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Efficacy and Safety of Propofol Sedation During Urgent Upper Gastrointestinal Endoscopy – A Prospective Study

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A B S T R A C T

The aim of this study was to investigate both the efficacy and safety of sedation with propofol during urgent therapeutic gastroscopy in patients with upper gastrointestinal bleeding. This prospective study included a total of 110 patients. Propofol was administered intravenously at the starting dose of 1 mg/kg body weight and was followed by repeated doses. Oxygen saturation and heart rate were monitored by pulse oxymetry. The mean dose of propofol administered was 161 ± 49 mg. Urgent upper GI endoscopy under propofol sedation was successful in 98% of cases. Endoscopists rated the sedation as good in 83.6%, satisfactory in 14.5%, and poor in 1.8% of patients. Potentially harmful drop in oxygen saturation below 85% was observed in 5.5% of patients, whereas a temporary drop in heart rate below 50 beats/min was observed in 11.8%, not requiring any intervention. Almost 93% of patients could not remember the beginning or the end of the intervention. This data demonstrates that sedation with propofol is suitable for use in patients with upper gastrointestinal bleeding undergoing urgent endoscopy.

Key words: *gastrointestinal endoscopy, sedation, propofol*

Introduction

Over the past two decades, endoscopy has evolved from being a diagnostic tool to being the initial therapeutic intervention of choice in acute upper gastrointestinal (GI) bleeding. Remarkable advances have been made in the therapeutic endoscopy of bleeding upper GI lesions, including various hemostatic techniques such as hemoclips, loops and ligations and various forms of thermal or injec-

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tional methods[1,2]. Such therapeutic endoscopic procedures are frequently prolonged, and require optimal patient co-operation.

Propofol is a relatively new intravenous sedative hypnotic that is used for the induction and maintenance of conscious sedation in GI endoscopy. Based on its use in gastroscopy[3,4], colonoscopy[5,6], and ERCP[7,8], propofol has been proved to be a suitable sedative in gastroenterological endoscopy. Furthermore, in recently published clinical trials intravenous sedation with propofol was found to be more effective than sedation with midazolam[9–11]. However, to our knowledge, there is no prospective study that has assessed the safety and efficacy of propofol for conscious sedation during urgent endoscopic procedures in patients with upper GI bleedings. Therefore, the aim of this prospective study was to investigate the efficacy and safety profile of sedation with propofol during urgent therapeutic gastroscopy in patients with upper GI bleeding that included many elderly individuals with multiple comorbidity problems, typical of the patient profile currently seen in major hospitals worldwide.

Patients and Methods

Between January 2001 and December 2001, patients admitted for upper GI bleeding in the Endoscopy Unit of the Division of Gastroenterology at the University Hospital »Sestre milosrdnice«, Zagreb, were considered for the study. Upper GI bleeding was suspected only if medical staff members witnessed hematemesis and/or melena, observed bloody nasogastric aspirate or detected black, tarry material on digital rectal examination. Patients were included in the study if the emergency upper GI endoscopy has been done under sedation with propofol alone. Use of additional sedative or analgesic drugs was not allowed. Exclusion criteria included pregnancy, patients under the age of 18 or older than 80 years, those who could not give informed consent, patients with severe congestive heart failure, torrential hemorrhage with persistent shock, unconsciousness or known hypersensitivity to propofol. Patients on regular dialysis, patients with heart rate lower than 40 beats per minute and those with tachyarrhythmias, or baseline oxygen saturation lower than 85% were also excluded from the study.

This prospective and nonrandomized study included a total of 110 patients who underwent urgent upper GI endoscopy. Written consent was obtained from each patient, and the local ethics committee had approved the study.

Endoscopic setting

All urgent upper GI endoscopies were done with Olympus EVIS 140 video endoscopes by skilled endoscopists, each with at least five years experience in the treatment of patients with upper GI bleeding. Urgent endoscopy was always performed within six hours of hospital admission.

Following endoscopy, the endoscopist filled out a questionnaire rating the adequacy of sedation as: (1) good (complication-free intervention with adequately sedated patient), (2) satisfactory (restless patient; the procedure was successfully completed), and (3) poor (intervention had to be aborted due to the insufficient sedation or severe side effects). Separate questions were related to the presence of any adverse effects and possible interventions. The length of the endoscopic procedure has also been recorded.

