as an initial Loading dose and a Maintenance dose. A Loading dose is determined based on the volume of distribution and the initial plasma drug concentration. Following initial administration, the drug is redistributed to tissues and eliminated as well. To maintain the desired plasma drug concentration, a Constant Rate Infusion (CRI) should be initiated. The infusion rate is determined by the clearance of the drug and the plasma drug concentration (based on pharmacokinetic studies). The depth of the anaesthesia can be maintained by either a continuous infusion or by intermittent boluses of drug. To perform TIVA, the use of a target-controlled infusion (TCI) set is recommended. TIVA can also be administered manually (i.e., without a TCI pump), thorough a fixed infusion rate in syringe pump. Premedication with an anticholinergic like glycopyrrolate and a short acting benzodiazepine like midazolam is recommended as adjuvants in TIVA. The advantages and disadvantages of TIVA should be considered on individual case basis, while choosing it as an anaesthetic protocol.

Ketamine is a potent analgesic; its anaesthetic and analgesic effects have been suggested to be mediated by different mechanisms. Ketamine in subanaesthetic doses with propofol has gained attention in total intravenous anaesthesia4 because of its powerful analgesic action in a small dose without causing myocardial and respiratory depression. Ketamine also causes some degree of sympathetic stimulation, which tends to counter balance the cardiovascular effects of propofol. It has very high margin of safety, no irritation of the veins and no negative influence on ventilation or circulation except the disadvantage of producing hypertension and psycho mimetic emergence phenomena[3].

Fentanyl on other hand is the most frequently used opioid in clinical anaesthesia today. Fentanyl is synthetic opioid analgesic, which has rapid onset and short duration of action and has been used in combination with propofol for total intravenous anaesthesia satisfactorily[3].

II. MATERIALS AND METHODS

This randomised, single blinded clinical study was conducted at department of Anaesthesiology of Narayan Medical College and Hospital Sasaram, Bihar for period of April 2022 to March 2023.

Inclusion criteria:

A total of 76 patients of either sex, aged between 18-45 years of age with an ASA physical status I and II, who were posted for short surgical procedures, with a duration of surgery less than 30 mins (like fibroadenoma of breast excision, circumcision, dilatation and curettage, dilatation and evacuation etc.) that require TIVA.

Exclusion criteria:

Patients refusing to participate in the study, having Basal Metabolic Index (BMI)>35kg/m^2, known allergy or contraindications to either study drugs, patients with head injury, seizure disorder, congestive cardiac failure, haemorrhagic disorder, chronic kidney diseases or neurological disorders.

Sample size calculation:

PS Power and Version 2.1.30, February 2003, was used for sample size calculation. Sample size was calculated taking a difference of wake fulness or recovery score of 0.20 as clinically acceptable margin [3]. Sample size thus, required in either arm was estimated to be 34. Taking a 10% attrition, the study subjects recruited in each arm was 38.

Procedure:

After taking written informed consent from the patients and a detailed preanesthetic check-up, the patients were randomly divided into two equal groups, each comprising of 38 patients, by opening sealed envelopes. After receiving the patients in the operation theatre, monitors were attached and an intravenous cannula of 18G secured, following which the patients were preloaded with Lactated Ringer's Solution @10 mL/kg body weight. All the patients in either of the groups were given supplemental oxygen flow at the rate of 6L/min via face mask and were then premedicated with injections of glycopyrrolate 0.2 mg, midazolam 0.03 mg/kg and ondansetron 4 mg intravenous 2 minutes before induction. In a single 50 mL syringe, a mixture of propofol-ketamine or propofol-fentanyl was prepared by using an aseptic technique for delivery via an infusion pump. In case of group A (n=38), a propofol ketamine solution (1:1) was prepared by mixing 4 mL ketamine (50 mg/mL) with 20 mL of 1% propofol (10 mL/kg), a total of 24 mL of solution. In case of group B (n=38), a propofol-fentanyl solution (1:1) was prepared by mixing 4 mL (50 µg/mL) of fentanyl with 20 mL of 1%

