Volume-4, Issue-9, Sept-2015 • ISSN No 2277 - 8160

Research Paper | Medical Science

Ketofol Anaesthesia for Short Gynaecological and Obstetric Procedures in ASA 1 & 2 Patients

Dr Rama Selvam Associate Professor, ACS Medical College and Hospital Velapanchavadi

ABSTRACT

Propofol and ketamine are intravenous anaesthetic agents. They are used for induction of Anaesthesia as their effect lasts for 20 minutes. Ketamine causes sympathetic stimulation where as propofol causes cardiac depression and decrease in PVR. However ketamine provides best analgesia and propofol only causes sleep and rapid recovery. The combination of these two drugs for short gynaecological procedures is the aim of my study and has proved to be effective . Both these drugs together maintain the haemodynamic stability and provided good recover with no adverse effects. The effect of Ketofol in this randomized, double blinded study was done compare the quality of Anaesthesia

KEYWORDS : TIVA,ketofol, hallucination, NMDA receptor, PONV PVR

Introduction

Ketamine is an IV anesthetic that is commonly for minor gynaecological procedures.when we add Propofol to ketamine, it counteracts the sympathetic stimulation seen with Ketamine used alone. Ketamine + Propofol were solely used for procedures. ASA 1&2 patients we in the study group and all were given 50 mg Ketamine and 50 mg Propofol (1:1) after giving 0.2 mg Glycopyrolate and 1 mg Midazolam as premedication .so this randomized, double blinded study was designed to compare the quality of analgesia. However all the procedures last-Ed for less tha half hour.Heart rate, noninvasive arterial blood pressure (NIBP), oxygen saturation (SpO_2), end tidal carbon dioxide ($Etco_2$) and incidence of any side effects were recorded. There were no significant hemodynamic changes in both groups after induction. However, there was no nausea and vomiting as Propofol itself has an antiemetic activity. Also the hallucinations of ketamine were counteracted by 1mg Midazolam .

Procedures selected for the study were short gynaecological and obstetric cases,Included missed abortions, fractional curettage, and vulval and vaginal cyst excision

Ketamine is a dissociative anaesthetic agent, classified as an NMDA receptor antagonist and has also been found to bind to opioid receptors and sigma receptors, and provides good analgesia. Propofol a short-acting intravenous sedative agent used for the induction and maintenance of anaesthesia ,It provides no analgesia(2).

In my study, all the patients received Glycopyrolate 0.2 mg and Midazolam 1 mg as premedication .Ketamine 50mg and Propofol 50 mg were given in combination .

All the patients had perfect haemodynamic stability, adequate depth of anaesthesia, clear headed recovery, no post operative nausea and vomiting .

Methods:

100 patients, (50 Gynaec and 50 obs)American Society of Anesthesia (ASA) class I and II scheduled for minor gynaecological and obstetric procedure.. Approval obtained from local ethical committee . Consent for TIVA (Total intravenous anaesthesia) taken from the patient's attenders. Obese patients, anaemic, epileptic , asthmatic, cardiac disease patients were excluded from my study.

Oxygen 4 l/mt by mask was given to all patients.

Pre anaesthesia assessment was done to evaluate if that patient fulfils the criteria of study and for fasting instruction and night sedation.

Morning of surgery I V cannula 18 G was started on left hand for all patients and Ringer lactate infusion started.Glycopyrolate 0.2 mg and Midazolam 1mg intravenous as premedication . Baseline measurements included Non Invasive Blood Pressure (NIBP), heart rate, respiratory rate, and pain faces scale recorded. The level of sedation was determined by Ramsay Sedation Scale[6]. A blinded observer who was being used to assess the depth of sedation of patients.

***Ramsay Sedation Scale[6]**

Patient is anxious and agitated or restless, or both

Patient is co-operative, oriented, and tranquil

Patient responds to commands only

Patient exhibits brisk response to light glabellar tap or loud auditory stimulus

Patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus

Patient exhibits no response

Fig 1: Pain Faces Scale

Ketamine 50 mg + Propofol 50 mg was loaded in a10 ml syringe and another 10 ml syringe with Ketofol (same combination) was kept as stand by. After giving Glycopyrolate and Midazolam premedication , 10 ml of blous dose Ketofol was give to the patient and gynaecologist was allowed to proceed .