Anesthetic procedure and monitoring of patients

Endoscopic procedures were carried out without tracheal intubation. Sedation was performed exclusively with propofol administered by a skilled nurse who was present throughout the procedure. Propo-

fol (Propofol® 1%, Fresenius Kabi, South Africa; Diprivan®, Astra Zeneca, Great Britain) was administered intravenously at the starting dose of 1 mg/kg body weight and was followed by repeated doses of 20 mg intravenously at two-minutes intervals until complete sedation had been achieved (maximal sedation level without response). The maximal initial dose of propofol was set subjectively at 200 mg. If the maximal dose did not lead to sufficient sedation or if severe side effects occurred, intervention has been aborted. Sedation was maintained by administering a bolus of 10 to 20 mg of propofol intravenously every time the patient's resistance was noted, making the endoscopic procedure difficult to perform.

All patients received supplemental oxygen (10 L/min) via a nasal cannula.

Oxygen saturation and heart rate were monitored by pulse oxymetry (Spenser Otis 3000, USA). Blood pressure was measured at 5-minute intervals during the first 15 minutes of the intervention, and then every 10 to 15 minutes afterwards.

Hypoxia was defined as oxygen saturation below 85% over at least 30 seconds. Adverse reactions such as injection pain, coughing reflex, headache and phases of apnea were also recorded.

The recovery time after completion of the upper GI endoscopy was measured using the Stewart score, which assessed respiration, consciousness and motor coordination[12].

All patients were carefully monitored for a minimum of one hour prior to the admittance to the Intensive Care Unit where any delayed effects of sedation were also documented.

Statistical analysis

All values were reported as means ± standard deviations or medians where appropriate. Statistical analysis was performed using the Mann-Whitney U-test where appropriate (Statistica for Windows, Statsoft Inc., USA). Values of $p< 0.05$ were considered significant.

Results

A total of 110 patients who underwent urgent upper GI endoscopy received propofol. There were 49 women and 61 men, mean age 55±13 years (range 22 to 78 years). Some patients' characteristics with respect to potential impact on degree and quality of sedation were presented in Table 1.

TABLE 1
CHARACTERISTICS OF 110 INVESTIGATED PATIENTS (49 FEMALES, 61 MALES), AGE RANGED FROM 22 TO 78 YEARS (55±13)

	N (%)
Alcohol abuse	63 (57.3%)
Smokers	70 (63.6%)
Regular use of sedative or psychotropic drugs	19 (17.3%)
Shock	8 (7.3%)
Hemoglobin concentrations (g/L)	27 (24.5%)
Comorbidity	
Cardiovascular disease	48 (43.6%)
Liver cirrhosis	40 (36.4%)
Respiratory disease	12 (10.9%)
Diabetes mellitus	10 (9.1%)
Renal failure	9 (8.2%)
Mortality	3 (2.7%)

During urgent endoscopy the cause of upper gastrointestinal bleeding was identified in 109 patients (99%), (Table 2). Interventional hemostatic procedures during urgent upper GI endoscopy have been used in 79 patients (71.8%). Median of duration of urgent upper GI endoscopy under propofol sedation was 39 minutes (ranging 10 to 90 minutes).

The mean dose of propofol administered was 161±49 mg (with a range of 80

TABLE 2
ENDOSCOPIC DIAGNOSES AND HEMOSTATIC PROCEDURES (N=110)

Endoscopic diagnosis	N (%)
Peptic ulcer bleeding	54 (49.1)
Hemoclip therapy	28
Injection therapy	12
Without therapy	14
Esophageal variceal hemorrhage	23 (20.9)
Variceal ligation	11
Injection therapy	8
Variceal obliteration	4
Bleeding Mallory-Weiss tears	8 (7.3)
Hemoclip therapy	3
Without therapy	5
Bleeding gastric erosions	7 (6.4)
Argon plasma coagulator	1
Without therapy	6
Bleeding portohypertensive gastropathy	5 (4.5)
Argon plasma coagulator	2
Without therapy	3
Bleeding gastric carcinoma	4 (3.6)
Argon plasma coagulator	2
Without therapy	2
Bleeding watermelon stomach	2 (1.8)
Argon plasma coagulator	2
Gastric variceal hemorrhage	2 (1.8)
Variceal obliteration	2
Bleeding angiectasiae	2 (1.8)
Ligation	1
Hemoclip therapy	1
Bleeding Dieulafoy lesion	2 (1.8)
Argon plasma coagulator	1
Hemoclip therapy	1
Unknown	1 (0.9)