propofol (10 mg/mL), a total of 24 mL. Induction was done with ketamine 10 mg/kg + Propofol 1mg/kg in group A and fentanyl 1.5 µg/kg + Propofol 1.5 mg/kg and achievement of induction in both the groups were considered with a Ramsay Sedation Scale (RSS) of 6. In both groups, maintenance of anaesthesia was achieved with continuous infusion of the prepared solutions for either group respectively at a rate of around 20 mL/hour or more, as per required to maintain the RSS score of 6. Haemodynamic parameters and RSS were observed continuously and recorded at intervals of every 5 minutes during operation. Neither any muscle relaxant was used nor the patients were intubated. After completion of the surgery or end of the skin closer depending on the type of surgery, infusion was stopped and patients were transferred to the recovery room, Postanesthesia Care Unit (PACU) with oxygen support at the rate of 6L/min and vitals were monitored for 1 hour. Duration of surgery, awakening time (defined as the time from the first administration of the drug to the opening of eyes to verbal commands after surgery). Total sedation time (awakening time) was defined as the time, from the first administration of the drug to the opening of eyes to verbal commands after surgery. Recovery time was defined as the time taken from stopping the infusion of the study drug to the point when the patients will achieve a Modified Aldrete Score of more than or equal to 8 [13]. After ensuring a modified Aldrete score ≥8 patients were shifted to the surgery ward. Postoperative analgesia is assessed by Visual Analogue Scale (VAS).

Statistical Analysis:

Statistical Package for Social Sciences software version 20.0 (IBM) was used for statistical analysis and descriptive analysis was done in the form of proportion for categorical variables, mean [Standard Deviation (SD)] or median {Interquartile range (IQR)} for continuous variables. Data were checked for normal distribution using tests (Shapiro-Wilk normality test) for normality and parametric or non-parametric test was performed accordingly. Student's t-test was used for quantitative data and Chi-square test for qualitative data. A p-value of less than 0.05 was considered statistically significant.

III. Results:

[Table/Fig-1] shows that the age and sex difference with ASA distribution were similar.

Parameters		Group A (n=38)	Group B (n=38)	p-value
Age (in years) (Mean±SD)		27.16±7.59	27.32±5.66	0.502
Gender	Male	14	15	0.813
	Female	24	23	
ASA	I	22	23	0.796
	II	16	15	

[Table/Fig-1]: Distribution of study subjects according to age, gender and ASAstatus.

ASA: American society of anesthesiologists

[Table/Fig-2] shows that the time of awakening and difference of recovery time among the two groups were not statistically different, although both were slightly more among group B. The postoperative pain score was less among the patients of group A than group B, although it was not statistically significant.

Criteria	Group A (n=38)	Group B (n=38)	p-value
Time of awakening	23.68±3.35	24.34±2.66	0.521
Recovery time	27.82±3.58	29.26±3.19	0.084
VAS Score	0.32±0.47	0.45±0.50	0.241

[Table/Fig-2]: Distribution of study subjects according to time of awakening,recovery time and postoperative VAS score.

[Table/Fig-3-5] show that the mean heart rate, systolic blood pressure, respiratory rate was significantly more among the subjects of group A than group B.

[Table/Fig-6] shows that the occurrence of hypotension and bradycardia were statistically more among the subjects of group B than group A patients.

However, the occurrence of nausea among both the groups was similar. Among the other side effects, there was no complication like emergence reaction, agitation, increased oral secretions in this study and only one patient in group A and two in group B had nausea but no vomiting.

Time (minutes)	Heart rate		p-value
	Group A	Group B	
1	81.55±8.42	76.21±7.17	0.007
2	77.82±8.45	70.32±7.23	<0.001
3	75.08±8.02	64.45±6.97	0.001
4	72.95±8.78	61.18±5.10	<0.001
5	71.68±8.85	60.37±5.10	0.001
10	72.45±8.30	65.05±4.01	<0.001
15	74.79±7.78	68.89±3.68	<0.001
30	79.92±8.06	73.26±4.51	0.001

[Table/Fig-3]: Distribution of heart rate among the patients (n=38).

