

Review

Sedation in Gastrointestinal Endoscopies [Part 1]

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SUMMARY

Endoscopy, both of the upper and the lower gastrointestinal tract remains difficult and sometimes painful procedures to be performed with the patients fully awoken. On the other hand, sedation and analgesia must be approached as a complex procedure requiring high-level skills and knowledge, since it requires preparedness, diligent monitoring and risk awareness. Knowledge of patient's co-morbid state and selection of sedation agents that will not exacerbate its baseline status is also a prerequisite.

Keywords: Endoscopy, conscious sedation.

Improvement in gastrointestinal endoscopy has substantially broadened the diagnostic and therapeutic skills of gastroenterologists. Gastrointestinal endoscopies are painful procedures that cause discomfort and anxiety. Sufficient patient co-operation is important for a successful and safe completion of gastrointestinal examinations. Sedation offers a lot of advantages. It reduces pain, discomfort and stress in patients undergoing unpleasant and prolonged procedures and contributes to patients' accepting them. Moreover, it reduces the danger of injuries during endoscopies due to inappropriate co-operation and contributes to the endoscopist's comfort. Sedation also improves endoscopic quality, especially in children and elderly patients with whom cooperation is difficult.

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Sedation practices differ from one country to another and even vary within the same country. These differences may reflect many different factors. These include the personal preferences and training of the endoscopist, the availability of anesthetic services, the need to train colleagues in endoscopic techniques, the cost and availability of monitoring equipment, differences in the availability and use of common drugs, and particularly, the expectations of the patients.¹

In the UK and USA sedation is widely used in endoscopies. In France 80% of colonoscopies are performed under general anaesthesia while in Germany and Finland, by contrast, most examinations are conducted without any form of sedation.¹

According to the American Society of Anesthesiologists, sedation is a continuum of progressive impairment in consciousness ranging from minimal sedation (anxiolysis) to general anesthesia (Table 1). The purpose of this continuum is to teach the concept that patients can move in a fluid manner between the states of sedation.²

Successful performance of endoscopic procedures can be achieved with patients in either moderate or deep sedation or general anesthesia; however, moderate sedation is generally considered adequate to control the pain and anxiety of routine endoscopic examinations and to achieve adequate amnesia.³

At this level of sedation, medications are used to create central nervous system suppression that allows the completion of the procedure, while patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. At this level of sedation, ventilatory and cardiovascular functions are unaffected, which means that there is no need for invasive airway support and there is verbal response.^{4,5}

Moderate sedation differs from deep sedation in that

Table 1. Definitions of clinical states of sedation as proposed by the American Society of Anaesthesiologist's Task Force on Sedation and Analgesia by Non-anaesthesiologists (5).

Sedation Level	Characteristics
Minimal sedation/anoxiolysis	<ul style="list-style-type: none"> • A drug-induced state during which patients respond normally to verbal commands • Cognitive function and coordination may be impaired • Ventilatory and cardiovascular functions are unaffected
Moderate sedation/analgesia	<ul style="list-style-type: none"> • A drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation • No interventions are required to maintain a patent airway and spontaneous ventilation is adequate • Cardiovascular function is usually maintained
Deep sedation/analgesia	<ul style="list-style-type: none"> • A drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully following repeated or painful stimulation • Ability to independently maintain ventilatory function may be impaired • Patients may require assistance in maintaining a patent airway and spontaneous ventilation may be inadequate • Cardiovascular function is usually maintained
General anesthesia	<ul style="list-style-type: none"> • A drug-induced loss of consciousness during which patients are not arousable, even by painful stimulation • Ability to independently maintain ventilatory function is often impaired • Patients often require assistance in maintaining a patent airway and positive pressure ventilation may be required because of depressed spontaneous ventilation or drug-induced depression of neuromuscular function • Cardiovascular function may be impaired

deep sedation is accompanied by loss of consciousness and verbal response. This means that the level of care must be the same as general anesthesia.⁶ It must be noted that conscious and deep sedation is determined by clinical parameters so their evaluation is subjective.⁷

Although clinicians may target a specific level of sedation, it is not always possible to predict how each patient will respond to sedative or analgesic medications. Clinicians commencing sedation/analgesia intending to produce a given level of sedation should be able to rescue patients whose level of sedation has become deeper than initially intended. For conscious sedation, this implies the ability to manage a compromised airway or hypoventilation in a patient who responds purposefully after repeated or painful stimulation. For deep sedation, this implies the ability to manage respiratory or cardiovascular instability in a patient who does not respond purposefully to painful or repeated stimulation.⁵

Targeting moderate sedation is the goal, but in clinical practice some patients will transiently be in lighter or deeper levels of sedation. Targeting conscious levels results in an overall safer profile than targeting deep levels and should result in a substantial safety margin for non-anesthesiologists.

