Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2017/241

Original Article

# Comparison of Ketamine and Propofol in Combination with Fentanyl and Midazolam in Total Intravenous Anaesthesia for Minor Gynecological Procedures

**V Krithika[1], R Amudharani[2], Heber Anandan[3]**

[1]Senior Assistant Professor, Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tirunelveli, Tamil Nadu, India, [2]Professor, Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tirunelveli, Tamil Nadu, India, [3]Senior Clinical Scientist, Department of Clinical Research, Dr. Agarwal's Healthcare Limited, Chennai, Tamil Nadu, India

## Abstract

**Background:** Total intravenous anesthesia (TIVA) is commonly employed for anesthetizing patients for minor gynecological procedures such as dilatation and curettage.

**Aim:** The aim of this study is to compare the effectiveness of ketamine and propofol in combination with fentanyl and midazolam in TIVA for minor gynecological procedures.

**Materials and Methods:** This is a prospective randomized study of 20 patients of ASA physical status 1 or 2 divided into two groups. One group received TIVA with propofol, fentanyl, midazolam, and glycopyrrolate whereas the other group received TIVA with ketamine, fentanyl, midazolam, and glycopyrrolate. Hemodynamic parameters, oxygen saturation during anesthesia, and adverse effects if any were noted and recorded during a 15 min interval after administration of the induction drug.

**Results:** A significant increase in heart rate and blood pressure responses were observed during a 15 min interval period following ketamine administration for induction compared to propofol. There were instances of desaturation ($SpO_2$ < 92%) in 4 cases belonging to propofol group which was treated with jaw thrust and bag and mask ventilation with $O_2$ support.

**Conclusion:** Ketamine produced an adequate plane of anesthesia with minimal side effect profile than propofol when combined with other agents in TIVA.

**Key words:** Fentanyl, Ketamine, Midazolam, Propofol

## INTRODUCTION

Propofol is an alkyl phenol, highly lipid soluble and is insoluble in aqueous solution. The formulation most commonly used is that of 1% propofol, 10% soybean oil, and 1.2% purified egg phospholipid added as emulsifier, with 2.25% of glycerol as a tonicity-adjusting agent and sodium hydroxide to change the pH to 7. Ethylenediaminetetraacetic acid is added for its bacteriostatic activities. Midazolam and propofol mutually affect the pharmacokinetics of each other.[1] Midazolam induces hemodynamic alterations, which reduce hepatic perfusion inturn decreasing propofol uptake by the liver due to its high extraction ratio property. In the presence of propofol, plasma midazolam is administered in a smaller central compartment from which midazolam is cleared and distributed less rapidly to peripheral tissues. Thus, the action of midazolam is intensified.[2] The same holds true when propofol is administered with opioids. Ketamine is a water-soluble drug chemically related to phencyclidine with pH 3.5-5.5 in commercial solutions and n-methyl-d-aspartate receptor antagonists. It produces dissociative anesthesia which is characterized by catalepsy, light sedation, amnesia, and marked analgesia. Unlike other types

Access this article online

www.ijss-sn.com

Month of Submission : 03-2017
Month of Peer Review : 04-2017
Month of Acceptance : 05-2017
Month of Publishing : 05-2017

**Corresponding Author:** R Amudharani, Professor, Department of Anaesthesiology, Tirunelveli Medical College Hospital, Tirunelveli, Tamil Nadu, India. Phone: 9894039383. E-mail: drkrith@gmail.com

of anesthesia, the eye lash, corneal and laryngeal reflexes are not lost, and muscle tone actually increases. It produces profound analgesia even in subhypnotic doses and this lasts after recovery of consciousness. It does not depress the cardiovascular and respiratory system. Low dose alfentanil increases the $V_d$ and clearance of ketamine. In addition, alfentanil increases the distribution of ketamine into the brain. This is observed with other opioids also.[3] Hence, the potentiation of effect of the induction agent with their addition in total intravenous anesthesia (TIVA) mixtures. A combination of agents reduces the cardiovascular and respiratory side-effects of the induction agents in our study with potentiation of their actions when combined. The study compares the pharmacodynamics of propofol and ketamine mixed with premedicant in the selected group of patients.[4]

### Aim

The aim of this study is to compare the effectiveness of ketamine and propofol in combination with fentanyl and midazolam in TIVA for minor gynecological procedures.