Time (minutes)	Systolic blood pressure		p-value
	Group A	Group B	
1	122.63±8.04	118.26±6.84	0.030
2	120.55±8.51	112.47±7.06	<0.001
3	117.18±8.93	106.03±6.50	0.001
4	115.87±7.84	102.97±6.56	<0.001
5	114.87±6.85	103.21±5.93	<0.001
10	115.89±7.30	106.97±5.31	0.001
15	117.97±6.73	110.97±5.23	<0.001
30	121.97±6.57	116.24±5.87	0.001

[Table/Fig-4]: Distribution of Systolic Blood Pressure (SBP) among the patients (n=38).

Time (minutes)	Respiratory rate		p-value
	Group A	Group B	
1	14.11±0.95	12.58±0.75	<0.001
2	12.84±0.85	12.08±0.85	0.001
3	12.45±0.95	11.32±0.66	<0.001
4	11.97±0.78	11.11±0.45	<0.001
5	11.92±0.67	11.26±0.64	<0.001
10	12.66±0.90	11.87±0.57	0.001
15	13.34±0.87	12.47±0.60	<0.001
30	14.37±0.91	13.39±0.49	0.001

[Table/Fig-5]: Distribution of Respiratory rate (RR) among the patients (n=38).

Criteria	Group An (%)	Group B n (%)	Totaln (%)	p-value
Hypotension	02 (5.3)	28 (73.7)	30 (39.5)	<0.001
Bradycardia	03 (7.9)	20 (52.6)	23 (30.3)	<0.001
Nausea	01 (2.6)	02 (5.3)	3 (3.9)	0.556

[Table/Fig-6]: Distribution of study subjects according to hypotension, bradycardiaand nausea (n=38).

A p-value of less than 0.05 was considered statistically significant

IV. Discussion

TIVA (Total Intravenous Anaesthesia), the anaesthetic procedure of choice for short surgical procedures, is generally conducted using propofol based anaesthesia. However, due to lack of its analgesic property, several other drugs have been used as supplemental analgesic, among which ketamine and fentanyl are

most commonly used. Few studies have shown propofol-ketamine having a better result than propofol-fentanyl though a definitive conclusion needs further research [2,10-12].

This study was thus done to compare the induction, maintenance of anaesthesia, awakening and recovery characteristics following anaesthesia with propofol-ketamine and propofol-fentanyl combinations for TIVA by studying the incidences of any adverse effects in adult patients undergoing short surgical procedures.

In the present study, continuous infusion of propofol-ketamine (group A) and propofol-fentanyl (group B) were used to maintain a steady state sedation level, by achieving a RSS of 6. Intraoperatively, there was not much difference among the total dose of drugs required in either of the groups to maintain a steady state level. Similarly, awakening time, recovery time among the patients of either group were also found to be non-significant.

However, regarding haemodynamic, heart rate was found to significantly reduced in group B (after achieving RSS 6) at 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 10 minutes, 15 minutes; whereas the Systolic Blood Pressure (SBP) also showed significant decrease in patients of group B at those same time intervals. Respiratory Rate (RR) started decreasing more at group B and became statistically significant (p-value<0.05) at 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 10 minutes, 15 minutes, 30 minutes as well in this study.

Tajoddini S and Motaghi M, compared the sedative, analgesic effects as well as safety characteristics of ketamine-propofol and fentanyl-propofol combinations in painful emergency procedures [10]. They found that the ketamine-propofol group provided superior analgesia and sedation with faster recovery and lesser adverse events in comparison to the fentanyl-propofol group.

Reddy BAP et al., compared the intraoperative haemodynamic responses as well as postoperative spontaneous eye opening and PONV after injection of propofol-ketamine and propofol-fentanyl in 100 patients undergoing short surgical procedures under TIVA [11]. They concluded that haemodynamic responses were better in propofol-ketamine group with lesser adverse effects, though patients in propofol-fentanyl had superior postoperative recovery.

