National Consensus on the Use of Sedation Drugs in the Gastrointestinal Endoscopic Procedures

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ABTRACT

Gastrointestinal endoscopy is rapidly developing and several gastrointestinal endoscopy equipment are available for both diagnostic and therapeutic purposes. Proper sedation is critical in performing endoscopic procedures, both for patients and physicians. This consensus is used as a guideline and not as a legal standard in performing endoscopic services. This consensus explained the definition, indication, contraindication, and complication prevention during sedation. Factors affecting the need of sedation is patient factors, procedure factors, and sedation level. Diagnostic or therapeutic upper gastrointestinal tract endoscopy which not complicated can be performed with minimal sedation or moderate sedation, while deep sedation can be considered for longer and more complex procedures. Furthermore, assessment and selection of sedation was explained, followed by the guide to choose pharmacological sedation and analgesics. Currently, diazepam, midazolam, propofol, fentanyl, and pethidine is the most likely used sedation during gastrointestinal endoscopy, with midazolam as the preferred medication of choice. This consensus also explained the antidote of each drug and the recovery after procedure. This consensus aimed to improve gastrointestinal endoscopic procedure services in Indonesia.

Keywords: *diazepam, fentanyl, gastrointestinal endoscopy, midazolam, national consensus, pethidine, propofol, sedation*

ABSTRAK

Endoskopi saluran cerna saat ini telah berkembang pesat dan berbagai peralatan telah tersedia baik untuk keperluan diagnostik maupun terapeutik. Sedasi yang tepat sangatlah penting selama prosedur endoskopi, baik untuk pasien maupun dokter. Konsensus ini menjadi petunjuk dan bukan menjadi standar baku dalam pelayanan endoskopi saluran cerna. Konsensus ini menjelaskan definisi, indikasi, kontraindikasi, dan pencegahan komplikasi dari penggunaan sedasi. Faktor yang memengaruhi pemilihan dan kebutuhan sedasi terdiri atas faktor pasien, faktor prosedur, dan tingkat sedasi yang diharapkan. Endoskopi saluran cerna baik untuk diagnostik maupun terapeutik yang tidak kompleks membutuhkan sedasi yang minimal atau sedang, sementara sedasi dalam dibutuhkan pada prosedur yang kompleks dan panjang. Lebih lanjut lagi, pengkajian dan penentuan kebutuhan sedasi dijelaskan, kemudian dilanjutkan dengan penduan memilih obat-obatan sedasi dan analgesik. Saat ini, diazepam, midazolam, propofol, fentanyl, dan pethidine merupakan obat sedasi yang paling sering digunakan dalam prosedur endoskopi saluran cerna, dengan midazolam masih menjadi obat pilihan berbagai ahli endoskopi saluran cerna. Konsensus ini juga menjelaskan antidotum dari tiap obat dan pemantauan pemulihan pasien pasca prosedur. Konsensus ini bertujuan untuk memperbaiki pelayanan endoskopi saluran cerna di Indonesia.

Kata kunci: *diazepam, endoskopi saluran cerna, fentanyl, konsensus nasional, midazolam, pethidine, propofol, sedasi*

INTRODUCTION

Gastrointestinal (GI) endoscopy is an examination to evaluate the structure of the upper and lower gastrointestinal mucosa in detail through a camera located at the end of the scope.[1] Nowadays, gastrointestinal endoscopy is rapidly developing and several gastrointestinal endoscopy equipments are available, including esophagogastroduodenoscopy, enteroscopy (single baloon or double baloon), endoscopic retrograde pancreatography (ERCP), endoscopic ultrasonography (EUS), and colonoscopy.[1,2] The use of gastrointestinal endoscopic equipments not only can be used for diagnostics but also for therapeutic procedures.[1,2]

Several endoscopic procedures can be performed using gastrointestinal endoscopic equipment, such as ligation or sclerotherapy of esophageal or gastric varices, upper or lower gastrointestinal polypectomy, oesophageal dilatation either with savary spark or with pneumatic dilatation, pylorus dilation, stent application of upper or lower gastrointestinal, upper and lower gastrointestinal hemostasis, foreign body extraction, endoscopy mucosal resection (EMR), endoscopy submucosal disection (ESD) or fine needle aspiration through EUS. In the field of hepatobiliary, ERCP can be used for sphincterotomy procedures, stone extraction, and installation of common bile duct stent (CBD).[1]

