Endoscopist-Administered Propofol Sedation Is Safe – a Prospective Evaluation of 10,000 Patients in an Outpatient Practice

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Abstract

Background & Aims: Due to improved patient satisfaction and its pharmacological benefits, more endoscopic procedures are carried out with the use of propofol. However, recent rulings in the USA challenge endoscopist-administered propofol sedation. We evaluated the safety of endoscopist-administered propofol sedation in a German outpatient practice. Methods: During a period of 65 months, we prospectively evaluated 10,000 patients who received endoscopic procedures. During 377 endoscopic procedures we performed extensive blood pressure observation. Propofol was administered via intermittent i.v. bolus titration by trained practice nurses under the supervision of the gastroenterologist. Oxygen saturation, heart rate and blood pressure were recorded constantly during the procedure and adverse cardiopulmonary events were monitored by the endoscopy team. A major respiratory event was defined as an episode of apnea or laryngospasm requiring assisted ventilation. Results: 13,764 endoscopic procedures were recorded in 10,000 patients (7,349 esophago-gastro-duodenoscopies (ESD), 6,415 colonoscopies); 9,654 patients were sedated with propofol (ESD: 115 ± 35; colonoscopy: 155 ± 52; combined: 199 ± 55 mg) and 346 patients had endoscopic examination without sedation. 0.03% of the patients received mask ventilation due to apnea and in 0.39% minor events of hypoxemia (oxygen saturation < 90%) were recorded. Bradycardia and arterial hypotension occurred in 0.07% and 0.24% of the patients. Patients with adverse events were significantly older than patients without (P < 0.001). Conclusion: The low number of adverse events recorded in this prospective study concludes that endoscopist-administered propofol sedation is a safe procedure. It does not seem likely that additional support of an anaesthetist would further improve patient’s safety, and particularly cost-efficiency.

Key words


Introduction

Several studies were able to show that endoscopic procedures performed under sedation lead to higher acceptance in the population [1,2]. More and more procedures are now performed under sedation and therefore improve patient comfort and increase the willingness to undergo repeat procedures [3,4]. Thus, proper sedation regimens are a key feature sustaining the acceptance of endoscopic procedures such as colorectal cancer screening programs. The use of the sedative propofol has significantly increased over the past years due to its pharmacological benefits with rapid onset and short duration of action [4] resulting in quick patient recovery upon completion of the procedure [5]. Randomized studies showed that acceptance and satisfaction of endoscopic procedures were significantly increased by the use of propofol [6-11] and a meta-analysis of 12 randomized colonoscopy trials reported significantly fewer adverse side effects for propofol than benzodiazepines [12]. Therefore, the German guidelines for endoscopic sedation favour the use of the sedative propofol for gastrointestinal sedation [13]. Despite numerous studies, there still exist controversial discussions within the medical community whether propofol administration is safe when given by endoscopists. Some anaesthesiologists argue that endoscopist-administered propofol sedation is unsafe. However, this assumption is not based on scientific evidence but on a warning contained in the package insert that propofol should only be given by persons trained in the administration of general anaesthesia. In addition, a ruling
from the Centers for Medicare and Medicaid Services (CMS) in the USA has challenged endoscopist-directed propofol administration. The CMS released revised Interpretive Guidelines related to the Hospital Conditions of Participation governing Anaesthesia Services (42 CFR 482.52), requiring an anaesthesiologist to oversee the administration of propofol for colonoscopy. Anaesthesia-assisted sedation results in highly increased costs [14] that not only threaten routine endoscopic procedures but also programs such as colorectal cancer screening. The aim of this prospective study with 10,000 cases in an out-patient gastroenterology practice is to evaluate the safety of endoscopist-administered propofol sedation.

Methods

The study was approved by the ethics committee of the University of Heidelberg, Germany. The examinations were carried out in the senior author’s outpatient practice in Heidelberg. The study was conducted from October 2006 to January 2012 with the aim to evaluate a total number of 10,000 patients. All endoscopic procedures were recorded prospectively. The following variables were registered: patient’s age, sex, indication for the procedure, endoscopic diagnosis, adverse effects, propofol dose, co-medication, completeness of colonoscopy (cecum intubation rate), and combination with gastroscopy and polypectomy.

