Risks and Benefits of Propofol and Midazolam for Sedation during Upper Gastrointestinal Endoscopy in Egyptian Cirrhotic Patients

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ABSTRACT

Background: Upper gastrointestinal (GI) endoscopy, either diagnostic or therapeutic, is frequently performed under conscious sedation in cirrhotic patients. The standard agent, on the other hand, is not yet well established.

Objective: Comparison between propofol and midazolam for conscious sedation during upper GI endoscopy in patients with liver cirrhosis in terms of safety and effectiveness. **Patients and methods:** Sixty cirrhotic (Child-Pugh A or B) patients, at Al-Azhar University Hospitals' Endoscopy Unit, were included in the study and randomly assigned to either propofol group (30 patients) or midazolam group (30 patients). Patients aged 18 to 65 years with known chronic liver disease who presented for upper GI endoscopy for routine variceal screening or banding were eligible. Patients with advanced or decompensated liver disease (Child score >10) were excluded. Sedation was administered by an anesthesiologist. **Results**: Our results observed clearly that the recovery time, patient satisfaction, and the incidences of hypoxia differ significantly between groups. **Conclusions:** propofol is safe and effective when compared to midazolam for sedation during upper GI endoscopy in cirrhotic patients.

Keywords: Propofol, Midazolam, Cirrhosis, Upper GI Endoscopy.

INTRODUCTION

Upper GI endoscopy is performed regularly in patients with chronic liver disease to evaluate for portal hypertension complications such as esophageal varices [(1)]. Patients are routinely sedated to make the procedure simple and more pleasant for them [(2)].

The selection of a sedative agent is critical to ensuring safe and effective upper GI endoscopy. Sedation targets include patient safety, providing analgesia and amnesia, accomplishing the upper GI endoscopy, and quickly returning the patient to pre-sedative levels [(3)]. Because of its amnestic properties, midazolam outclasses older benzodiazepines [(4)]. Midazolam alone, with or without opioids, is the most commonly used sedative regimen in our endoscopy unit but the prolonged half-life in patients with liver failure is a red flag [(5)]. Propofol is frequently used as a substitute for midazolam in patients with impaired hepatic or renal function because it does not require dose adjustment [(6)]. Propofol is a hypnotic agent that influences moderate to deep sedation (conscious). It is quickly metabolized in the hepatocytes before being excreted by the renal tubules [(7)]. Propofol has several advantages due to its rapid onset, shorter length of action, and rapid recovery of cognitive abilities [(8)].

However, whether propofol provides the same benefits in high-risk groups, such as patients with liver cirrhosis, is mysterious. Deficient protein synthesis, disrupted drug metabolism, and affected hepatic blood flow in patients with chronic liver disease may affect the bioavailability of drugs, placing patients undergoing endoscopy at a greater likelihood of negative events [(8)].

This designed research's main goal was to compare the effectiveness and safety of propofol and midazolam in cirrhotic patients undergoing endoscopy. Numerous comparative trials [(9)] have been carried out to evaluate their effectiveness and tolerability. Some of these experiments failed to detect a significant statistical difference between midazolam and propofol due to small sample sizes. Other trials ascertained that propofol sedation has the potential benefits of shorter recovery time, shorter discharge time, higher postanesthesia recovery scores, greater sedation, and better patient cooperation, with no raise in side effects [(10, 11)].

PATIENTS AND METHODS

Sixty patients with known chronic liver disease (cirrhosis), at Al-Azhar University Hospitals' Endoscopy Unit, were enrolled in the study and randomly assigned to either propofol or midazolam for sedation. Patients aged 18 to 65 years with known chronic liver disease (Child-Pugh class A or B) who presented for upper GI endoscopy for routine variceal screening or banding was eligible. Patients with advanced or decompensated liver disease (CP score >10), GI bleeding within the previous month, hepatic encephalopathy, advanced medical disease, known allergy to the sedative, active alcohol or illicit drug abuse, or refusal to participate were excluded. Written informed consent from all patients enrolled in the study.

As shown in table (1), 30 patients were assigned to the propofol group (group 1), while the remaining 30 patients were assigned to the midazolam (group 2). Sedation was administered by an anesthesiologist.