The purpose of sedation and analgesic endoscopy is to reduce anxiety, discomfort in patients, reduce psychic trauma, and achieve optimal endoscopic examination results.[2,3,4] The patients' comfort depends on the skill of the operating doctor and supported by sophisticated equipment, and also no less important is the sedation given during the gastrointestinal endoscopic procedures. Furthermore, proper sedation may also assist the physician in performing endoscopic procedures.[4] The sedation procedures for gastrointestinal endoscopic procedures in the world and especially in Indonesia are not the same, from no sedation, to mild sedation, to deep sedation/general anesthesia.[2] Currently the use of deep sedation, in particular propofol, has been widely used in gastrointestinal endoscopic procedures.[5,6,7] Similarly, sedative analgesic drugs such as fentanyl or pethidine are also widely used.[2,6] Accordingly with that matter, a consensus was drawn up by an agreement of gastrointestinal endoscopy experts representing all branches in Indonesia to serve as a reference in the daily gastrointestinal endoscopic action. This consensus is used as a guideline and not as a legal standard in performing endoscopic services.

Definition of Sedation

Sedation can be defined as drug-induced level of awareness suppression.[3] The purpose of sedation and analgesia is to reduce anxiety and discomfort in patients, improve the quality of examination, and reduce patients' memory of examination process.[3] According to guideline from American Society of Anesthesiologist (ASA), sedation and analgesia consist of a continuation of the patient's condition starting from minimal sedation (ansiolysis) to general anesthesia (Table 1).[8] Changes in sedation levels from conscious sedation to general anesthesia can occur unintentionally with little change in the dose of sedation used.[8]

Factors Affecting the Need for Sedation and Degree of Sedation

Several things to consider in the provision of sedation for the procedures of gastrointestinal endoscopy include patient factors and procedure factors, are as follows: (1) Patient factors: age, health status, current medication, anxiety level before procedure, pain tolerance; (2) Procedure factors: degree of examination's invasiveness, degree of discomfort caused by endoscopic procedure, the need or not for patient immobilization during the procedure, duration of examination; (3) Sedation level. Level of sedation consists of minimal sedation, moderate sedation, deep sedation and general anesthesia. The response during sedation and its effects on respiratory tract, ventilation and cardiovascular function can be seen in Table 1.[3,5,9]

Table 1. Levels of sedation and anesthesia and their effects[9]

	Minimal sedation (ansiolysis)	Moderate sedation/ conscious sedation	Deep sedation	General anesthesia
Response	Normal response with verbal stimulation	Responsive to verbal or tactile stimulation	Responsive to recurrent stimulation/ pain	Unresponsive with pain stimulation
Airway	Not affected	No intervention required	Intervention can be required	Intervention often required
Spontaneous ventilation	Not affected	Adequate	Can be inadequate	Often inadequate
Cardiovascular function	Not affected	Usually controlled	Usually controlled	Can be disturbed

Indications, Contraindications, and Complications Prevention of Sedation Indication of Sedation

Rigid and flexible sigmoidoscopy, rectal endosonography. In this case, routine sedation is not required. Moderate sedation is an option for anxious patients, pain anticipation, or therapeutic procedures. Upper gastrointestinal endoscopy as well as diagnostic and therapeutic colonoscopy without complication may be done with sedation. In a complicated procedure or takes a long time, (e.g. ERCP, endosonography), deep sedation may be needed or by request of the patient.