A key principle in the administration of sedation is to titrate sedative medications in incremental doses to desired sedative effect.

Certain patient characteristics like age, comorbidities, body mass, race, previous responses to sedation and current use of oral narcotics or benzodiazepines may help predict the dosage required to achieve adequate sedation level to complete the procedure. The exact dose that will be successful in a given patient is impossible to accurately predict. This is because the pharmacologic response of individual patients to specific agents is variable. Therefore, clinicians attempting to achieve moderate sedation must deliver an initial bolus selected through a process of clinical estimation and then titrate the drug by incremental dosing to the desired effect. The general process is to start with a low dose; assess the response of the patient's sedation level, ventilatory function and cardiovascular status; and proceed gradually with titration.

Adequate knowledge of pharmacokinetic properties of the agents is crucial when commencing sedation (Table 2).

Over the last 20 years, midazolam has substituted diazepam in most endoscopic units. Midazolam has shorter duration of effect compared with diazepam and has better

Table 2. Pharmacological properties of sedation agents for endoscopy

Pharmacokinetics				
Sedation agent	Onset of action (min)	Duration of action	Elimination half-life	Metabolism/excretion
Meperidine	5	2-4h	2-7h	Hepatic; excreted in urine
Midazolam	1.0-2.5	2-6h	1.8-6.4h	Hepatic and intestinal; Excreted in urine
Fentanyl	≤1.5	1-2h	2-7h	Hepatic; excreted in urine
Propofol	<1	3-10min	Triphasic: 2.2min, 20min, 8h	Hepatic; excreted in urine

amnesic properties. Although benzodiazepines alone or in combination with opioids has excellent sedative properties it is far from being the ideal sedative agent. Several tragic deaths occurred when benzodiazepines were first used. Nevertheless, since the 1980s, the use of benzodiazepines, often in combination with an analgesic, has become standard practice in the United States and many parts of Europe.^{8,9}

However, even in the 1990s, a remarkable morbidity (1:200 to 1:2,000) and occasional mortality were still being reported with its use.^{10,11}

Many clinical trials have documented the feasibility of endoscopies without any sedation.^{12,13}

The increasing technical complexity of endoscopic procedures frequently requires deeper levels of sedation. Even for purely diagnostic endoscopy, sedation can be advantageous for patient comfort and for achievement of higher-quality procedures. Time consuming endoscopies of the gastrointestinal tract like ERCP and EUS require deep sedation and thus the use of centrally acting powered sedative medications.

Propofol is a particularly popular choice for induction and maintenance of deep sedation. During the last few years, propofol sedation for gastrointestinal endoscopy has increased significantly, reaching an estimated 50,000 procedures.¹⁴

The pharmacokinetic profile of propofol makes it a very suitable sedative agent for endoscopic procedures.^{15,16} It has excellent amnesic effect, rapid onset of action, and short half-life, 4 minutes compared with 30 minutes for midazolam.¹⁷ Clinical trials comparing iv propofol (plus or minus a small dose of benzodiazepine or opioid) with intravenous benzodiazepines (either alone or in combination with an opioid) continue to appear. Enthusiasm for the drug's use continued to be high in reports published during the last years.¹⁸⁻²¹

There is no dispute regarding propofol's superiority over benzodiazepines (plus or minus an opioid), in terms

of both its extremely rapid onset of action (literally within one arm-brain circulation time) and the patient's relatively short recovery time once the intravenous infusion is discontinued.¹⁸⁻²⁵

What of course is the greatest worry for the sedation-endoscopist, is its safety profile when no anesthesiologist is available to assist in the event of a respiratory arrest. Debate continues as to whether propofol should be administered by the medical assistant or registered nurse, or alternatively by some form of patient-controlled system.^{6,26-30}

Safety parameters during endoscopic procedures.

Sedation and analgesia used by non-anesthesiologists outside the operating room may increase the risk of ventilatory and cardiovascular suppression. In order to secure an adequate level of sedation/analgesia, minimizing the above mentioned risks, the American Society of Anesthesiologists has introduced guidelines for sedation and analgesia by non-anesthesiologist.⁵ The purpose of these Guidelines is to allow clinicians to provide their patients with the benefits of sedation/analgesia while minimizing the associated risks.

According to these guidelines, patients must be [a] evaluated before the examination according to their past medical history, physical examination, laboratory parameters, medications, allergies, airway evaluation and fasting; and [b] must be under monitoring/recording during and after the procedure.