## MATERIALS AND METHODS

This is a prospective randomized controlled study conducted in the Department of Anaesthesiology at Tirunelveli Medical College Hospital, Tirunelveli, Tamil Nadu, India.

### Inclusion Criteria

Minor gynecological procedures belonging to the American Society of Anesthesiologists risk 1 or 2. Age 25-50 years, body mass index: 18.5-25.

### Exclusion Criteria

Patients not satisfying inclusion criteria, patients with systemic hypertension/diabetes mellitus/cardiac disease/reactive airway disease. Boyle's machine with circle $CO_2$ absorber circuit, emergency drugs, endotracheal tube's, laryngoscope, and resuscitation kit kept ready. All the patients were premedicated with midazolam 0.05 mg/kg and glycopyrrolate 0.01 mg/kg followed by fentanyl 1 μg/kg. After 3 min, the patients were induced with ketamine (K group) 0.5 mg/kg or propofol (P group) in the dose of 1 mg/kg. Vital parameters such as $SpO_2$, HR, blood pressure (BP) (systolic, diastolic) at baseline, pre-induction, at 1, 3, 5, 10, and 15 min after induction were monitored. Any adverse effects such as hypotension, bradycardia, and reduction in $SpO_2$ were noted and treated with supplemental $O_2$, IV fluids and jaw thrust if needed.

## RESULTS

When compared between both groups, a statistically significant increase in heart rate (HR) was observed with ketamine at 1, 3, 5, 10, and 15 min after induction. A significant increase in diastolic BP was observed at 1, 3, 5, and 10 min after induction with ketamine. A highly significant increase in systolic BP value at 3 min after induction with ketamine compared to propofol was observed. A somewhat significant increase in systolic BP at 5 and 10 min after induction with ketamine was observed. There was no statistically significant difference in oxygen saturation decline in both groups up to 10 min after induction, but at 15 min after induction, there was a significant drop in $SpO_2$ levels after propofol administration in 4 patients. The desaturation episodes were treated with jaw thrust and bag and mask ventilation with supplemental $O_2$. All the patients in both the groups showed no movement during the beginning of the procedure (Tables 1-3).

## DISCUSSION

A statistically significant increase in HR and systolic and diastolic BP responses after inducing with ketamine was due to the cardiovascular stimulatory effect of the drug. The subanesthetic doses of ketamine used for the study purpose were sufficient to prevent patient movement and provided good depth of anesthesia during the procedure due to pre-medication with fentanyl and midazolam before the procedure.[5] Addition of midazolam prevented emergence delirium associated with ketamine use in some patients. The increase in secretions brought about by the use of ketamine was suppressed by the use of glycopyrrolate administered in pre-medication.[6] A statistically significant reduction in $SpO_2$ values observed at 15 min post-inductions with

**Table 1: Comparison of HR responses between two groups**

| HR | Group | Mean±SD | *P* value |
|---|---|---|---|
| Baseline | P | 82.10±11.99 | 0.009 |
| | K | 97.80±12.13 | |
| Pre-induction | P | 79.80±12.09 | 0.001 |
| | K | 101.20±11.55 | |
| Induction | P | 83.20±13.21 | 0.002 |
| | K | 103.20±10.88 | |
| 1 min | P | 91.00±11.16 | 0.003 |
| | K | 109.20±12.04 | |
| 3 min | P | 90.00±10.69 | 0.001 |
| | K | 110.00±10.51 | |
| 5 min | P | 89.60±9.88 | 0.001 |
| | K | 110.80±12.61 | |
| 10 min | P | 90.80±8.56 | 0.001 |
| | K | 110.50±13.28 | |
| 15 min | P | 90.20±9.55 | 0.002 |
| | K | 109.00±13.37 | |

