Original Research Article

Indian Journal of Anesthesia and Analgesia
2018; 5(3): 402-408
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.5318.8

Comparitive Evaluation of Propofol with Ketamine versus Propofol with Fentanyl in Total Intravenous Anaesthesia for Day Care Surgeries

R. Yogarajan[1], Edger Nelson[2]

[1,2]Assistant Professor, Department of Anaesthesiology, Critical Care & Pain Medicine, Sree Balaji Medical College & Hospital Chrompet, Chennai, Tamil Nadu 600044, India.

Abstract

Aim of the Study The aim of the study is to compare the recovery times when Propofol with Fentanyl or Propofol with Ketamine are used for maintenance of anaesthesia in day case surgery and also to determine which agent combination is suitable to make the patient home fit at the earliest.

Keywords: Propofol; Ketamine; Fentanyl; Day Care Surgeries.

Introduction

An ideal general anaesthetic should provide quick and pleasant induction, predictable loss of consciousness, stable operating conditions, minimal adverse effects, rapid and smooth recovery of protective reflexes and psychomotor functions. The current practice is to use a balanced anaesthesia technique with depth of anaesthesia, analgesia and relaxation produced by different drugs in combination.

This study was conducted to evaluate and compare two drug combinations of Total Intravenous Anaesthesia using Propofol with Ketamine and Prop ofol with Fentanyl and to study the analgesic characteristics and recovery characteristics following anesthesia with these techniques. The development of anesthesia since its introduction has been erratic, long periods of stagnation being occasionally broken by improvement and advances. General anesthesia has undergone a vast number of improvements and modifications and even its recently modified form total intravenous anesthesia (TIVA; induction as well as maintenance of anesthesia with intravenous agents only) has undergone many improvements ever since its introduction into clinical practice.

TIVA has many advantages over inhalational anesthesia such as

- No operating room pollution
- Minimal cardiac depression
- Lesser neurohumoral response
- Decreased oxygen consumption
- Avoids distension of air -filled spaces within the patient's body, thus producing optimum operating conditions for the surgeon
- Avoids postoperative diffusion hypoxemia
- Decreases the incidence of postoperative nausea and vomiting (PONV)
- In day care surgery for rapid recovery.

Moreover, TIVA can be used not only in well - equipped hospital setting but at remote location also with only oxygen and ventilation facilities.

Corresponding Author: Edger Nelson, Assistant Professor, Critical Care & Pain Medicine, Sree Balaji Medical College & Hospital Chrompet, Chennai, Tamil Nadu 600044, India.
E-mail: raj_udpm@yahoo.co.in

Received on 20.12.2017, **Accepted on** 17.01.2018

Various drugs have been tried from time to time in TIVA. Since no single drug can provide all the characteristics of an ideal intravenous agent, several drugs are used in different combinations to provide balanced anesthesia in TIVA, that is, amnesia, hypnosis and analgesia.

Aim of the Study

The aim of the study is to compare the recovery times when Propofol with Fentanyl or Propofol with Ketamine are used for maintenance of anaesthesia in day case surgery and also to determine which agent combination is suitable to make the patient home fit at the earliest.

Materials and Methods

This study was carried out in the General Surgery theatre, Sree Balaji Medical college hospital, Chennai after obtaining institutional approval.

The aim of the study was to compare the Phase I and Phase II recovery times when Propofol with Fentanyl or Propofol with Ketamine are used for the maintenance of anaesthesia in day case procedures and also to determine which agent is suitable to make the patient home fit at the earliest.

Study Design

The study was a randomized prospective study.

Selection of Cases

Forty patients undergoing Day Case surgeries were selected for the study. Their age ranged from 18 to 50years. All the patients were assessed and those with normal clinical, biochemical radiological and hematological parameters were selected. Informed written consent was obtained from all the patients. Each patient was ran domly allocated to either the Fentanyl or the Ketamine group bylots. The groups were named 'F' for Fentanyl and 'K' for Ketamine

Inclusion Criteria

- Age group between 18 to 50 years
- Normal biochemical and hematological parameters
- ASA class I, II
- No known hypersensitivity to eggs or sulpha drugs
- Airway MPC 1, 2 and 3
- Minor Surgical and Obstetric procedures
- Surgery lasting less than 90 minutes duration
- Patients normally able to ambulate well
- Educated attender who can understand and carryout instructions

