ORIGINAL ARTICLE

# Comparison of Efficacy of Propofol Versus Midazolam in Endoscopy: A Randomized Controlled Trial

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## ABSTRACT

**Objectives:** To compare the efficacy of propofol versus midazolam in terms of sedation 2-minutes after bolus administration of both drugs in endoscopy.

**Study Design:** Randomized Controlled Trial.

**Place & Duration:** Department of Anaesthesiology, Surgical Intensive Care Unit and pain management, Dow University of Health Sciences and Civil Hospital Karachi from February to August 2015.

**Material & Methods:** Total 122 adult patients who underwent elective upper gastrointestinal endoscopies were selected. Patients were randomly allocated into two groups, A and B having 61 patients in each. Intravenous midazolam was then administered to group A while group B received propofol. The main outcome measure was efficacy of drugs to achieve adequate sedation on the basis of Modified Observer's Assessment of Alertness/Sedation Score. The SPSS version 11 was applied to the data.

**Results:** Majority of patients (27%) were between 51-60 years of age group with mean (±SD) age was 49.48 (±12.98) years. Males were more than females. Intravenous propofol was effective in 95.1% of cases in comparison to midazolam which was found effective in 82% ($p < 0.05$).

**Conclusion:** Intravenous propofol is effective in achieving adequate depth of sedation when compared with midazolam.


**Key Words:** Midazolam, Propofol, Endoscopy, Sedative, Gastrointestinal.

## INTRODUCTION:

Endoscopy is a medical procedure used to view the digestive tract, and other internal organs, non-surgically through the use of an endoscope.[1] It is performed under sedation and considered to be a day case procedure.[2] Traditionally, sedation for endoscopies was provided by the gastro-enterologist.[3] However, modern-day endoscopic procedures are complex and require full attention of the gastroenterologist along with complete co-operation of the patient.[4]

This necessitates the administration of drugs by anesthetist to accomplish effective sedation without any complications and in addition, facilitates patient compliance while achieving quick and complete recovery.[5]

Conventionally, deep sedation is attained with benzodiazepines and narcotics.[6] Midazolam (usually in combination of other agents, such as nalbuphine/meperidine) is frequently use by anesthesia providers for sedating patients prior to endoscopy,[7,8] but due to prolonged recovery, its role has been overtaken by propofol.[9] Propofol is an ultra-short acting hypnotic agent that provides sedation amnesia and hypnotic effects.[10] Although, propofol is valuable in endoscopic procedures due to its rapid onset, quick recovery and has less effects on oxygen saturation as compared to midazolam,[11] much controversies exist in literature when comparing both propofol and midazolam in terms of level of sedation. Krugliak *et al.*,[12]


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observed statistically significant difference in sedative amnesia with propofol administration in contrast to midazolam. Correspondingly, Wehrmann et al.,[11] recommended the use of propofol as a consequence of its safe and effective sedative effects. Contrary to this, Kongkam and colleagues[13] encountered no differences in level of sedation after administration of both drugs during endoscopic retrograde cholangiopancreaticography (ERCP). A research reports that 80% of patients achieved adequate sedation with midazolam as compared to 97.5% of patients with propofol ($p<0.001$).[14] Still, there is no final consensus about satisfactory sedative effects. Furthermore, no local study has been conducted in this regard. Therefore, this study aimed to compare the efficacy of midazolam versus propofol in terms of sedation in endoscopy, as the need for a local study to evaluate the efficacy of both drugs will go a long way to settle this dispute and would be instrumental in developing local and international protocols regarding the use of most appropriate drug for providing sedation during endoscopies.