to 390 mg). The individual propofol dose used was mainly dependent on body weight and the duration of the procedure. There was also a significant difference between the dose of propofol used and the presence of hepatic failure (determined as a bilirubin concentration above 40 mmol/L with at least twofold increase in AST and ALT concentrations), (106 ± 31 mg vs. 176 ± 44 mg, p<0.001), (Table 3).

Sedation efficacy

Urgent upper GI endoscopy under propofol sedation was successful in 98% of cases (108 out of 110 patients). Endoscopists rated the sedation as good in 92 patients (83.6%), satisfactory in 16 patients (14.5%), and poor in two (1.8%), (Figure 1). Te two patients in whom urgent endoscopy under propofol sedation was not successful had advanced alcoholic liver cirrhosis and both required therapeutic procedures relating to esophageal variceal hemorrhage and a bleeding Dieulafoy stomach lesion, respectively (in patient with bleeding esophageal varices endoscopy had to be aborted due to insufficient sedation, whereas in patient with a bleeding Dieulafoy's lesion severe side effect occurred: an epileptic seizure with short apnea and a prolonged decrease in oxygen saturation – completely reversible after withdrawal of the endoscope and without consequence during the follow-up period). In these patients, endoscopy had been successfully performed immediately after the unsuccessful sedation with

TABLE 3
DOSES OF PROPOFOL IN PATIENTS WITH AND WITHOUT HEPATIC FAILURE (N=110)

	Number of patients	Dose of propofol (mg) X ± SD
Hepatic failure	40 (36.4%)	106±31
No hepatic failure	70 (63.6%)	176±44*

* p<0.001

propofol, but this time without any form of sedation.

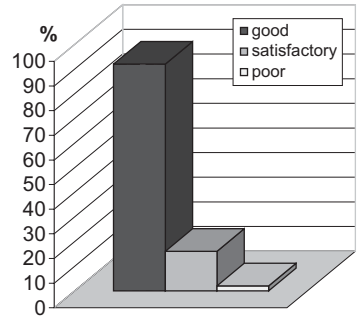

Fig. 1. Sedation quality as rated by the endoscopist.

Vital signs and adverse effects

The mean decline in oxygen saturation (initial oxygen saturation versus lowest oxygen saturation during the endoscopy) was 5±3%. Potentially harmful drop in oxygen saturation below 85% was observed in six patients (5.5%). Oxygen desaturation was short-lasting in five patients (4.5%). Endoscopic suction in all those patients resulted in a fast increase in oxygen saturation. In only one patient, an epileptic seizure and short-time apnea developed. After withdrawal of the endoscope, the patient started to breath spontaneously and the epileptic attack stopped before any additional medication was given and assisted ventilation was applied. She did not develop any late sequels from the event.

A temporary drop in heart rate below 50 beats/min was observed in 13 patients (11.8%), but did not require any intervention. In only one patient undergoing propofol sedation, tachyarrhythmia (with a median heart rate of 200 beats/min) occurred, without any signs of hypotension or hypoxia. Ten minutes after the therapeutic procedure had been successfully performed and endoscope has been withdrawn, tachyarrhytmia stopped spontaneously. No residual effects had been observed during the follow-up period.

Mean decrease in the mean arterial blood pressure (initial blood pressure versus minimal blood pressure value during the endoscopy) was 12±9 mmHg.

In only one patient with significant hypotension and shock, hypotension was prolonged (lasting more than one hour after the intervention).

Pain at the injection site was noted in only one patient.

Transient hiccups were present in a majority of patients (59 out of 110 patients, 53.6%), whereas cough reflex was seen in only 6 (5.5%) patients.

Patient's recovery

All patients who underwent urgent upper GI endoscopy under intravenous propofol sedation had achieved the total Steward score by 30 minutes. Almost 93% of patients (102 out of 110 patients) could not remember the beginning or the end of the intervention.