Exclusion Criteria

- Patient not willing
- ASA class III and above
- Known hypersensitivity to eggs or sulpha allergy
- Patient with known psychiatric disorder

Major surgeries requiring overnight hospital stay

- Surgeries near or involving the airway
- Patient having difficulty in walking
- No attender or attender not educated enough to carry out instruction

Materials

1. Boyles machine
2. Syringe infusion pump
3. Appropriate drugs in preloaded syringes
4. Appropriate sized Laryngeal Mask Airways
5. Functioning Laryngoscope with appropriate size blades
6. Appropriate sized Endotracheal tubes
7. Equipment and drugs for resuscitation
8. Suxamethonium for emergency use in airway control

Methods

Pre-Operative Preparation

Patients were assessed pre-operatively, procedure was explained to the patient and informed consent obtained. They were assessed with particular attention for any contraindications. The tests for recovery and the importance of strictly following instructions were emphasized.

Premedication

All the patients received Glycopyrrolate 5μg/Kg premedication fifteen minutes before induction.

Conduct of Anesthesia

On arrival of the patient in the operating room, monitors like pulseoximetry, Non invasive BP and ECG were connected and baseline values of HR, BP and SpO2 were recorded. An intravenous access was obtained in the nondominant arm.

Patients were randomly allotted by lots to Group F or Group K. Patients allocated to group F were induced with Propofol 2mg/Kg I.V. and Fentanyl 2ìg/Kg. An appropriate sized Laryngeal Mask Airway was introduced and its correct position confirmed. No muscle relaxants were used. In case of any movement by the patient, an additional bolus of Propofol 0.5mg/Kg was given.

Patients in group K were indu ced with Propofol 2mg/Kg I.V. and Ketamine 0.5mg/Kg. An appropriate sized Laryngeal Mask Airway was introduced and its correct position confirmed. No muscle relaxants were used. In case of any movement by the patient, an additional bolus of Propofol 0.5mg/Kg was given.

Fentanyl Group

Immediate post induction, this group of patients received a continuous infusion of Propofol from a syringe pump.(B Braun Melsungen 'S' series) according to the following scheme: -

- 12 mg/kg/h ´ 10 min (200 mcg/kg/min)
- 10 mg/kg/h ´ 20 min (167 mcg/kg/min)
- 8 mg/kg/h ´ 1 h (133 mcg/kg/min)
- 6 mg/kg/h maintenance (100 mcg/kg/min)

In addition, they were connected to the Bain breathing circuit with 66% Nitrous oxide and 33% Oxygen. The patient spontaneously ventilated througho ut the procedure. Any spontaneous movement was tackled with a 20mg bolus of Propofol. Supplementary Fentanyl 1μg/Kg bolus was given intraoperatively if the procedure extended beyond 1 hour.

Ketamine Group

Immediate post induction, this group of patients received a continuous infusion of Propofol from a syringe pump.(B Braun Melsungen 'S' series) according to the following scheme: -

- 12 mg/kg/h ´ 10 min (200 mcg/kg/min)
- 10 mg/kg/h ´ 20 min (167 mcg/kg/min)
- 8 mg/kg/h ´ 1 h (133 mcg/kg/min)
- 6 mg/kg/h maintenance (100 mcg/kg/min)

In addition, they were connected to the Bain breathing circuit with 66% Nitrous oxide and 33% Oxygen. The patient spontaneously ventilated throughout the procedure. Any spontaneous movement was tackled with a 20mg bolus of Propofol. Supplementary Ketamine 0.5mg/kg bolus was given every 20 minutes intraoperatively.

Parameters Studied

Time to Phase I Recovery: This is the time taken to the discontinuation of Propofol Aldrete time when the score is ≥ 9

Time to Phase II Recovery: This is the time taken from discontinuation of Propofol to the time when the PADSS score is ≥ 9. It is also taken as the time to Home readiness.