El-Rab NAG et al., made a comparative study between propofol-ketamine and propofol-fentanyl combinations in paediatric patients undergoing upper gastrointestinal endoscopy [12]. They studied 60 children aged 6-12 years and concluded that propofol-ketamine provided better haemodynamic stability with comparable recovery and adverse effect profiles.

Sharma R et al., did a randomised, double-blind study on 100 adult patients, giving slow bolus of premixed injection of either ketamine-propofol (1 mg/kg) or fentanyl-propofol (1.5 mg/kg) followed by TIVA infusion to a predetermined sedation level using RSS for short orthopaedic procedures [2]. They reported a significant decrease (p-value<0.001) in the pulse rate, systolic and diastolic blood pressure in intraoperative and postoperative period in group 2 (fentanyl propofol group) whereas there was significant rise in pulse rate, systolic and diastolic blood pressure in group 1 (ketamine-propofol group). Respiratory depression was more pronounced in group 2. Mean total sedation time as well as recovery time was significantly prolonged in group 2 compared to group 1.

Kurdi MS et al., conducted a prospective randomised double-blind study among 60 adult females scheduled for elective tubal sterilisation by mini laparotomy in which the patients received a slow bolus injection followed by Ketofol containing ketamine: Propofol (1:1) (group A), ketamine: propofol (1:2) (group B), and fentanyl: propofol (group C) to a predetermined sedation level using RSS [14]. Considering the onset of sedation, intraoperative sedation score, and recovery time, group C (fentanyl-propofol) patients were less sedated than counter parts in group A and B. Considering the verbal rating scale for pain postoperatively, group C patients had poor analgesia compared to group A and B. They found that ketamine-propofol provides better sedation level, better hemodynamic and respiratory stability compared to fentanyl-propofol.

Similarly, Akhondzadeh R et al., in their study, comparing the effects of propofol-fentanyl with propofol-ketamine to sedate patients undergoing endoscopic retrograde cholangiopancreatography outside the operating room, found that the lower amount of pain and apnoea in propofol- ketamine group [15].

In another study done by Singh Bajwa SJ et al., propofol-fentanyl combination produced a significantly greater fall in pulse rate and in both systolic and diastolic blood pressures as compared to propofol-ketamine during induction of anaesthesia [3]. Propofol-ketamine combination produced stable hemodynamics during maintenance phase.

Similar findings were also found in studies done by Tosun Z et al., Goyal R et al., Nalini KB et al., Khutia SK et al., in all of which haemodynamic status were found to be well maintained in ketofol group with equally acceptable anaesthesia, recovery, analgesia and side-effect profiles [16-19]. The findings of all these studies thus corroborate with the findings of this present study.

V. Conclusion:

Thus, from this study we can well conclude that ketamine when combined with propofol can provide better analgesia with adequate haemodynamic stability and minimal side effects in comparison to Fentanyl during procedural sedation in adult patients undergoing short surgical procedures. Therefore, propofol-ketamine combination provides us with a perfect option for providing TIVA, particularly in daycare procedures.