Monitoring the patients under any level of sedation is very important for their safety. The response of patients to commands serves as a guide to their level of consciousness. Verbal response provides an indication that the patients are breathing. Patients whose only response is reflex withdrawal from painful stimuli are deeply sedated, approaching a state of general anesthesia and should be treated accordingly. Continuous monitoring of pulmonary ventilation and oxygenation by observation or auscultation and pulse oxymeter correspondingly is very impor-

tant. Continuous monitoring of respiratory rate by observation or capnography and possible apnoea detection by capnography is critical.

Electrocardiogram during deep sedation and during conscious sedation in patients with significant cardiovascular disease or dysrhythmias must be monitored continuously. Blood pressure should be measured at 5 min intervals during the procedure, unless such monitoring interferes with the procedure. Heart rate per minute should be measured every 5 minutes.

Exhaled carbon dioxide should be considered for all patients receiving deep sedation and for patients whose ventilation cannot be directly observed during moderate sedation.

Monitoring parameters must be recorded at 5 min intervals once a stable level of sedation is established. A designated individual other than the person performing the procedure should be present to monitor the patient's status throughout procedures performed with sedation/analgesia. Persons using sedation and analgesia must be trained in pharmacology and the practice of sedation.

The presence of an individual capable of establishing a patent airway, positive pressure ventilation, and resuscitation (i.e. advanced life-support skills) during a procedure is imperative.

Wherever sedation is used during gastrointestinal endoscopic procedures, emergency equipment must be present and checked. Emergency equipment is presented in Table 3.

Table 3. Emergency equipment necessary for safety sedation during gastrointestinal endoscopic procedures.

Equipment for intravenous line placement
Stethoscope, equipment for blood pressure measurement
Oxygen supply
Suction
Pulse oxymeter
Face masks in different sizes
Rhinopharyngeal and oropharyngeal airways [different sizes]
AMBUE with oxygen reservoir bug
Laryngeal masks [different sizes]
Elastic bougie
Intubation equipment [laryngoscope with blades in different sizes, endotracheal tubes in different sizes, cuff-syringe]
Reversal agents: Flumazenil and naloxone [for benzodiazepines and opiates reverse respectively]
Emergency medications [adrenaline, atropine, antiarrhythmic medications, etc]
Defibrillator
Electrocardiograph

Esophago- Gastro- Duodenoscopy

Sedation during upper gastrointestinal endoscopy increases patient tolerance, quality and diagnostic accuracy of the examination. Nevertheless, increases the duration of the procedure, side effects and cost.^{31,32} The use of sedation in therapeutic Esophago- Gastro- Duodenoscopy (EGD) is widely accepted. In contrast, its use in diagnostic EGD is controversial and the decision for its use depends on the patient's desire and the endoscopist's point of view.^{33,34}

The patient's desire to receive sedation during upper GI endoscopy varies significantly from country to country. Most patients in France and in the USA request iv sedation, whereas in Japan, Germany, Poland, Spain and Sweden the majority of patients expect nothing but local pharyngeal anesthesia.^{35,36}

In a recent study, in about 50% of ESGE-related countries, less than 25% of patients are sedated for a routine diagnostic UGI endoscopy.³⁷ In a big endoscopic unit in the UK there has been a dramatic decrease in the sedation rate for outpatient gastroscopies over a 10-year period, from 70% to only 32%.³⁵

In the study by Heuss, the proportion of Swiss endoscopists who never use sedation for routine endoscopies has dwindled from more than 25% in 1990 to less than 5% in 2003.³⁶ In a study from Italy, the use of sedation during gastroscopy increased from 69% to 86%.³⁸

The benefit of EGD when under sedation, has been addressed in numerous studies, but remains controversial. Many studies that suggest a beneficial effect are not placebo controlled or adequately blinded as they either include selected patients or took place in countries where sedation during endoscopy was popular.³⁹

It is difficult to compare results from several studies because there are no international criteria or scales to measure the patient's EGD acceptance or the endoscopist's difficulties. It is also controversial if the results from studies could have any clinical application.

A study from Canada shows that although diagnostic EGD sedation is more costly, it remains the most efficacious strategy when increasing clinical efficacy. These data may differ for elderly patients in whom a non-sedation strategy may dominate.⁴⁰

There are two controlled studies where EGD sedation was performed in countries where sedation is not popular. These studies examine the hypothesis that gastroscopies performed on sedated patients are better tolerated, were easier and more accurate for endoscopists.^{39,41} Both stud-

ies took place in countries where sedation during endoscopy was not popular. Although in these studies patients tolerate EGD without sedation, EGD with sedation was better tolerated. A paradox in the study from Finland³⁹ is that EGD was technically more complex for endoscopists when sedation was used. In their study, the authors recommended the use of sedation in younger patients.