Patients in both the groups did not differ significantly with respect to the demographic data as well as duration of surgery and anaesthesia

The mean pulse rate was 75±4 for Group K and 77±8 for Group F at base line level and was statistically insignificant. There was slight increase in pulse rate after induction in both the groups which was statistically insignificant

The mean systolic blood pressure was 117±6 for Group K and 120±5 for Group F which was statistically insignificant. However there was statistically significant fall in systolic blood pressure in the Group F (P value 0.0001)

Table 1: Demographic data

Variables	Group (K) N=20	Group (P) N=20	P Value
Age (Years)	35±13	38±15	0.80
Weight (Kgs)	53±11	53±13	0.52
Sex (m/f)	14/16	11/19	0.54
Time of Surgery (mins)	49±6	51±4	0.051
Time of Anaesthesia (mins)	58±7	59±5	0.38

Table 2: Mean pulse rate

Time	Group (K) n=20	Group (F) n=20	p Value
Pre OP	7 5±4	77±8	0.181
After	82±4	84±5	0.068
Induction			
5 mins	80±5	83±7	0.061
10 mins	80±6	80±7	0.931
15 mins	80±6	77±6	0.093
20 mins	81±7	79±6	0.063
25 mins	81±5	79±5	0.069
30 mins	79±5	77±6	0.128
40 mins	79±6	78±5	0.327
50 mins	78±6	76±5	0.211
60 mins	79±5	78±4	0.243

Table 3: Mean systolic blood pressure

Time	Group (K) N=20	Group (F) N=20	p Value
Pre OP	1 17 ±6	120±5	0.15
After Induction	116±14	107±9	0.0001
5 mins	117±8	115±11	0.470
10 mins	117±7	115±12	0.273
15 mins	116±7	118±17	0.630
20 mins	116±6	117±16	0.634
25 mins	117±7	120±18	0.218
30 mins	117±6	114±12	0.152
40 mins	116±7	112±10	0.019
50 mins	116±6	114±12	0.230
60 mins	117±7	113±10	0.075

Table 4: Mean diastolic blood pressure

Time	Group (K) N=20	Group (F) N=20	p Value
Pre OP	77±7	75±6	0.17
After	74±5	73±6	0.54
Induction			
5 mins	77±4	76±6	0.10
10 mins	77±7	75±5	0.07
15 mins	77±6	74±6	0.08
20 mins	78±6	76±7	0.07
25 mins	77±6	75±7	0.30
30 mins	77±6	76±7	0.65
40 mins	76±7	75±7	0.44
50 mins	77±6	75±6	0.25
60 mins	76±5	74±6	0.12

Table 5: PONV

Nausea/Vomiting	Group (K) N=20	Group (F) N=20	p Value
Yes	2/20	3/20	0.74
No	18/20	17/20	

Table 6: Phase I Recovery

Duration of Phase I	Group (K) n=20	Group (F) n=20	p Value
Recovery Time	12±2	13±3	0.492

Table 7: Phase II Recovery

Duration of Phase II	Group (K) n=20	Group (F) n=20	p Value
Recovery Time	29±4	47±8	0.046

The mean diastolic blood pressure for the Group K was 77±7 and 75±6 for Group F at baseline level which was statistically insignificant. After induction there were statistically no significant changes in both the groups.

Post operative nausea and vomiting was noted in 2 patients in Group K and 3 patients in Group F which was statistically insignificant.

The mean time for Phase I recovery in Group K was 12±2 and Group F was 13±3 which was statistically not significant.

The mean time for the Phase II recovery in Group K was 29±4 and Group F was 47±8. There was a statistically significant difference in the time up to Home readinesses and was significantly shorter with Propofol with Ketamine group than with Propofol with Fentanyl Group (P value – 0.046).

Discussion

The growing importance of ambulatory surgery during the past decade has led to the development of efficient anaesthetic techniques in terms of quality and safety of anesthesia and recovery. In these challenging objectives, intravenous techniques have played an important role, as they provide safe, efficient, and cost-effective anaesthesia in the ambulatory setting. Among the numerous intravenous drugs, propofol, with its fast a nd smooth onset of action, short duration of action, and low incidence of postoperative side effects appears to be the anaesthetic of choice in this situation.

In last few decades, many new sedative -hypnotic drugs with improved induction, maintenance and recovery profiles have been introduced into clinical practice. Kay B Rolly. Anesthesiol Belgca concluded that Propofol is a substituted phenol anaesthetic, and is associated with smooth induction, good maintenance and rapid recovery.

Greifenstein FE, De Vault M: A study of a 1 -aryl cyclohexyl amino for anesthesia identified that Ketamine, a powerful analgesic has a high margin of safety. John Stone M, Evans V, Baigel S: Sernyl in their study Dissociative anesthesia further pharmacological studies and fi rst clinical experience with phencyclidine derivative found out that ketamine produces no negative influence on ventilation or circulation. Corssen G, Domino EF quoted that the main disadvantage of ketamine is emergence delirium.

