

## Original Article

# PROCEDURAL SEDATION AND ANALGESIA FOR ERCP: A COMPARATIVE STUDY OF THE PROPOFOL AND KETAMINE-PROPOFOL COMBINATION (KETOFOL)

Nadia Bano\*, Shahid Rasool\*\*, Ahmed Raza\*\*\*

\* Assistant Professor, Department of Anaesthesia and Intensive Care, Madinah Teaching Hospital (MTH), Faisalabad.

\*\* Assistant Professor, Department of Medicine, Madinah Teaching Hospital (MTH), Faisalabad.

\*\*\* Medical Officer, Department of Anaesthesia and Intensive Care, Madinah Teaching Hospital (MTH), Faisalabad.

## ABSTRACT:

**OBJECTIVE:** The aim of this study was to find a near ideal drug for procedural sedation and analgesia for patients undergoing ERCP.

**STUDY DESIGN:** A randomized control study was carried out for comparison.

**SETTING & DURATION:** This study was conducted at department of anaesthesia and intensive care, Madinah Teaching Hospital, Faisalabad from August 2014 to July 2015.

**SAMPLE SIZE:** The group under study consisted of 146 ASA I & II status patients undergoing ERCP.

**METHODS:** The patients were randomly divided into two groups A and B. Group A patients were to receive Propofol and Group B patients were to receive Ketamine-Propofol (Ketofol).

**RESULTS:** As compared to Propofol Group (group A), Ketofol group (group B) showed significant hemodynamic stability. The frequency of hypotension was 27.4% in group A as compared to 12.3% in group B. Respiratory drive was maintained in both groups. Requirement for post procedure analgesia was significant in group A being 16.4% as compared to 2.7% in group B. Time of onset and offset were also significantly shorter in group B.

**CONCLUSION:** It is concluded that Ketofol offers stable hemodynamics, adequate sedation and analgesia for patients undergoing ERCP. It also offers quick onset and offset of sedation. So it is a near ideal agent for procedural sedation and analgesia for ERCP.

**KEY WORDS:** ERCP, Propofol, Ketofol, Ketamine-Propofol, Ketamine.

## INTRODUCTION:

ERCP (Endoscopic Retrograde Cholangiopancreatography) is a procedure frequently carried out in department of Gastroenterology. The procedure requires adequate relaxation and amnesia for the patient while maintaining cardiorespiratory status of the patient. Satisfaction of operator and comfort of patient is very important for a successful procedure. A number of drugs are

being used for this purpose such as opioids, benzodiazepines, sedative and hypnotic agents. An ideal agent for ERCP should provide stable hemodynamics, less respiratory depression,

*Corresponding Author:*

Nadia Bano

Assistant Professor, Department of Anaesthesia and Intensive Care, Madinah Teaching Hospital (MTH), Faisalabad.

E-mail: drsaab@gmail.com

gastroenterologist's satisfaction and comfort of patient. However there is no ideal drug which offers all these benefits.

Propofol is the most commonly used drug for ERCP. The drug has a quick onset and recovery, provides adequate relaxation<sup>1</sup> but unfortunately it leads to hemodynamic instability due to profound peripheral vasodilatation. It also leads to severe respiratory depression<sup>2</sup>. It lacks analgesic properties. All these effects add up to patient's discomfort.

Ketamine is a complete anesthetic agent leading to sedation, amnesia and analgesia<sup>3</sup>. It causes sympathetic stimulation which in turn causes a rise in blood pressure, cardiac output and heart rate. It causes less depression of ventilatory drive. However it is associated with undesirable effects such as emergence delirium, agitation and nightmares<sup>4</sup>. These effects can be abolished by the concurrent use of benzodiazepines and Propofol.

Since both drugs have an entirely opposite hemodynamic and respiratory effects we can combine both drugs to get stable hemodynamics and respiration of patient. Further combining Propofol and ketamine blunts undesirable CNS effects of ketamine.

So we used both Propofol alone and Ketofol in our study, hoping to find a near ideal agent for procedural sedation analgesia.

## **MATERIAL AND METHODS:**

### **SETTING:**

This study was conducted at department of anaesthesia and intensive care, Madinah Teaching Hospital.

### **DURATION OF STUDY:**

The study was carried out from August 2014 to July 2015.