## MATERIAL & METHODS:

The current study was a randomized controlled trial conducted in the department of Anaesthesiology, Surgical Intensive Care Unit and pain management, Dow University of Health Sciences and Civil Hospital Karachi, for three from February to August 2015. The sample was calculated to be 122 patients, using open EPi, version 2. All the 122 patients who underwent elective upper gastrointestinal endoscopies were selected during study period on the basis of predetermined criteria. The sample was collected by non-probability purposive technique. The inclusion criteria consists of; age of patients between 20-70 years of either gender, ASA status I & II, and elective patients for upper gastrointestinal endoscopy. The exclusion criteria consists of; Patients with clinically significant hepatic, renal or respiratory disease, or taking any anxiolytic drug within 24 hours prior to endoscopy, & those having allergy to study drugs.
A total of one hundred and twenty two patients undergoing elective upper gastrointestinal endoscopy; fulfilled the inclusion criteria, were included in the study. Informed consent was taken from each patient and/or their attendants to participate in this study. Those who did not give consent were excluded and similar number of patients was recruited. Patients were randomly allocated in two groups: Group A (n=61) ((Midazolam), and Group B (n=61) (Propofol) by using the lottery method to minimize sampling bias. Patients in group A received intravenous midazolam (0.07mg/kg) over 30 seconds whereas intravenous propofol (1.5mg/kg) over 30 seconds was administered to patients in group B.

At the beginning of procedure, non-invasive monitoring of patient's vitals (heart rate and blood pressure), electrocardiography, and oxygen saturation ($SpO_2$) were taken and continuously checked throughout the procedure. The patients who were allocated to the propofol group were given intravenous propofol in a dose of 1.5mg/kg over 30 seconds with 10 mg increments at 30 seconds intervals, up to two minutes. Correspondingly, intravenous midazolam, in a dose of 0.07 mg/kg over thirty seconds with 1 mg increments at 60 seconds interval up to two minutes, was administered to the patients who had been allocated to midazolam group. The syringes with the study drugs were prepared by a doctor who was not involved in collection of the data and analysis of the result. The study drugs were administered by researcher/on duty anaesthetist under supervision of consultant anesthetist.

The sedation scoring after two minutes was assessed using criteria of Modified Observer's Assessment of Alertness/Sedation (MOAAS) and leveled as being alert, light, moderate, deep, and deep sleep according to sedation scoring. The final outcome (efficacy of sedation) was determined as effective and ineffective. These parameters were evaluated by researcher / consultant anesthetist who supervised the sedation procedure. The findings were documented on a pre-designed proforma. It included the patients name, age, gender, hospital registration number, ASA status (I and II), group of patients (A and B), sedation scores (5, 4, 3, 2 or 1), sedation levels (alert, light, moderate, deep, deep sleep) and final outcome i.e. efficacy of sedation (effective and ineffective). All

proforma were filled by independent observer not participating in the study to minimize bias.

Data was analyzed by using SPSS version 11 on computer. Mean and standard deviation was computed for numerical variables like age; whereas frequency and percentages were employed to assess the categorical variables like gender, ASA status, sedation levels and final outcome (i.e. efficacy of sedation). Chi-square test was used to compare the final outcome. Statistical significance was taken at $p < 0.05$. Stratification was done with regard to age, gender and ASA status to control the effect modifiers.

## RESULTS:

The youngest patient enrolled in this study was 25 years old while the oldest was of 69 years. Thirty three patients fell in the age group of 51-60 years that is 27%. Fifteen patients (12.3%) were in between 20-30 years of age, twenty (16.4%) were in between 31-40, twenty four (19.7%) in 41-50 and thirty (24.6%) in 61-70 years of age groups. Mean (±SD) age was 49.48 (±12.98) years. Out of the 15 patients in 20-30 years of age group 9 (14.8%) were in group A while 6 (9.8%) were in group B. Mean (±SD) age was 50.13 (±12.63) years in group A, while mean (±SD) age was 48.81 (±13.39) years in group B (Table 01). A total of 74 (60.7%) patients were male whereas forty eight (39.3%) were female. (Fig. 01) Male to female ratio was 1.54: 1. The number of males in group A was 35 (57.4%) while 26 (42.6%) were females. Correspondingly, group B had 39 (63.9%) males and 22 (36.1%) females (Fig. 01). A total of 70 (57.4%) patients belonged to the ASA I classification, whereas 52 (42.6%) patients were found to be of ASA II status in this study. Out of these, the number of ASA I patients in group A were 38 (62.3%) and ASA II were 23 (37.7%). Group B had 32 (52.5%) ASA I status patients and 29 (47.5%) ASA class II patients. (Table 02)