Susan M. Steele, Karen C. Nielsen, Stephen M on their study on Ambulatory Anesthesia and Perioperative Analgesia identified that fentanyl, a phenylpeperidine derivative has analgesic potency 50 -100 times that of morphine. But it is associated with respiratory depression and post operative nausea and vomiting.

Joshi, Girish P., Inagaki, Yoshimi, et al; Molloy, Mary E, Buggy, Donal J, Scanlon, Patrick in their study on using the Laryngeal Mask Airway concluded that it is ideal for Daycase anaesthesia.

Figueredo Eduardo, Vivar-Diago, Miguel, Mu no z-Blanco, Francisco, found that post operative throat discomfort following anaesthesia using laryngeal mask depends on the type of ventilation. Spontaneous ventilation causes less discomfort than controlled ventilation. McCrory, Connail R., McShane, Alan J., in a study comparing non premedicated and premedicated patients in ambulatory surgery, concluded that reflux of gastric contents occurs only in non premedicated patients. With adequate premedication, reflux or micro aspiration did not occur. The use of Laryngeal mask airway for our study was based on the above studies

Patients in both the groups did not differ significantly with respect to the demographic data as well as duration of surgery and anesthesia which are consistent with those of Guit j.b. et al in their study used propofol 2 mg/kg for induction, maintenance with propofol 12 mg/kg/hr for first 30 minutes, 9 mg/kg/hr for next 30 minutes and then 6 mg/kg/hr thereafter. Ketamine was used as 0.5 mg/kg for induction followed by maintenance dose of 0.5 mg/kg every hour. It was compared with fentanyl 2 μg/kg bolus and 1μg/kg every hour for maintenance. Propofol-ketamine combination resulted in hemodynamically stable anesthesia without the need for additional analgesics as cited by Guit JB, Koning HM in their study Ketamine as analgesic for total intravenous anesthesia with Propofol. We followed a similar protocol in our study.

There was gradual increase in mean pulse rate in propofol-ketamine group and in propofol -fentanyl group which returned to baseline after 30 and 15

minutes respectively. Guit jb et al have also reported that heart rate was stable except for an increase in mean h eart rate by 24% after induction in propofol -ketamine group. heart rate does not change significantly after an induction dose of propofol. Propofol either resets or inhibits baro-reflector reflex. There is reduction in the techycardic response to hypotension which coincides with the study Effects of Propofol anesthesia on baroreceptor activity in humans by Cullen PM, Turtle M, Prys Roberts C Sigmoid EK, Kothary SP et al found out that ketamine causes release of nor epinephrine which can be b lo ck ed by benzodiazepine in their study Diazepam for prevention of the rise in plasma catecholamine caused by ketamine. Fentanyl causes dose dependent decrease in heart rate. Carotid sinus baro receptor reflex control of heart rate is markedly depressed by fentanyl. These findings are also consistent with those of Badrinath.S, Michail N. Avramov, M Shadrick, Thomas R. Witt, and Anthony D. Ivankovich who in their study concluded that, ketamine induced tachycardia and hypertension was not evident in hemodynamic response of patients treated with the propofol-ketamine combination.

Hui TW et al also concluded that heart rate and peripheral vascular resistance are increased due to ketamine.

Heart rate is frequently slowed with more significant vagotonic effects of large doses of propofol. The effect of individual drugs on heart rate and blood pressure counterpart each other when used in combination.

There was fall in systolic blood pressure in propofol fentanyl group after induction as compared to propofol - ketamine group. Guit jb et al have also reported similar trend though both groups were haemodynamically stable.

The hemodynamic stability of propofol -ketamine combination makes it suitable for use during outpatient anesthesia. Which was evident from Schuttler J, Schuttler M et al study Optimal dosage strategies in TIVA using Propofol-Ketamine, Anesthesia

In our study both groups did not differ significantly in relation to the time to Phase I recovery but there was a statistically significant difference in the time up to 'Home readiness' between the two groups. The time up to Phase II recovery was significantly shorter with Propofol with Ketamine than with Propofol with Fentanyl.

Propofol seems to be effective in eliminating the side effects of subanaesthetic dose of ketamine in humans. Which was similar to the study The effects of small dose ketamine on Propofol sedation: Respiration post operative mood perception, cognition and p ain by Mortero RF, Clark LD., Tolan MM, Metz RJ, Tsueda K Hypotension (<20% of basal blood pressure) was reported in 5 patients of propofol-fentanyl group which was corrected by fluid infusion. There was no difference in surgery and recovery time, incid ence of PONV requiring treatment in either of the groups.