### **SAMPLE SIZE:**

After fulfilling the inclusion criteria 146 patients were taken, in which 73 were placed in group A and 73 in group B. ERCP was carried out in group A by using Propofol and in group B by using Ketofol respectively.

### **SAMPLING TECHNIQUE:**

Consecutive (Non Probability) sampling technique was used.

## **SAMPLE SELECTION:**

### **INCLUSION CRITERIA:**

- American society of anesthetist (ASA) grade I and II patients.
- Patients with stable hemodynamics.

### **EXCLUSION CRITERIA:**

- Patients with increased risk of aspiration.
- History of allergy to drugs under study.
- Psychiatric illness.
- History of substance abuse.

## **STUDY DESIGN**

Randomized control trial

## **DATA COLLECTION PROCEDURE**

After ethical approval and informed written consent, 146 patients prepared in gastroenterology department prepared for ERCP were selected according to inclusion criteria.

Using lottery method patients were randomly divided into two groups A and B. Group A patients were to receive Propofol and group B patients were to receive Ketamine-Propofol Combination (Ketofol).

Data of the patients was recorded including age, height, weight, ASA status, baseline blood pressure, heart rate and SpO<sub>2</sub>.

A senior anesthesiologist was responsible for patient randomization and drug administration while resident doctor collected the data throughout the procedure. Both the patient and resident doctor were unaware of the drug being used.

It was confirmed that patient had nothing per oral for last 8 hours. IV cannula was passed and Lactated Ringer was started @ 6-8 ml/kg. No premedication was used. Patients were monitored for B.P., heart rate, SpO<sub>2</sub> and ECG throughout the procedure. Oxygen was given @3L/min via nasal cannula. All parameters were recorded at the start of procedure then every 5 minutes.

Group A patients received Propofol 1% (10mg/ml) @3-5mg/kg while group B received Ketofol 1:2(Propofol 10mg/ml @2mg/kg and Ketamine 50mg/ml @1mg/kg). The infusion was started in group A with Propofol@6-10mg/kg/hr and in group B with Ketofol @

0.03ml/kg/min (Ketamine 30 µg/kg/min and Propofol 60 µg/kg/min). The infusion was stopped 5-7 minutes prior to end of procedure. B.P., heart rate, SpO<sub>2</sub> and ECG were recorded at the start of the procedure and then every five minutes. Special record was made of any untoward event. Hypotension was defined as systolic blood pressure less than 90mmhg, bradycardia was defined as heart rate less than 60/min and respiratory depression was defined as SpO<sub>2</sub> less than 92%. Hypotension was treated with IV fluids and bradycardia with atropine 0.5mg IV. Time of onset was taken as time from administration of drug to time for loss of consciousness while time of offset was taken as time between cessation of anesthesia and consciousness of patient.

Patients were discharged from PACU meeting following criteria:

- Conscious and oriented
- Stable hemodynamics
- Pain free
- No postoperative nausea vomiting

## DATA ANALYSIS PLAN

Data was analyzed using SPSS (version 20)

- Mean and standard deviation was calculated for quantitative variables i.e. time of onset, time of offset, age, weight, height and ASA status.
- Frequency and percentages were presented for qualitative variables i.e. hypotension, bradycardia, respiratory depression and post procedure analgesia.
- Chi square test was applied to compare gender, ASA status, hypotension, bradycardia, respiratory depression and post procedure analgesia.
- Independent sample t-test was used to compare age, height, weight, onset and offset time.

P value < 0.05 was considered significant.

**Table 1: Demographic Data**

Group	N	Gender [M/F]	Age (Years)	Height (cm)	Weight (Kg)	ASA Status [I/II]
Group A	73	23/50	47.97±13.88	161.30±9.79	67.23±11.93	43/30
Group B	73	32/41	51.49±15.75	164.89±10.37	66.07±10.71	33/40

Hemodynamic stability was marked in group B. The incidence of hypotension in group A being 27.4% as compared to 12.3% in group B which is statistically significant (p=0.023). However significant bradycardia was not observed in either group (p=1.000). Respiratory drive was maintained in both groups (p= 0.560). [Table 2]

**Table 2: Cardiorespiratory Changes**

Variable	Group A (n=73)		Group B (n=73)		P
	No of Pts.	%age	No of Pts.	%age	
<b>Bradycardia</b>	2	2.7%	2	2.7%	1.000
<b>Hypotension</b>	20	27.4%	9	12.3%	0.023
<b>Respiratory depression</b>	2	2.7%	1	1.4%	0.560