Table (1): Patient groups

Propofol group	Midazolam group
30 patients	30 patients
The initial dose of propofol was 0.5 mg/kg; the maintenance dose was 10-20 mg bolus at 60 s intervals.	The initial dose of midazolam was 3 -5 mg, and the maintenance dose was 0.5 to 1 mg every 2-3 minutes up to a maximum cumulative dose of 10 mg or 0.1 mg/kg of body weight.

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According to the most recent laboratory data, all patients had upper GI endoscopy, liver ultrasound, and liver function (serum albumin, total bilirubin, aspartate transaminase [AST], alanine transaminase [ALT]), CBC, the international normalized ratio [INR], and serum creatinine was assessed. The Child-Turcotte-Pugh (CTP) score was estimated in cirrhotic patients based on laboratory findings and physical examination. Throughout the procedure and in the recovery room, baseline data for oxygen saturation were collected.

We compared the two groups in terms of; Time to complete recovery (patient awake), a 10-point visual analog scale was used to assess patient satisfaction [1 = least satisfied, 10 = most satisfied] and Hypoxia [defined as SpO2 < 90%].

Ethical approval: The study was approved by the Ethics Board of Al-Azhar University number "HGID.Deplt._-Med.Research_Liv.GIT.Dis._000128" and an informed written consent was taken from each participant or their parents in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis: Quantitative data were presented as mean and standard deviation (SD), and were compared by independent t-test. Qualitative data were presented as frequency and percentage and were compared by Chi-Square test. P < 0.05 for any parameters was considered significant. The analysis of data was made using the SPSS; PC+ version 22 computer program.

RESULTS

Table (2): Demographic characters of the examined patients

	Groups	N	Mean ± Standard Deviation	p-value
Age	Propofol	30	56.50±8.06	0.003 **
	Midazolam	30	49.20±10.02	
Sex	Propofol	30		1
	Male		15 (50 %)	
	Female		15 (50 %)	
	Midazolam	30		
	Male		15 (50 %)	
	Female		15 (50 %)	

** = Highly significant at (P < 0.01)

Table (2) shows that the demographic characteristics that include age of the examined patients differ significantly among propofol and midazolam groups.

Table (4): Recovery time among examined patients

	Groups	N	Mean ± Standard Deviation	p-value
Recovery time	Propofol	30	6.21±1.44	0.001 **
	Midazolam	30	31.08±4.88	

** = Highly significant at (P < 0.01)

Table (3) shows that, the recovery time was significantly longer in the midazolam than in the propofol group

Table (4) Patient satisfaction score among examined patients

	Groups	N	Mean± Standard Deviation	p-value
Patient satisfaction score	Propofol	30	8.93±0.78	0.001 **
	Midazolam	30	8.23±0.82	

** = Highly significant at (P < 0.01)

Table (4) shows that the patient satisfaction scores differed significantly between patients of the two studied groups

Table (5): Hypoxia incidences among examined patients

	Groups	N	%	p-value
Hypoxia	Propofol	30		0.01 **
	NO	30	100	
	Yes	0	0	
	Midazolam	30		
	NO	24	80	
	Yes	6	20	

** = Highly significant at (P < 0.01)

Table (5) shows that the incidences of hypoxia differed significantly between the patients of the two studied groups, the higher incidence of hypoxia was observed in the midazolam group.

DISCUSSION

Cirrhotic patients frequently undergo an upper endoscopy to screen for or treat varices or portal hypertensive gastropathy. These endoscopic procedures are usually uncomfortable; thus, pre-endoscopy sedation is recommended [(4)]. There are currently no guidelines for sedation in cirrhotic patients, and few studies have been conducted to evaluate sedation in cirrhotic patients. Each sedative drug had a distinctive profile of safety and efficacy. As a result, the hunt for the safest and most beneficial drug or drugs is keeps going [(12)].

In terms of recovery time, our study cleared that a highly significant difference between the two groups studied was found. Longer recovery times were reported in the midazolam group, while shorter recovery times were reported in the propofol group, demonstrating propofol's clear superiority in this context [31.08 ± 4.88 minutes, while in the propofol group it reached 6.21±1.44 (P < 0.01)].