In group A, 21 (34.4%) patients achieved deep sleep level, 29 (47.5%) sleep level, 04 (6.6%) moderate sedation, 6 (9.8%) light sedation and 01 (1.6%) patient was awake. (Fig. 03) In group B, 40 (65.6%) patients achieved deep sleep level, 18 (29.5%) sleep level, 01 (1.6%) had moderate sedation, 02 (3.3%) had light sedation and no patient was awake. (Fig.04) Intravenous midazolam was effective in achieving adequate sedation at 2-minutes after bolus administration in 50 (82%) of patients whereas intravenous propofol was effective in adequate sedation at 2-minutes after bolus administration in 58 (95.1%) of the patients. This study demonstrated that intravenous propofol was statistically more effective in achieving adequate sedation when compared with intravenous midazolam ($p = 0.023$). (Table 03)

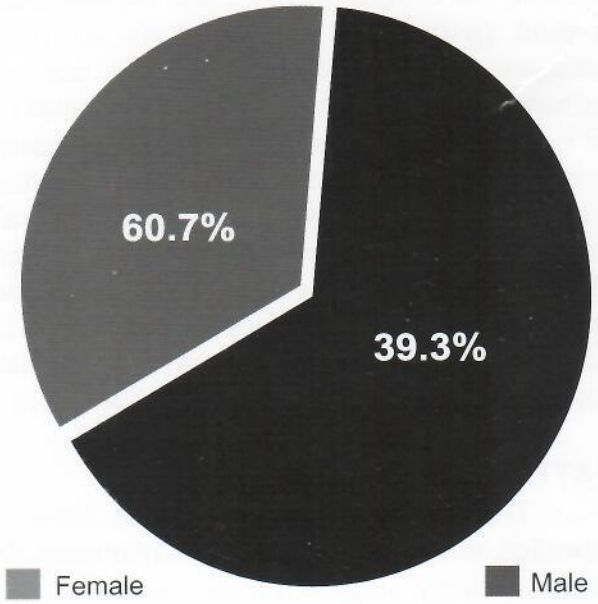


**Fig. 01: Gender Distribution (n=122)**

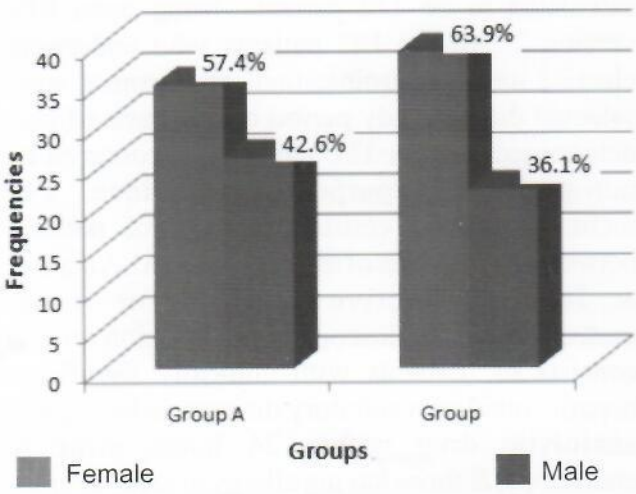


**Fig. 02: Gender Distribution According to Groups (n=122)**

**Table-01: Age Distribution**

| Age of Patients (years) | Group A (Midazolam Group) | | Group B (Propofol Group) | | Total | |
|---|---|---|---|---|---|---|
| | (n = 61) | % | (n = 61) | % | (n =122) | % |
| 20-30 | 09 | 14.8 | 06 | 9.8 | 15 | 12.3 |
| 31-40 | 11 | 18 | 09 | 14.8 | 20 | 16.4 |
| 41-50 | 12 | 19.7 | 12 | 19.7 | 24 | 19.7 |
| 51-60 | 14 | 23 | 19 | 31.1 | 33 | 27 |
| 61-70 | 15 | 24.6 | 15 | 24.6 | 30 | 24.6 |