Practical training of the endoscopist team contains training of advanced cardiac life support, airway-management with mask ventilation and intubation, training on propofol administration and a written examination. The courses for gastroenterologists and their endoscopic teams are run by anesthesiologists or gastroenterologists. 1-day or 3-day courses are certified by the DGVS (Deutsche Gesellschaft für Verdauungs- und Stoffwechselkrankungen) and the DEGEA (nurses association). A yearly course in emergency resuscitation is recommended for the members of the endoscopy team.

Propofol administration

Sedation is voluntary and is offered to all patients scheduled for endoscopy. 96.5% of the endoscopic procedures were performed under sedation. Exclusion criteria included allergy to propofol or its components, patients with severe morbidity (ASA class III and higher from cardiopulmonary cause), and sleep apnea. Subjects with ASA class III from a non-cardio-pulmonary source were included in the study. The excluded patients requesting sedation were sent to an inpatient endoscopic department. Propofol was administered by intermittent intravenous bolus titration to the necessary level of sedation as clinically judged by the practice nurse and the endoscopist. In most cases, depending on the age, body weight and co-morbidity we started with a 40 mg bolus followed by 20 mg boluses after 40-60 seconds, respectively, until the subjects reached the level of conscious sedation. Propofol was the only sedative used in this study; combined sedation regimens were not applied. All the patients received supplemental oxygen at a flow rate of 2 L/min. The practice nurse administering propofol had no other tasks except to monitor the patient and administer sedation in continual cooperation with the endoscopist. Another individual assisted the endoscopist with the technical performance of the procedure. The monitoring consisted of continuous measurement of oxygen saturation and heart rate and of measurement of blood pressure before bolus injection of propofol and at 5 minute intervals thereafter.

During two months (March and April 2008) in 377 endoscopic procedures (199 colonoscopies and 178 gastroscopies) the blood pressure was recorded automatically in 2-minute-intervals and before the examination. Additionally the anamnestic systolic blood pressure was documented if known by the patient.

The data were displayed on a monitor placed next to the endoscopy monitor so that the endoscopist could see simultaneously the endoscopic picture and the vital data of the patient.

The primary clinical assessment of the patient included measurement of respiratory effort by visual assessment, by palpation of the chest wall and abdominal excursion, and/or by sensation of exhaled breath. In the case of a respiratory event during upper GI endoscopy, the endoscope was withdrawn within a few seconds; whereas, in the case of a respiratory event during colonoscopy, the endoscope was handed over immediately to the second practice nurse, so the gastroenterologist was able to manage ventilation of the patient.

Definition of adverse events

An event was defined as an episode of apnea or laryngospasm requiring assisted ventilation, which in all cases was bag-mask. All events involved clinical evidence of prolonged poor or absent respiratory effort or laryngospasm that was judged clinically to warrant assisted ventilation. Minor events of hypoxemia were defined as oxygen desaturation below 90% for more than 30 seconds and a rapid spontaneous normalization after verbal and tactile stimulation and supplementation with oxygen. Bradycardia was defined as a heart rate below 60/min. Medical intervention was performed at a heart rate below 40/min. Hypotension was defined as systolic pressure < 90 mmHg and saline was infused when the systolic pressure dropped below 80 mmHg.

Statistics

Statistic calculation was carried out with the use of Mann-Whitney Rank Sum Test and the paired t-test as the age distribution and the target values were adequately normally distributed. The influence of the total dose of propofol as independent variable on systolic blood pressure and heart rate was evaluated by linear regression with the mathematical formula

\[ Yi = a + b \times xi \]

where \( Yi \) represents the maximal decrease of systolic blood pressure (or heart rate) in the ith patient and \( xi \) the dose of propofol in the ith patient. The coefficients \( a \) and \( b \)
describe the linear correlation for all patients. In this case the Zero-hypothesis means that the maximal decrease of the systolic blood pressure (or heart rate) does not change with the total dose of propofol and therefore, b is not significantly different from zero.

Results

In the 10,000 evaluated patients 13,764 endoscopic procedures were performed: 7,349 esophago-gastro-duodenoscopies (EGD) and 6,415 colonoscopies were recorded in 5,473 women and 4,527 men. The cecum intubation rate of all the colonoscopies was 99.15%. The mean age of the 10,000 patients was 51.8 years.