Time of onset and offset varied markedly between two groups (p=0.000) and (p=0.000) respectively which was statistically significant. Ketofol group showed quick onset of sedation and recovery as compared to Propofol group. [Table 3]

**Table 3: Onset and Offset of Sedation**

Variable	Group A (n=73)	Group B (n=73)	P
<b>Onset (mean time in Minutes)</b>	2.23±0.36	1.16±0.30	0.000
<b>Offset (mean time in Minutes)</b>	18.56±1.92	12.41±1.39	0.000

In group A 16.4% of patients required post procedure analgesia as compared to 2.7% in group B which was statistically significant(p=0.005). [Table 4]

**Table 4: Requirement for Post-Procedure Analgesia**

Variable	Group A (n=73)		Group B (n=73)		P
	No of Pts.	%age	No of Pts.	%age	
<b>Required Post-Procedure Analgesia</b>	12	16.4%	2	2.7%	0.005

**RESULTS:**

Both groups were comparable with regard to age, weight and ASA status. However height differed significantly between two groups despite random allocation.

**DISCUSSION:**

ERCP is a commonly performed procedure in gastroenterology department. The anesthesia for this procedure is challenging as patient is positioned prone and the airway is shared with endoscopist. Spontaneous ventilation is favored in this procedure. Deep sedation, adequate analgesia as well as cardiorespiratory stability is very important for patient and endoscopist satisfaction. Since no single drug offers all the benefits, the purpose of this study was to find a near ideal agent for procedures like ERCP.

In our study Ketofol showed a quick onset and quick offset as compared to Propofol group. These results were supported by Sherin et al during bronchoscopic removal of sharp pin inhalation<sup>5</sup>. Ehab et al also showed shorter hospital stay with Ketofol for minor orthopedic procedures<sup>6</sup>. However similar onset, efficacy and sedation were noticed in both groups with more consistent depth with Ketofol in study carried out by Andolfatto et al in 2012<sup>7</sup>. Rapid recovery was seen in children with hematological diseases in Ketofol group as well as satisfactory level of sedation without significant adverse effects<sup>8</sup>. In Gastrointestinal

endoscopy shorter recovery time was observed in Ketofol group when compared to Propofol while hemodynamic stability was similar in both groups<sup>9</sup>. Similarly early recovery was seen when small dose of ketamine was added to Propofol sedation by Mortero FR et al<sup>10</sup>.

We observed greater hemodynamic stability and less respiratory depression with Ketofol as compared to Propofol. It was supported by Ozgul et al while comparing both drugs for insertion of laryngeal tube suction (LTS) II<sup>11</sup>. Smichney Nathan J observed improved hemodynamics when Ketofol was used as induction agent<sup>12</sup>. Hamzeh Hosseinzadeh found that Ketamine-Propofol Combination (Ketofol) offers more hemodynamic stability when compared to Propofol Etomidate mixture<sup>13</sup>. Similarly it was studied that Ketofol is associated with more respiratory depression and hemodynamic stability in elderly patients for placement of LMA<sup>14</sup>. Nashwa Samy ELZayyat et al observed hemodynamic stability with Ketofol in critically ill rheumatic cardiac patients undergoing c-section<sup>15</sup>.

We found that Ketofol offered adequate analgesia and sedation and less demand for post procedure analgesia. It is supported by Etane Victoria Willman and Gary Andolfatto<sup>16</sup>. This is further supported by Henry David and Joseph Shipp, however they observed similar respiratory depression in both groups<sup>17</sup>. Ayman A. Abdellatif concluded that Ketofol offers adequate sedation, analgesia and early recovery<sup>18</sup>.

**CONCLUSION:**

It was concluded that as compared to Propofol during ERCP Ketofol provides hemodynamic stability, quick onset and offset of sedation. It provides adequate analgesia during procedure and is associated with less post procedure pain and analgesia requirement. It leads to satisfaction of operator as well as comfort of patient. So Ketofol meets the criteria of a near ideal drug for procedural sedation and analgesia for ERCP.