Mean age (±SD) = 49.48 (±12.98) years
Mean age (±SD) in group A and B=50.13 (±12.63) years and 48.81(±13.39) years respectively.

**Table-02: ASA Status**

| ASA Status | Group A (Midazolam Group) (n=61) | Group B (Propofol Group) (n=61) | * Total (n=122) |
|---|---|---|---|
| ASA I | 38 (62.3) | 32 (52.5) | 70 (57.4) |
| ASA II | 23 (37.7) | 29 (47.5) | 52 (42.6) |

* Data is shown in numbers followed by percentages in parentheses.

**Table-03: Outcome (Effectiveness of Drugs) (n=122)**

| Effective-ness | Group A (Midazolam Group) (n=61) | Group B (Propofol Group) (n=61) | * p-value |
|---|---|---|---|
| Effective | 50 (82) | 58 (95.1) | 0.023 |
| Ineffective | 11 (18) | 3 (4.9) | |

* Data is shown in numbers followed by percentages in parentheses.
* using chi-square test; df=1

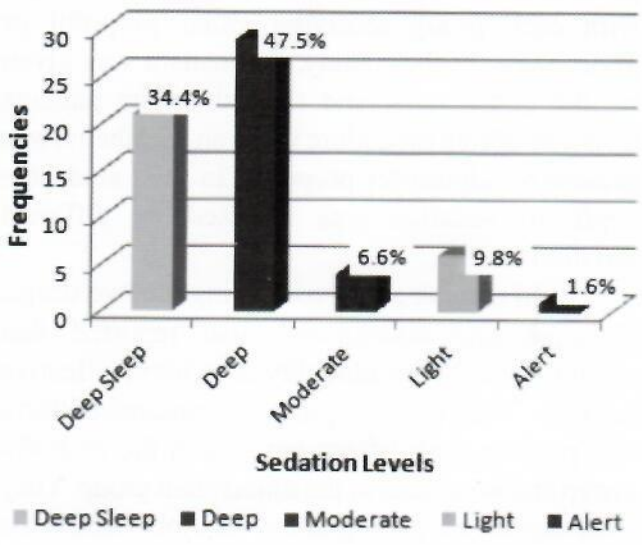


**Fig. 03: Sedation Levels of Group A (n=61)**

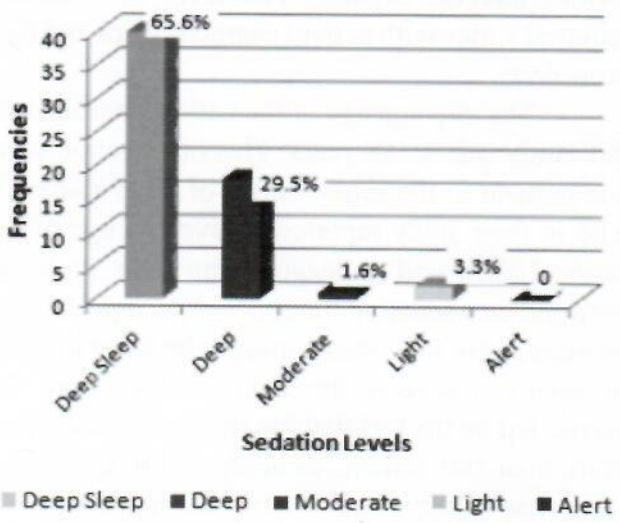


**Fig. 04: Sedation Levels of Group B (n=61)**

## DISCUSSION:

The current study reveals that intravenous propofol was significantly more effective in achieving adequate sedation at 2-minutes after bolus administration when compared with intravenous midazolam. Propofol was effective in 95.1% of the cases as compared to midazolam which was effective in 82% of the patients.