Discussion

The need for proper sedation of patients with upper gastrointestinal bleeding during urgent upper gastrointestinal endoscopy is evident particularly if technically demanding endoscopic procedures have to be performed. Interventional therapeutic procedures during upper gastrointestinal bleeding sometimes last more than one hour, are potentially unpleasant to the patient, and therefore are not acceptable without sedation.

Propofol, 2.6 diisopropylphenol is an ultra-short acting sedative hypnotic agent that has received much attention, for use during gastrointestinal endoscopy[13]. Propofol may be ideal for sedation of bleeding patients during urgent upper gastrointestinal therapeutic procedures because

of its rapid onset of sedative action, easy titrability, and short duration of effect[14]. The results of this prospective and controlled study clearly demonstrate that propofol provides very effective sedation during urgent upper gastrointestinal endoscopy performed in patients with upper gastrointestinal bleeding. Endoscopists rated the sedation as good or satisfactory in more than 98 percent of cases. It is very important to emphasize that interventional hemostatic procedures have been done in more than 83 percent of patients, and that median of duration of urgent endoscopy under propofol sedation was 39 minutes.

Adverse reactions of propofol are rare and have only brief duration, as a result of its short half-life. Respiratory depression and cardiovascular adverse effects such as hypotension or bradycardia have been associated with propofol use[15]. However, in majority of clinical studies no serious complications were observed upon propofol sedation although these studies were carried out mostly on patients with relatively good general health[3–11].

Despite the fact that in our study there were many elderly individuals with multiple, and in many cases significant comorbidity, serious complications were seen in a very small percentage of patients suggesting that the propofol safety profile in elderly seems to be comparable to the one in young adults. According to our observations, significant problems regarding both the efficacy and safety of propofol can be associated with propofol administration in patients with advanced liver failure. There is a strong correlation between the individual propofol dose used and the presence of significant hepatic failure. It seems possible that the high overall dosage of propofol is directly related to the adverse effects since most of our patients in whom we observed cardiorespiratory adverse effects of propofol were patients with liver failure.

As has been noted in previous studies, the predominant cardiovascular effect of propofol is a reduction in the systemic vascular resistance, which may induce hypotension[16]. Despite the fact that the decrease in mean arterial pressure has been also observed among patients in this study, it must be emphasized that only one patient with significant hypotension and shock had prolonged hypotension after the sedation with propofol, but without any clinically relevant consequences.

In conclusion, this data demonstrates that sedation with propofol is suitable for use in patients with upper gastrointestinal bleeding undergoing urgent endoscopy. Although the complication rate is very low and complications are of short duration close monitoring of the sedated patient is mandatory.

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DJELOTVORNOST I SIGURNOST SEDACIJE PROPOFOLOM TIJEKOM URGENTNE ENDOSKOPIJE GORNJEG DIJELA PROBAVNOG SUSTAVA: PROSPEKTIVNA STUDIJA

S A Ž E T A K

Cilj ove prospektivne studije bio je istražiti sigurnost i djelotvornost propofola u sedaciji tijekom endoskopskih zahvata u bolesnika s krvarenjem iz gornjeg dijela probavnog sustava. U studiju je bilo uključeno 110 bolesnika u kojih je načinjena urgentna endoskopija. Propofol je primijenjen intravenski u početnoj dozi od 1 mg/kg tjelesne težine, uz dodavanje lijeka do postizanja potpune sedacije. Saturacija kisikom i srčana frekvencija praćeni su putem pulsnog oksimetra. Prosječna doza primijenjenog propofola je bila 161 ± 49 mg. Hitna endoskopija gornjeg dijela probavnog sustava bila je uspješna u 98% slučajeva. Endoskopičari su ocijenili sedaciju kao dobru u 83,6%, zadovoljavajuću u 14,4% te lošu u 1,8% bolesnika. Potencijalno opasan pad u saturaciji kisikom ispod 85% zabilježen je u 5,5% bolesnika, dok je kratkotrajna bradikardija (<50 otkucaja/min) zamijećena u 11,8% bolesnika, ali nije zahtijevala nikakav terapijski pristup. Gotovo je 93% bolesnika imalo amneziju za sam početak i kraj endoskopskog zahvata. Ovi podaci pokazuju da je sedacija propofolom pogodna za sedaciju bolesnika s krvarenjem iz gornjih dijelova probavnog sustava u kojih je potrebno učiniti hitnu endoskopiju.