In most European countries sedation in diagnostic EGD was electively applied. Some factors that could predict which patients will need sedation are young age,^{39,42} patient anxiety⁴² and the presence of intense vomit reflexes.^{42,43} However, the final decision about which patient needs sedation during EGD influenced by the patients^{34,44} and the endoscopist's point of view^{37,44} does not seem to change after training in sedation methods.³⁷

EGD without sedation has some advantages.⁴⁴ It does not have complications related with sedation, it does not need nursing or accompanied person to transfer the patient, the cost is reduced and possibly the duration of the examination. It also enables immediate conversation about examination findings between patient and endoscopist. As regards cost-effective relationship, some studies support that endoscopy without sedation maybe increases examination cost because the reduced patient tolerance could result in examination miss and repetition of examination under sedation.⁴⁴

There is one study on cost-effectiveness that compares diagnostic gastroscopy with and without sedation. This Canadian study shows that although sedated diagnostic EGD is more costly, it remains the most efficacious strategy by increasing clinical efficacy. This may differ for elderly (>75 years) patients in whom an unsedated strategy may dominate.⁴⁰

An alternative method of conventional EGD is one without sedation by small diameter instruments (3-6 mm) introduced by nose or mouth.⁴⁵⁻⁴⁹ Due to the small diameter of instrument, the endoscopy is better tolerated by patients and there is no need for sedation but only some local anesthetic application to nostrils, pharynx or hypo-pharynx.⁵⁰

In Europe and the USA, there are many studies that compare conventional EGD under sedation with EGD by small diameter instruments. Results from these studies do not differ as regards patient and endoscopist acceptance and diagnostic accuracy.⁴⁷⁻⁵³ But there are no studies that compare EGD by small diameter instruments with conventional EGD without sedation.

Sedation in diagnostic EGD was carried out with a variety of drugs. In ESGE (European) countries the most

popular medications are midazolam and propofol.^{54,55} These medications were administered by an endoscopist or nurse but it is not known if they had adequate training in resuscitation or sedation using medications.^{56,57} For EGD performed in outpatients, propofol may be the ideal substance.⁵⁵⁻⁵⁹ However, the dosage needed to smoothly perform upper endoscopies may be slightly higher than that for colonoscopies and may thus be accompanied by an increased risk of apnoea.⁶⁰⁻⁶²

Nevertheless, the short procedure time corresponds very well to the effect of the drug. After an adequate level of sedation has been reached, propofol enables most EGDs to be performed without further incremental application of the drug while still achieving a perfect amnesia. Patients are able to communicate immediately after the procedure and can be discharged after 20 min, although they should not be allowed to drive.

In the USA due to the increased use of propofol as well as medicoligal issues, sedation is administered by an anaesthesiologist or registered nurse (nurses trained in sedation practice) in 30% of endoscopies. Only 8% of US gastroenterologists use propofol without the presence of anaesthesiology training clinicians.⁶³

It is important to note that 8 in 12 ESGE countries, where sedation was administered by anesthesiologists, the percentage of sedation use during diagnostic EGD is less than 25%. In contrast, in countries like Switzerland, where propofol does not have to be administered by anesthesiologists, there is an increased use of sedation and propofol during EGD.³⁶

More specific meta-analysis of 12 original studies has shown that propofol sedation during gastroscopy was safer compared to other sedative agents.³¹ The pooled odds ratio for developing hypoxemia or hypotension under sedation with propofol compared with other sedative agents was 0.85 (95% CI 0.33±2.17).³¹ Although there are a lot of data regarding the safety profile of propofol administered by trained nurses and endoscopists, the use of this medication was restricted only to anesthesiologists in some countries.^{2,36,43,56,57}

Premedication with orally administered midazolam in adults and children undergoing diagnostic and therapeutic upper endoscopy is optional.^{58,59,60,64} Oral midazolam offers smooth onset of sedation before the administration of iv sedation. In addition, it not only reduces patient anxiety prior to the procedure, but it also reduces the doses of iv sedation and consequently the accompanying complications.^{60,64}

Local pharyngeal anesthesia improves tolerance of EGD without sedation^{61,62} but its use is controversial when sedation is used.⁶³ Meta-analysis of 53 studies shown that local pharyngeal anesthesia improves patient's tolerance and performance of EGD under sedation.⁵⁹ In ESGE countries, local pharyngeal anesthesia was applied in most unsedated EGDs and in 60% of sedated EGDs.³⁷

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