SD: Standard deviation, HR: Heart rate, K: Ketamine, P: Propofol

**Table 2: Comparison of systolic and diastolic BP between two groups**

| Systolic and diastolic BP | Group | Mean±SD | *P* value |
|---|---|---|---|
| Systolic baseline | P | 118.20±11.49 | 0.839 |
| | K | 117.20±10.12 | |
| Diastolic baseline | P | 76.00±7.06 | 0.516 |
| | K | 73.90±7.13 | |
| Systolic pre-induction | P | 118.40±10.70 | 0.462 |
| | K | 115.20±8.18 | |
| Diastolic pre-induction | P | 76.20±6.29 | 0.352 |
| | K | 73.60±5.87 | |
| Systolic induction | P | 115.00±9.85 | 0.049 |
| | K | 106.00±9.19 | |
| Diastolic induction | P | 72.00±5.50 | 0.145 |
| | K | 67.50±7.55 | |
| Systolic 1 min | P | 108.80±9.94 | 0.156 |
| | K | 115.10±9.05 | |
| Diastolic 1 min | P | 66.40±6.31 | 0.046 |
| | K | 74.90±10.84 | |
| Systolic 3 min | P | 106.20±9.68 | <0.0001 |
| | K | 127.90±10.88 | |
| Diastolic 3 min | P | 66.60±4.53 | 0.002 |
| | K | 79.20±9.98 | |
| Systolic 5 min | P | 107.40±10.54 | 0.001 |
| | K | 129.00±12.94 | |
| Diastolic 5 min | P | 67.40±7.06 | 0.003 |
| | K | 83.80±13.55 | |
| Systolic 10 min | P | 111.00±9.01 | 0.002 |
| | K | 124.80±8.19 | |
| Diastolic 10 min | P | 69.80±5.03 | 0.009 |
| | K | 79.00±8.59 | |
| Systolic 15 min | P | 113.80±9.45 | 0.106 |
| | K | 120.80±8.95 | |
| Diastolic 15 min | P | 74.00±7.89 | 0.263 |
| | K | 77.20±3.82 | |

SD: Standard deviation, BP: Blood pressure, K: Ketamine, P: Propofol

**Table 3: Comparison of $SPO_2$ saturation levels between two groups**

| $SPO_2$ | Group | Mean±SD | *P* value |
|---|---|---|---|
| Baseline | P | 98.40±1.71 | 0.115 |
| | K | 99.40±0.84 | |
| Pre-induction | P | 98.10±1.66 | 1 |
| | K | 98.10±1.60 | |
| Induction | P | 96.00±1.94 | 0.137 |
| | K | 97.10±1.10 | |
| 1 min | P | 90.80±2.97 | 0.145 |
| | K | 92.80±2.90 | |
| 3 min | P | 97.80±2.15 | 0.124 |
| | K | 96.30±2.00 | |
| 5 min | P | 97.50±2.37 | 1 |
| | K | 97.50±1.90 | |
| 10 min | P | 97.30±2.63 | 0.196 |
| | K | 98.60±1.58 | |
| 15 min | P | 97.40±2.72 | 0.023 |
| | K | 99.60±0.70 | |

SD: Standard deviation, K: Ketamine, P: Propofol

propofol but not before that is similar to the observation of the study published in pediatrics journal.

Hasanein and El-Sayed studied that ketamine/propofol combination in the ratio 1:4 provided better sedation quality than fentanyl/propofol combination with less side-effects in the form of hypotension, bradycardia, apnea, and reduction of $SpO_2$ levels.[7]

In a study published in Tehran University Medical Journal, TIVA with propofol is found to be more suitable than midazolam for patients undergoing D & C.[8]

In a study done by Miner *et al.*, there was a higher rate of subclinical respiratory depression in patients administered ketamine than propofol during TIVA contrary to the results in our study. However, the dose which they used is 1 mg/kg followed by 0.5 mg/kg every 3 min, which is grossly more than the subanesthetic doses of 0.5 mg/kg administered in our study.[9]

## CONCLUSION

Ketamine is safer to administer in subanesthetic doses in combination with other agents in TIVA with less to absent serious side effects such as apnea/hypotension/bradycardia than propofol.

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**How to cite this article:** Krithika V, Amudharani R, Anandan H. Comparison of Ketamine and Propofol in Combination with Fentanyl and Midazolam in Total Intravenous Anesthesia for Minor Gynecological Procedures. Int J Sci Stud 2017;5(2):178-180.

**Source of Support:** Nil, **Conflict of Interest:** None declared.