During the procedure, patients were put on Hudson oxygen mask 4l/mt with a CO_2 sampling port. All patients were monitored with NIBP, electrocardiography (ECG), Pulse oximetry(SpO_2), heart rate (HR), and end tidal carbondioxide($EtCO_2$). The measurement started before commencement of the intravenous (IV) line and continued fifteen minutes after induction. The patients were also assessed for apnoea, which was defined as the loss of respiratory efforts for more than 20 seconds or fall of SpO_2 below 95%. Small movements during procedure were treated with incremental doses of Ketofol . There was perfect intraoperative haemodynamic stability.

After the completion of the procedure, the total drug requirement was noted. Patients were transferred to postoperative room when an Aldrete score[7] 9-10 was confirmed, The postoperative room nurses were blinded to the study medication received by the patients. The incidence of any episode of , agitation, hallucination, pain,postoperative nausea and vomiting (PONV) or any other side effects was noted. The patients vital signs were assessed at 5- minute interval. Patients were discharged on the second postoperative day to be in the safer side.

Descriptive variables were analyzed using Students *t*-test and X^2 test as appropriate using SPSS software statistical computer package

version 15. Differences between the groups in mean blood pressure (BP),heart rate(HR), end-tidalCO_2, oxygen saturation and ketofol requirements were compared using analysis of variance with repeated measures. A *P* value < 0.05 was considered to be statistically significant. Values are expressed as meanSD.

Results:

ASA I&II cases used for the study.

100 patients divided broadly into 2 groups of 50 patients each.

Group 1 - Gynaecological patients

5 Bartholin cyst
12 vaginal cyst
10 cervical polyp
22 fractional curettage

Group II - Obstetric patients

10 displaced Cu T
10 encirclage operation
5 manual removal of placenta
25 missed/ incomplete abortion

All minor obstetric and gynaecological procedures lasting for less than half hour.

Exclusion criteria were, epileptic, asthmatic, severe anaemia, cardiac illness and obese patients. Intraoperative monitoring of blood pressure, heart rate, ECG, SpO2, ETCO2 and respiratory rate. All the patients had perfect haemodynamic stability and clear headed recovery with no immediate post operative pain. No agitation or hallucination due to ketamine. Gynaecologist were also highly comfortable with the technique.

None of our patients landed in either LMA or Emergency intubation due to inadequate plane of anaesthesia or desaturation due to any other cause.

Table 1. Demographic Characteristics, Intraoperative Management, and Recovery Times of Patients in the Study Groups

Parameters	Group 1	Group 2
Number	50	50
Age (yr)	30 - 45	25 - 35
Weight (kg)	48	70
ASA physical status	1&2	1&2
Amount of drug Ketofol bolus (ml)	10	10
Average propofol concentration (mg/ml)	5	5
Average ketamine concentration (mg/ml)	5	5
Procedure time(mts)	25	30
Intraoperative complications	Nil	Nil
Time to ambulation (hrs)	2 hrs	2hrs
First call for pain	2 hrs	2 hrs
Time to actual discharge (day)	2nd POD	2nd POD

Ketamine 50 mg and Propofol 50 mg was taken in 1:1 concentration.
-Group I Gynaec patients, Group 2 Obstetric patients
-ASA = American Society of Anesthesiologists.

Five patients in group II and one patient in group I had pain and discomfort during the middle of procedure which was overcome by incremental boluses of infusions.

The time to ambulation in group I and II patients was 2 hrs while readiness to discharge was on the second day for safer side. Pre procedural visit was done previous night to evaluate if that patient fulfils the criteria of study and for fasting instruction. In the preoperative waiting area, an IV cannula was inserted in left cream. Baseline measurements included Non Invasive Blood Pressure (NIBP), heart rate, respiratory rate, and pain faces scale was performed on all patients.

Discussion:

The goals of procedural sedation are to provide an adequate level of sedation while minimizing pain and anxiety, maximizing amnesia, minimizing the potential for adverse drug-related events, controlling behavior, and maintaining a stable cardiovascular and respiratory status. A number of studies have demonstrated that the combination of ketamine and Propofol (ketofol) for sedation is safe and effective. The combination of the two agents appears to reduce side effects of each medication used alone, and allows for a rapid recovery time[1].