Propofol dosage

346 endoscopic procedures (321 gastroscopies, 25 colonoscopies) were performed without sedation. Combined examinations were only performed with the use of propofol. For EGD, the mean propofol dose administered was 115.6 mg (SD ± 35.9 mg), for colonoscopy 155.6 mg (SD ± 52.9 mg). The 3,764 patients that received a combined examination of EGD and colonoscopy received a mean propofol dose of 199.1 mg (SD ± 54.9 mg).

Adverse events

Of the 10,000 patients who had received endoscopic examination, we recorded 91 adverse events (0.91%). There was no case resulting in death or requiring endotracheal intubation; neurological sequelae or other permanent injury were also not recorded. Assisted ventilation was necessary in 3 cases due to apnea. Hypoxemia, defined as an O$_2$-saturation below 90% occurred in 39 patients (0.39%). Since no case of laryngospasm was observed the overall respiratory event rate was 0.42%. Of the 7 patients with bradycardia (0.07%) intravenous application of atropine was performed in 5 patients. Of the 24 patients with a hypotensive episode during endoscopy 11 received saline infusions (0.11%). Bleeding occurred in 12 of the 13,764 endoscopic procedures performed (0.08%). Bleeding needed intervention in 7 cases and was treated with endoscopic clipping (n=1), APC beamer coagulation (n=1) or a combination of endoscopic clipping and APC beamer coagulation (n=5). In 2 patients the bleeding did not completely stop after intervention and they were transferred to the hospital (0.02%). Two patients suffered from nose bleeding after EGD but fully recovered without further therapy. Three patients were transferred to the hospital due to intestinal perforation after endoscopy (0.03%; Table I).

### Table I. Incidence of adverse events

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation</td>
<td>0%</td>
</tr>
<tr>
<td>Mask ventilation</td>
<td>0.03%</td>
</tr>
<tr>
<td>Minor events of hypoxemia</td>
<td>0.39%</td>
</tr>
<tr>
<td>Bradycardia, total</td>
<td>0.07%</td>
</tr>
<tr>
<td>Bradycardia, with medical intervention</td>
<td>0.05%</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0.12%</td>
</tr>
<tr>
<td>Perforation</td>
<td>0.03%</td>
</tr>
<tr>
<td>Arterial hypotension, total</td>
<td>0.24%</td>
</tr>
<tr>
<td>Arterial hypotension, with medical intervention</td>
<td>0.11%</td>
</tr>
<tr>
<td>Overall rate of adverse events</td>
<td>1.15%</td>
</tr>
</tbody>
</table>

Polypectomy was performed in 658 of the 6,415 patients who received colonoscopy (10.2%).

Propofol dosage had no significant impact upon overall adverse events in comparison to patients without adverse events. However, statistical analysis revealed that patients with adverse events were significantly older than patients not affected by sedation (P < 0.001; Table II).

The mean anamnestic systolic blood pressure was significantly lower (P < 0.001) compared to the value before the examination (Fig. 1). Propofol sedation decreased systolic blood pressure over 6 minutes. Eight minutes after the first injection, the blood pressure was not significantly different from anamnestic values.

### Discussion

Since endoscopic procedures performed under sedation lead to increased patient comfort, the majority of procedures are now carried out with the use of sedatives. A meta-analysis [12] was able to show that endoscopist-administered propofol sedation has comparable or even reduced risks of hypoxemia, hypotension or bradycardia than sedation regimens with benzodiazepines plus opioids. In addition, several studies evaluating the safety of nurse-administered propofol sedation showed minimal adverse effects [8-10,15-22]. However, recent administrative events may threaten the practice of endoscopist-directed propofol administration,
to anesthesia requiring airway management. The observed
increase in propofol dosage may result in a switch from deep sedation
from minimal, moderate and deep sedation to anesthesia.
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depth of sedation as a risk factor for oxygen desaturation
multivariate analysis the authors were able to identify greater
of the patients the saturation dropped below 90%. Using
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[25]. The ASA defined several levels of sedation ranging
from minimal, moderate and deep sedation to anesthesia.
Propofol has a narrow therapeutic window; therefore changes
in propofol dosage may result in a switch from deep sedation
to anesthesia requiring airway management. The observed
particular in the USA [23]. In 2005, the American Society
of Gastroenterology petitioned the FDA to remove the
requirement of general anaesthesia or monitored anaesthesia
care sedation that propofol should only be administered by
persons trained in the administration of general anaesthesia.
This petition was ultimately denied in 2010 [24]. With our
results we confirm former studies showing that endoscopist-
administered propofol sedation is indeed a safe procedure
even in an ambulatory practice of gastroenterology.

