Original Article

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

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**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.
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 but unfortunately it leads to hemodynamic instability due to profound peripheral vasodilatation. It also leads to severe respiratory depression. 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. 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. 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 SpO2. 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, SpO2 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, SpO₂ 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 SpO₂ 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.

A value < 0.05 was considered significant.

### Table 1: Demographic Data

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

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (n=73)</th>
<th>Group B (n=73)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of Pts.</td>
<td>%age</td>
<td>No of Pts.</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>2</td>
<td>2.7%</td>
<td>2</td>
</tr>
<tr>
<td>Hypotension</td>
<td>20</td>
<td>27.4%</td>
<td>9</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>2</td>
<td>2.7%</td>
<td>1</td>
</tr>
</tbody>
</table>

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]
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. Ehab et al also showed shorter hospital stay with Ketofol for minor orthopedic procedures. 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. Rapid recovery was seen in children with hematological diseases in Ketofol group as well as satisfactory level of sedation without significant adverse effects. In Gastrointestinal endoscopy shorter recovery time was observed in Ketofol group when compared to Propofol while hemodynamic stability was similar in both groups. Similarly early recovery was seen when small dose of ketamine was added to Propofol sedation by Mortero FR et al. 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. Smichney Nathan J observed improved hemodynamics when Ketofol was used as induction agent. Hamzeh Hosseinzadeh found that Ketamine–Propofol Combination (Ketofol) offers more hemodynamic stability when compared to Propofol Etomidate mixture. Similarly it was studied that Ketofol is associated with more respiratory depression and hemodynamic stability in elderly patients for placement of LMA. Nashwa Samy ELZayyat et al observed hemodynamic stability with Ketofol in critically ill rheumatic cardiac patients undergoing c-section. 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. This is further supported by Henry David and Joseph Shipp, however they observed similar respiratory depression in both groups. Ayman A. Abdellatif concluded that Ketofol offers adequate sedation, analgesia and early recovery.

Table 3: Onset and Offset of Sedation

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

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (n=73)</th>
<th>Group B (n=73)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Pts.</td>
<td>%age</td>
<td>No of Pts.</td>
<td>%age</td>
</tr>
<tr>
<td>Required Post-Procedural Analgesia</td>
<td>12</td>
<td>16.4%</td>
<td>2</td>
</tr>
</tbody>
</table>
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:

16. Willman E, Andolfatto G. A Prospective