The dose of Ketofol in group I. was higher than in group II as incremental doses of ketofol given for Gynaec patients to get the desired depth oanaesthesia and abort pain sensation which was due to much manipulation by surgeon for fractional curettage, in such infusion compared to group II. Propofol in the recommended dose of 2-2.5 mg/kg almost always causes fall in blood pressure .The induction doses of propofol are reduced considerably by combination with equal doses of ketamine. Ketamine had the additional advantage of better hemodynamic stability. Our results are consistent with Furuya et al and Hui et al who suggested that the minimal change observed in arterial pressure may be dose related and also because sympathomimetic actions of ketamine were effective in counter-acting the hemodynamic depression of propofol. There was a trend for pulse rate to increase after the induction in all the groups, but there was no occurrence of profound tachycardia in any group[8,9].

End-tidal CO_2 increased slightly after induction in both groups. In agreement with our results, Mildh et al and Persson et al who reported that ketamine-induced sympathoadrenal activation may account for improved ventilation, also arousal secondary to the subjective side effects of ketamine (e.g., perceptual changes and anxiety) may also contribute [12,13]. Also our results have confirmed the previous reports of Frey et al and Badrinath et al [14,15], suggesting that the combination of a small-dose ketamine with propofol improves ventilation during sedation.

We expect that the apnea and desaturation recorded in group I (10%) was due to the excessive salivation complicated the higher dose of ketamine in this group which led to impaired breathing and required airway support in 16% of such patients. While apnea and desaturation which happened in group II could be due to the higher infusion rate of propofol in ketofol combination.

Willman and Andolfatto published a study of 114 patients requiring procedural sedation and analgesia mainly for orthopedic procedures were given a 1:1 mixture of propofol and ketamine. Transient hypoxia occurred in 2.6% of patients, out of them one patient required bag valve mask ventilation. Three patients had an emergence reaction, one of whom received midazolam. No patient had vomiting or aspiration. Procedural success rate in this study without the use of adjunctive medications was 96.5%. Median time until recovery was 15 minutes (range 5 to 45 minutes) [16]. Furthermore, Akin et al compared propofol to propofol plus ketamine (3:1) in 60 patients between one and 13 years of age undergoing auditory brainstem response testing. There were no cases of desaturation in the ketofol group, but in the propofol group 4/30 experienced desaturation and 6/30 had apnea. The authors concluded that the addition of low dose ketamine to propofol reduced the risk of respiratory depression and the need for repeat medication administration[17].

The incidence of clinically significant psychotomimetic effects was noted in the large-dose ketamine group (group I). This could be a dose-dependent interaction of the excitatory anesthetic ketamine with a pure central nervous system depressant, such as propofol [18,19]. There were no post procedural psychotomimetic symptoms recorded in group II. In addition, the patients mood was significantly better in the recovery room and cognitive function recovered more rapidly in such group than those given higher dose of ketamine. Nagata et al and Mortero et al are coinciding with our results as they suggested that ketamine in sedative doses is associated with electroencephalographic activation. Furthermore, small-dose ketamine increases thalamic sensory output and arousal. Sedative effects of propofol may be partially antagonized by the arousal effects of ketamine[20,21]. While Akin et al in a trial of 40 adult patients undergoing endometrial biopsy, reported that the combination of propofol (1 mg/kg) plus fentanyl (1 g/kg) was compared to the combination of propofol plus ketamine (2:1). Time to recovery was similar; however time to discharge was longer in the ketofol group secondary to the increased presence

of adverse events including nausea, vertigo, and visual disturbances. These authors concluded that although both regimens seem safe, ketofol (2:1) had more adverse events leading to a longer time until discharge and had a lower overall patient satisfaction[22].

Badrinath et al, published One hundred female outpatients undergoing breast biopsy procedures under local anesthesia received an infusion of a solution containing propofol in combination with different doses of ketamine . The sedative infusion rate was varied to maintain a deep level of sedation and normal respiratory and hemodynamic functions. They reported that combination of propofol and ketamine (5:1) provides effective sedation/analgesia during monitored anesthesia care[15]. Our results suggest that our combination propofol and ketamine (4:1) was more suitable in procedural operations as Badrinath et al used their preferred combination (5:1) only in monitored anesthesia care and they supplement their sedation with local anesthesia infiltration.

Discussion.

In conclusion, propofol combined with ketamine (1:1) infusion for procedural operations contributed adequate sedation and analgesia without hemodynamic and respiratory depression or psychotomimetic side effects and appears to be a safe and useful technique for procedural operations in the ambulatory setting.