We therefore conclude that with Propofol with Ketamine is more efficacious in view of the time taken for the recovery compared to the Propofol with Fentanyl combination in elective day care surgi cal cases.

Conclusion

On comparing the recovery time and home readiness in Ambulatory Anaesthesia using Total Intravenous Venous Anaesthesia using agents Propofol with Fentanyl and Propofol with Ketamine, it was found that: -

- Propofol and Ketamine combination had a quicker recover
- Phase I recovery of both the groups were comparable
- Phase II recovery with Propofol and Ketamine was much shorter than Propofol and Fentanyl combination.
- The earlier Home Readiness in using Propofol with Ketamine combination makes it more advantageous than Propofol with Fentanyl in TIVA in day care surgeries.

References

1 . Wetcher PL: Anesthesia for ambulatory surgery 1990; 2nd Ed Philadelphia; Lippincott.

2. Hall MJ, Lawrence L: Ambulatory surgery in the United States, 1996. Adv Data 1998;12:1-16.

3. Manuel C Vallejo, Ryan C Romeo, Derek J Davis, Sivam Ramanathan: Propofol -ketamine versus propofol -fentanyl for outpatient laparoscopy, Comparison of postoperative nausea, emesis, analgesia and recovery. Journal of Clinical Anesthesia 2002;14:426-431.

4. Kortilla K, Ostman P, Faure E, Apfelbaum JL, Prunstis I, Eddawi M, et al. Randomized comparison of recovery after propofol, nitrous oxide versus thiopentone isoflurane - nitrous oxide anesthesia in

patients undergoing ambulatory surgery. Acta Anesthesiol Scand 1990;34:400 -03.

5. Jakobson J, Davidson S, Andreen M, Westgreen M. Opioid supplementation to propofol anesthesia for outpatient abortion: A comparison between alfentanil, fentanyl and placebo. Acta Anesthesiol Scand 1991; 35;767-70.
6. S Kaushik, Saigopal M, Rajini Sundar, Lalaniappan M, Mathew C. Comparative evaluation of propofol - ketamine and propofol -fentanyl in minor surgery. Indian J Anesthesia 2001;45(2):100 -103.
7. Kay B, Rolly G. ICI 35868 a new intravenous induction agent. Acta Anaes. Belgica.1977;28:303–16.
8. Kay B, Stephenson DK. Dose-response relationship for disoprofol (ICI 35868; Diprivan). Anuesthesiu 1981;36:863-7.
9. Greifenstein FE, De Vault M: A study of a 1 -aryl cyclohexyl amino for anesthesia. Anesth Analg 1958; 37:283.
10. Johnstone, B., Evans, V., Baigel, S. Sernyl in. Clinical Anesthesia. Brit. J. Anesth. 1959;31:433.
11. Corssen G, Domino EF. Dissociative anesthesia further pharmacological studies and first clinical experience with phencyclidine derivative CI -581, Anesth Analg 1966;4-8.
12. Susan M. Steele, Karen C. Nielsen, Stephen M. Ambulatory Anesthesia and Perioperative Analgesia 2005.
13. Guit JB, Koning HM. Ketamine as analgesic for total intravenous anesthesia with Propofol, Anesthesia 1991;46(12):1085-1086.
14. Cullen PM, Turtle M, Prys Roberts C. Effects of Propofol anesthesia on baroreceptor activity in humans. Anesth Analg 1987;66:1115.
15. Ebert T, Muzi M, Berens R et al. Sympathetic responses to induction of anesthesia in humans with Propofol or Etomidate, Anesthesiology 1992;76:725-8.
16. White M, P de Graft, B Renshof, E Van Kan, M Dzoljic. Pharmacokinetics of S (+) ketamine derived from target controlled infusion. Br J Anaesth 2006:96(3); 330-334.
17. AI-Khudhair, Gordon et al. Acute cardiovascular changes following Disoprofol: Effects in heavily sedated patients with coronary artery diseases, Anesthesia 1982;37:1007-1010.
18. Stephan H, Sonntag H et al. Effects of propofol on cardiovascular dynamics, myocardial blood flow and myocardial metabolism in patients with coronary artery disease, Br J Anaesth 1986;58:969-73.