**REFERENCES:**

1. Krauss B, Green SM. Procedural sedation and analgesia in children. *Lancet*. 2006; 367:766-80.
2. Bassett KE, Anderson JL, Pribble CG, et al. Propofol for procedural sedation in the emergency department. *Ann Emerg Med* 2003; 42:773-782.
3. Camu F, Vaniersbergh C. Pharmacology of systemic analgesics. *Best Pract Clin Anaesthesiol*. 2002;16:475-88.
4. Okamoto N, Nakai T, Sakamoto K, Nagafusa Y, et al. Rapid antidepressant effect of ketamine anesthesia during electroconvulsive therapy of treatment-resistant depression: comparing ketamine and propofol anesthesia. *J ECT*. 2010;26(3):223-7.
5. Mohamed S, Osman S. A comparison of ketofol and propofol for bronchoscopic removal of sharp pin inhalation. *AAMJ*. 2011;9:40-64.
6. Saeed E. Ketofol infusion as a procedural sedation and analgesia modality for minor orthopedic surgeries: evaluation of dose-outcome relation. *Ain shams journal of anesthesiology*. 2011;4-1:63-74.
7. Andolfatto G, Abu-Laban R, Zed P, Staniforth S, Stackhouse S, Moadebi S et al. Ketamine-Propofol Combination (Ketofol) Versus Propofol Alone for Emergency Department Procedural Sedation and Analgesia: A Randomized Double-Blind Trial. *Annals of Emergency Medicine*. 2012;59(6):504-512.e2.
8. Da Silva P, de Aguiar V, Waisberg D, Passos R, Park M. Use of Ketofol for procedural sedation and analgesia in children with hematological diseases. *Pediatrics International*. 2011;53(1):62-67.
9. Aydogan H, Aydogan T, Uyan A. Propofol-ketamine combination has shorter recovery times with similar hemodynamics compared to propofol alone in upper gastrointestinal endoscopy in adults. A randomized trial. *Acta Medica Mediterranea*. 2013;29:259-264.
10. Mortero R, Clark L, Tolan M, Metz R, Tsueda K, Sheppard R. The Effects of Small-Dose Ketamine on Propofol Sedation: Respiration, Postoperative Mood, Perception, Cognition, and Pain. *Anesthesia and Analgesia*. 2001;1465-1469.
11. Ozgul U, Begec Z, Karahan K, Ali Erdogan M, Said Aydogan M, Colak C et al. Comparison of Propofol and Ketamine-Propofol Mixture (Ketofol) on Laryngeal Tube-Suction II Conditions and Hemodynamics: A Randomized, Prospective, Double-Blind Trial. *Current Therapeutic Research*. 2013;75:39-43.
12. Smischney N, Beach M, Loftus R, Dodds T, Koff M. Ketamine/propofol admixture (ketofol) is associated with improved hemodynamics as an induction agent. *Journal of Trauma and Acute Care Surgery*. 2012;73(1):94-101.
13. Hosseinzadeh H, Eidy M, EJ Golzari S, Vasebi M. Hemodynamic stability during induction of anesthesia in elderly patients: propofol+ketamine versus propofol+etomidate. *journal of cardiovascular and thoracic research*. 2013;5(2):51-54.
14. Erdogan M, Begec Z, Aydogan M, Ozgul U, Yucel A, Colak C et al. Comparison of effects of propofol and ketamine-propofol mixture (ketofol) on laryngeal mask airway insertion conditions and hemodynamics in elderly patients: a randomized, prospective, double-blind trial. *Journal of Anesthesia*. 2012;27(1):12-17.
15. ELZayyat N, Hassan A, ELSakka A, Saad A. Ketamine/propofol (ketofol) versus propofol/fentanyl for induction of general anesthesia in parturients with rheumatic valvular lesions undergoing elective cesarean section. *Egypt J Cardiothorac Anesth*. 2013;7(2):79-84.
16. Willman E, Andolfatto G. A Prospective

- Evaluation of "ketofol" (Ketamine/Propofol Combination) for Procedural Sedation and Analgesia in the Emergency Department. *Annals of Emergency Medicine*. 2007;49(1):23-30.
17. David H, Shipp J. A Randomized Controlled Trial of Ketamine/Propofol Versus Propofol Alone for Emergency Department Procedural Sedation. *Annals of Emergency Medicine*. 2011;57(5):435-441.
18. Abdellatif A. Ketofol for outpatient transrectal ultrasound guided prostate biopsy. *ain shams journal of anesthesiology*. 2012;5-1:11-22.

Submitted for publication:	07.09.2015
Accepted for publication: After Revision	02.01.2016