REFERENCES

1. Aouad MT, Moussa AR, Dagher CM. Addition of ketamine to propofol for initiation of procedural anesthesia in children reduces propofol consumption and preserves hemodynamic stability. Acta Anaesthesiol Scand; 2008, 52 (4) : 561-5. | 2. Miner JR, Burton JH. Clinical practice advisory. Emergency department procedural sedation with propofol. Ann Emerg Med. 2007;50(2):182-7 | 3. Harrison N, Simmonds M. "Quantitative studies on some antagonists of N-methyl D-aspartate in slices of rat cerebral cortex". Br J Pharmacol 1985; 84 (2): 38191. | 4. Trissl LA, Gilbert DL, and Martinez JF: compatibility of propofol injectable emulsion with selected drugs during simulated Y-site administration, Am J Health-Syst Pharm 1997;54:1287-92 | 5. Wong DL, Hockenberry-Eaton M, Wilson D, Windelstein ML, Schwartz P. Wong's Essentials of Pediatric Nursing, 6th Edition.St. Louis: 2001; page 1301. | 6. Griffiths RD, Jones C. Recovery from intensive care. British Medical Journal 1999; 319: 427 9. | 7. Furuya A, Matsukawa T, Czaki M, Nishiyama T, Kume M, Kumazawa T. Intravenous ketamine attenuates arterial pressurechanges during induction of anesthesia with propofol. Eur JAnesthesiol 2001; 18: 88-92. | 8. Hui TW, Short TG, Hong W, Suen T, Gin T, Plummer J. Additive interactions between propofol and ketaminewhen used for anesthesia induction in female patients.Anesthesiology 1995; 82: 641-48. | 9. Akin A, Esmaoglu A, Guler G, et al. Propofol and propofol-ketamine in | 10. Pediatric patients undergoing cardiac catheterization. Pediatr Cardiol. 2005; 26:553-557. | 11. Goh PK, Chiu CL, Wang CY, et al. Randomized double-blind comparison of ketamine-propofol, fentanyl-propofol and propofol saline on haemodynamics and laryngeal mask airway insertion conditions. Anaesth Intensive Care. 2005; 33:223-8. | 12. Mildh L, Taittonen M, Leino K, KirvelO. The effect of low-dose ketamine on fentanyl-induced respiratory depression. Anaesthesia 1998; 53: 96570. | 13. Persson J, Scheinin H, Hellstrm G, et al. Ketamine antagonizes alfentanil-induced hypo-ventilation in healthy male volunteers. Acta Anaesthesiol Scand 1999; 43: 74452 | 14. Frey K, Sukhani R, Pawlowski J, et al. Propofol versus propofol-ketamine sedation for retrobulbar nerve block: comparison of sedation quality, intraocular pressure changes, and recovery profiles. Anesth Analg 1999;89:31721. | 15. Badrinath S, Avramov MN, Shadrick M, et al. The use of a ketamine-propofol combination during monitored anesthesia care. Anesth Analg 2000; 90: 85862 | 16. Willman EV, Andolfatto G. A prospective evaluation of ketofol (ketamine/propofol combination for procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2007; 49:23-30. | 17. Akin A, Esmaoglu A, Tosun Z, et al. Comparison of propofol with propofol-ketamine combination in pediatric patients undergoing auditory brainstem response testing. Int J Pediatr Otorhinolaryngol. 2005; 69:1541-1545. | 18. Mori K, Kawamata M, Mitani H, et al. A neurophysiologic study of ketamine anesthesia in the cat. Anesthesiology 1971;35:37383. | 19. Tomoda K, Shingu K, Osawa M, et al. Comparison of CNS effects of propofol and thiopentone in cats. Br J Anaesth 1993;71:3837. | 20. Nagata A, Nakao S, Miyamoto E, et al. Propofol inhibits ketamine-induced expression in the rat posterior cingulate cortex. Anesth Analg1998;87:141620. | 21. Mortero RF, Clark LD, Tolan MM, et al. The Effects of Small-Dose Ketamine on Propofol Sedation: Respiration, Postoperative Mood, Perception, Cognition, and Pain. Anesth Analg 2001;92:1465-9 | 22. Akin A, Guler G, Esmaoglu A, et al. A comparison of fentanyl-propofol with a ketamine-propofol combination for sedation during endometrial biopsy. J Clin Anesth. 2005; 17:187-90. |