Our findings are consistent with those of **Carlsson and Grattidge, [(13)]** who found that propofol, had better compliance, sedative effect, and faster recovery than midazolam, but they had similar amnesia.

Wang *et al.* [(14)] recommended propofol for upper GI endoscopy because it was both safe and effective in both

healthy and cirrhotic patients. Furthermore, it had a faster recovery and discharge time, better sedation, and higher patient satisfaction than midazolam, with no cardio-pulmonary side effects.

Poulos *et al.* [15] also advised that propofol to be chosen as the preferred sedation agent (even in patients with cirrhosis) because it was accompanied by faster recovery than midazolam-based sedation protocols. They also claimed that propofol is connected with patient satisfaction and decreased agony throughout the procedure. Likewise, **Correia *et al.*** [16] revealed results that were consistent with the current work.

Additionally, **Martinez *et al.*** [17] demonstrated that propofol sedation is safe in elderly populations, even though geriatrics are more vulnerable to complications. In a meta-analysis of 20 trials for sedation in cirrhotic patients, **Singh *et al.*** [18] realized that propofol was more effective than midazolam in terms of recovery time. Moreover, the use of propofol was linked to high levels of patient satisfaction.

Similarly, two studies done by **Sharma *et al.*** [19] and **Khamaysi *et al.*** [20] concluded that propofol was safe and did not aggravate minimal hepatic encephalopathy.

To add to that, **Riphaus *et al.*** [21] found that propofol has a good pharmacokinetic profile than benzodiazepine in terms of rapid recovery, and a similar level of amnesia without deterioration of psychometric score in cirrhotic patients.

In the current study, all patients tolerated propofol without experiencing any major side effects. This was in accordance with previous research on the safety of propofol in patients with liver cirrhosis [21]. Different pieces of literature indicate the advantage of propofol since it offers sustained sedation during the procedure and patients didn't complain of any discomfort. The findings of this study agree with those of **Watanabe *et al.*** [22] who found that patient satisfaction was significantly higher with propofol sedation than with midazolam.

However, our findings contradict those of **Koo *et al.*** [23] who discovered that midazolam and propofol have the same sedative effect, and there was no substantial difference in recovery time, endoscopy time, or oxygen saturation among the groups studied. Discrepancies in patient selection and cohort inequality could explain the apparent difference in our findings.

Rex *et al.* [24] reported that in a non-anesthesiologist-governed propofol, only four cases (from 200 patients included in the study) developed hypoxia with less than 90% O_2, all of which occurred during endoscopy. In addition, they stated that propofol was safely administered by a skilled nurse under the supervision of an endoscopist.

In our study, there was a significant difference in terms of complications (hypoxia) between the midazolam and propofol groups; hypoxia was less common in the propofol group; hypoxia was recorded in 6 out of 30 patients (20%), whereas no hypoxia (none) was reported in the propofol group. **Correia *et al.*** [16] disclosed that complications occurred in 22 of 210 patients (10.5%) and were not statistically different between the studied groups (8 of 110 (7.3%) of the midazolam patients and 14 of 100 (14%) of the propofol patients). **Amornyotin *et al.*** [25] revealed a difference in complication rates in cirrhotic patients who received propofol versus those who did not receive propofol. They demonstrated that propofol-based anesthesia is safer. In accordance with a comprehensive meta-analysis done by **Daneshmend *et al.*** [26] propofol provided more rapid sedation and recovery than midazolam did. Besides that, **Chernik *et al.*** [27] have proven that propofol outshines midazolam in cirrhotic patients.

Limitations exist in our research. The majority of the endoscopy procedures were not therapeutic and sedation with a gastroenterologist or trained nurses will need to be checked in further studies. Future studies are needed to outline the safety of propofol in advanced and decompensated liver disease (Child C).

To summarise, when administered by a trained anesthetist, propofol is safer and more effective than midazolam for sedation during endoscopy in patients with cirrhosis.

CONCLUSION

Propofol is superior to midazolam for sedation during endoscopic examination in patients with chronic liver disease. As an outcome, propofol could be recommended the initial sedative in our endoscopy units.

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