References

[1]. Matsuki A. A review of recent advances in total intravenous anaesthesia. Masui 1991;40(5):684-691.
[2]. Dunnihoo M, Wuest A, Meyer M, et al. The effects of total intravenous anaesthesia using propofol, ketamine, and vecuronium on cardiovascular response and wake up time. AANA J 1994;62(3):261-266.
[3]. Guit JBM, Koning HM, Coster ML. Ketamine as analgesic for total intravenous anaesthesia with propofol. Anaesthesia. 1991;46(1):24-7.
[4]. Akcaboy ZN, Akcaboy EY, Albayrak D, Altinoren B, Dikmen B. Gogus N, et al. Canremifentanil be a better choice than propofol for colonoscopy during monitored anesthesia care? Acta Anaesthesiol Scand. 2006;50:736-41.
[5]. Lichtenbelt BJ, Mertens M, Vuyk J. Strategiest ooptimise propofol-opioid anaesthesia. Clin Pharmacokinet. 2004;43:577-93.
[6]. Koo SW, Cho SJ, Kim YK, Ham KD, Hwang JH. Small-dose ketamine reduces the painofpropofol injection. Anesth Analg. 2006;103(6):1444-47.
[7]. Akhondzadeh R, Runassi N. Evaluation of analgesic effect of the ketamine on pain injection of propofol in patients undergoing general anesthesia. Int J Univ Pharm Life Sci. 2014;3:72-75.
[8]. Akhondzade R, Pipelzade MR, Gousheh MR, Sarrafan N, Mahmoodi K. Comparison ofthe analgesic effect ofintra-articular and extra-articular injection of morphine and ketaminecompound in arthrotomy lower limb surgery under spinal anesthesia. Pak J Med Sci. 2014;30(5):942-45.
[9]. Disma N, Astuto M, Rizzo G, Rosano G, Naso P, Aprile G, et al. Propofol sedation with fentany lormidazolam durin goes ophagogastroduodenos copy in children. Eur J Anaesthesiol. 2005;22(11):848-52.
[10]. Tajoddini S, Motaghi M. Sedative and analgesic effects of propofol-ketamine versus propofol-fentanyl for emergency department procedures. Hong Kong Journal of Emergency Medicine. 2022;29(4):212-19.
[11]. Reddy BAP, Kumari BG, Kumar VAK. A compartive study of ketamine and propofol versus fentanyl and propofol in total intravenous anaesthesia for short surgical procedures. MedPulse International Journal of Anesthesiology. 2019;2(3):238-43.
[12]. El-Rab NAG, El-Rahem MGA, Mohamed MK. A comparative study between propofol-ketamine and propofol-fentanyl for sedation during pediatric diagnostic upper gastrointestinal endoscopy. J Curr Med Res Pract. 2019;4:344-49.
[13]. Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth. 1995;7(1):89-91.
[14]. Kurdi MS, Deva RS. A comparison of two different proportions of ketofol with Fentanyl-Propofol for sedoanalgesia for tubal sterilization by minilaparotomy: A randomised double-blindtrial. J Obstet Anaesth Critical Care. 2015;5(2):84-89.
[15]. Akhondzadeh R, Ghomeishi A, Nesioonpour S, Nourizade S. A comparison between the effects of propofol-fentanyl with propofol-ketamine for sedation in patients undergoing endoscopic retrograde cholangiopancreatography outside the operating room. Biomed J. 20;39(2):145-49.
[16]. Tosun Z, Aksu R, Guler G, Esmaoglu A, Akin A, Aslan D, et al Propofol-ketamine vspropofol-fentanylfor sedation during pediatric upper gastrointestinal endoscopy. Paediatr Anaesth. 2007;17(10):983-88.
[17]. Goyal R, Singh M, Sharma J. Comparison of ketamine with fentanyl as co• induction in propofol anesthesia for short surgical procedures. Int J Crit Illn Inj Sci. 2012;2(1):17-20.
[18]. Nalini KB, Cherian A, Balachander H, Kumar CY. Comparison of Propofol and Ketamine versus Propofol and Fentanyl for puerperal sterilization, a randomised clinical trial. J Clin Diag Res. 2014;8(5):GC0l-04.
[19]. Khutia SK, Mandal MC, Das S, Basu SR. Intravenous infusion of ketaminepropofol can be an alternative to intravenous infusion of fentanyl-propofol for deep sedation and analgesia in paediatric patients undergoing emergency short surgical procedures. Indian J Anaesth. 2012;56(2):145-50

Dr. Siddhartha Das Roy, et. al.” A Comparative Study On Ketamine And Propofol Versus Fentanyl And Propofol For Total Intravenous Anaesthesia In Short Surgical Procedures In A Tertiary Care Hospital.*” IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 22(4),* 2023, pp. 17-22.