As described in Methods, propofol sedation was only
performed in patients with ASA class I, II and with class
III if classification was based on a non-cardio-pulmonary
source. The propofol sedation protocol was strictly adjusted
to the German S3 Guidelines for Sedation in gastrointestinal
endoscopy [13]. To decrease the rate of respiratory events
every patient received supplemental oxygen at a flow rate
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[25]. The ASA defined several levels of sedation ranging
from minimal, moderate and deep sedation to anesthesia.
Propofol has a narrow therapeutic window; therefore changes
in propofol dosage may result in a switch from deep sedation
to anesthesia requiring airway management. The observed
rate of hypoxemia in the present study did not lead to
increased propofol dosages since patients with hypoxemia
received even lower doses of propofol than the overall mean.
However, statistical analysis showed that patients with
hypoxemia were significantly older than patients unaffected
by sedation (P < 0.001). In addition, patients with adverse
events such as apnea (P = 0.039), bradycardia (P = 0.013),
or hypotension (P < 0.001) were significantly older than the
patients without adverse events (Table II). This goes in line
with the observation that action of propofol is dependent
upon patients’ age [26, 27] and that age-related deceleration
development can increase side-effects [28].

Seven patients (0.07%) in our study showed episodes
of bradycardia (< 60/min) and 5 patients therefore received
medical intervention. This rate of bradycardia is even lower
than the published incidence of 0.5% in a study of 3,000
colonoscopies [17].

Blood pressure significantly decreased after propofol
(Fig. 1). However, this decrease was in part a reversal
of the increased blood pressure recorded just before the
diagnostic procedures. At this time, systolic blood pressure
was significantly increased compared to the known values
remembered by the patients. Usually patients experience
fear of complications and of bad results. After the first bolus
of propofol this agitation will decrease rapidly. Arterial
hypotension leading to medical intervention is a rare event
(less than 1%) which was confirmed in former studies [11,
19, 20, 22]. But blood pressure monitoring during sedation
with propofol is recommended to avoid complications. We
did not use intravenous fluid infusions as a matter of routine
as this turned out not to be effective in a randomized study
[29].

Arterial hypotension occurred in 0.24% patients of whom
0.11% needed intravenous saline infusion. Since most of
the cardiovascular events occurred during colonoscopy or
combined examinations vagal responses during colonoscopy
might contribute to bradycardia and hypotension.

In comparison to literature data, the incidence of
respiratory and cardiovascular adverse events in the present
study are particularly low. This is probably due to the fact
that this study was carried out in an outpatient practice with a
higher rate of diagnostic procedures than in a hospital setting.
Another factor contributing to this low number of adverse
events might be the German S3 Guidelines for Sedation in
gastrointestinal endoscopy that specifies settings for safe
endoscopist-administered propofol sedation [13].

Given the very low rate of adverse events in the present
study, it does not seem likely that anesthetist-administered
propofol sedation would further improve the safety of
propofol sedation, and particularly cost-efficiency. However,
up to date there exists only one controlled trial comparing
endoscopist vs anaesthetist-administered sedation [30]. This
study consisted of 90 patients that underwent colonoscopy
and came to the conclusion that endoscopist-administered
propofol sedation offered a better level of satisfaction with
fewer side-effects. Despite the range of studies evaluating the
safety of endoscopist-administered propofol sedation, studies
observing adverse effects in anaesthetist-administered propofol sedation remain scarce. Despite the warning on the propofol product label, societies evaluating the safety of endoscopic propofol sedation need to take scientific evidence into account. In general, medical guidelines follow the highest possible evidence of the literature and are ranking higher than product labels. Classification systems such as the ASA criteria help to identify high risk patients that might benefit from more extensive observation of the sedation.

Conclusion
In the present study, we were able to show that endoscopist-administered propofol sedation is a safe procedure with a low incidence of adverse events.

Conflicts of interest
None to declare.

References