The development of gastrointestinal endoscopy has greatly expanded the diagnostic and therapeutic capabilities of gastroenterologists. Adequate patient tolerance is essential for successful completion of a safe examination and compliance with subsequent follow-up. As a result, endoscopists have developed skills in administering a variety of sedative and analgesic agents to facilitate procedures and enhance patient comfort[14].

A number of agents have been used to achieve a state of deep relaxation and analgesia. The most common approach to sedation for endoscopy is intravenous conscious sedation, which involves the administration of benzodiazepines alone or in combination with opiates to achieve moderate levels of sedation. A systematic review of 36 studies involving procedural sedation found that sedation provides a high level of clinician and patient satisfaction and a low risk of serious adverse events.[15] The level of sedation required varies with patient characteristics and the procedure.

The average age of the patients enrolled in this study was 49.48 years. This observation is in comparison to the observations of de Wit *et al.*,[16] who in their study reported an average age of 56 years. Cohen and colleagues[17] on their study of propofol as a sedative for endoscopy, reported the average age of their study group to be 59 years. The difference between the average age may be accounted by the fact that the study conducted had more than 800 patients as compared to this study which had a study population of 122 patients.

Horiuchi and associates[18] used propofol sedation for EGD in their study and they reported that in their study 52.4% of the patients were male and 42.5% female. This shows a male to female ratio of 1.35: 1. These results are comparable to that of this study which also showed a male to female ratio of 1.54: 1. In this study 60.7% of the patients were male and 39.3% females. Chin *et al.*,[19] in another study on comparison of sedation using midazolam and propofol, reported the ratio to be 2.15:1. This observation also supports the finding that majority of patients undergoing elective EGD are males.

It was observed in this study that the number of patients belonging to the ASA I category were 70 (57.4%) while 52 (42.6%) belonged to the ASA II. The same trend was reported by Cohen *et al.*,[17] who too reported this frequency to be 62% (ASA I) and 27% (ASA II). Both the groups formed in this study had similar number of ASA I patients, 38 (62.3%) and 32 (52.5%) in groups A and B respectively.

Overall midazolam achieved effective sedation in 82% of the patients while propofol achieved the same in 95.1% of the cases. Jung *et al.*,[14] in their study of sedation in ERCP using the same two drugs also reported a comparable result, stating effectiveness of midazolam to be 83% and that of propofol at 93%. They randomized eighty patients into two groups of forty(40) patients each, with each group receiving either propofol or midazolam. In their study, midazolam was given by the endoscopist and titrated to the patients response during procedure while an anesthetist was present to administer propofol. In their study the depth of sedation was assessed by different sedation scores.

In another study comparing the two drugs, Krugliak and colleagues[12] also reported that propofol is a better modality to achieve effective sedation. Their study population consisted of thirty two patients with fifteen patients in the propofol group and seventeen in the midazolam group. They used electroencephalogram as the tool to assess the depth of sedation for their study. Bo *et al.*,[20] conducted a meta analysis to compare midazolam

and propofol and concluded that the latter's use leads to shorter recovery time without an increase of cardiopulmonary side effects and provides adequate sedation. Databases included PubMed, Embase and Cochrane Central Register of Controlled Trials and they included six trials with a total of six hundred and sixty three patients. Lordan and colleagues[21] also arrived at the same conclusion in their study of two hundred and fifty two patients.

## CONCLUSION:

Intravenous propofol is effective in achieving adequate depth of sedation when compared with midazolam. Therefore, it should be used routinely in endoscopies in the future.

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