Table 2. Contraindication of moderate to deep sedation administration

Absolute	Relative
Patients in unstable condition: need to resuscitate first	Children Uncooperative patients (e.g. incompetent patient, mental disorders) Severe comorbidities Difficulties in airway Anticipation of the occurrence of intolerance to standard sedation

*For relative contraindications, consider anesthesiologist assistance.[10]

Prevention and Treatment of Sedation Administration Complications

Proper and careful dose administration especially for vulnerable and elderly patients is important to avoid cardiorespiratory depression during endoscopy. There is evidence that oxygen supplementation reduces the risk of hypoxemia during colonoscopy, although there is concern that when oxygen supplementation is given oxygen saturation levels no longer show ventilatory function and can mask CO_2 retention. However, the results of anesthesiologist surveys in Australia show that oxygen supplementation is routinely done. Expertise in dealing with airway obstruction and apnea is important to be mastered, including chin lift, jaw thrust, oropharyngeal tube installation, and nasopharyngeal tube. For a dangerous and lenghty respiratory condition requiring bag & mask ventilation. Antidotums such as naloxone and flumazenil are used when necessary as indicated. Further life support measures such as the use of laryngeal mask and endotracheal intubation are rarely needed in an outpatient setting.[9] For patients who have hypotension due to sedation drugs are given intravenous fluids. For endoscopic procedures which take place in hospitals, it is recommended to provide emergency rescue access.[9]

Assessment Before and During Endoscopic Procedures

Assessment Before Endoscopic Procedures

Important predictors of the adverse effects of sedation should be obtained from anamnesis and physical examination prior to procedure. Several important predictors can be seen in Table 2.

Table 2. Anamnesis and physical examination before endoscopic procedures[3,5,9]

Anamnesis	Physical examination
Significant heart or lung disease	Weight and body mass index
Neurologic disease, including a history of stroke, transient ischemic attack or seizure	Resting blood pressure, pulse rate, and breath frequency
Obesity, obstructive sleep apnea and other conditions affecting the airway such as a history of oropharyngeal surgery	Auscultation findings on lung and precordium examination
Snoring history or breath sound which suggestive of stridor	Physical state of the neck and oral cavity which can make positive pressure ventilation more difficult. Mallampati score is an indicator of the degree of difficulty of endotracheal intubation
Side effects reactions to sedation and anesthetic drugs	
Use of medicines, herbal therapy, and recreational drugs	
Use of alcohol and cigarettes	
The length of fasting performed by the patient	
Pregnant or possibly pregnant patient	

Assessment Before Endoscopic Procedures

In order for a safe endoscopy procedure to take place, careful assessment is required. Patients should always be under clinical supervision with particular attention to respiratory movement and response to verbal and tactile stimulation. At least one member of the endoscopic team specifically monitors the endoscopy patient. The person may be a medical practitioner trained on sedation and monitoring or a nurse working under endoscopist supervision. In addition, the pulse oximetry is measured continuously, the blood pressure is measured periodically, and the pulse rate is measured before, during, and after the procedure. Then all the measurement results are documented. Other monitoring techniques such as capnography which are more sensitive hypoventilation indicators than pulse oximetry or visual inspection can be used for patients with higher risk. The use of capnography has been shown to decrease the risk of desaturation when used during ERCP and EUS. EEGs have not been shown to benefit more in endoscopic procedures.[9]

Selection and Authority of Sedation, Selection of Sedation for Endoscopy

Generally, diagnostic or therapeutic upper gastrointestinal tract endoscopy which not complicated can be performed with minimal sedation or moderate sedation. Deep sedation can be considered for longer and more complex procedures, such as ERCP and EUS.[1,2,4]. Deep sedation or general anesthesia should be considered in patients who are difficult to handle with moderate sedation and are thought to be less responsive to sedation. Patients who are less responsive are patients who consume narcotics, benzodiazepines, alcohol, or long-term neuropsychiatric treatment.[1] In the daily practice of gastrointestinal endoscopic procedures, several things which can be done, among others: without sedation, with local anesthesia, with sedation and analgesic.[3]

Without Sedation

Endoscopy with a small diameter (less than 6 mm) or transnasal may increase upper gastric endoscopic tolerance so it can be performed without sedation. Generally, topical anesthesia is used for endoscopy without sedation. Older patients, men, patients who are not anxious, or patients without a history of abdominal pain may have better tolerance to undergo upper gastrointestinal endoscopy or colonoscopy should be considered for minimal or no sedation. For endoscopy without sedation, the type and level of monitoring should be adjusted per individual.

Topical Anesthesia

Topical anesthesia of pharyngeal spray with lidocaine, tetracaine, and benzocaine is often used for anesthetic purposes during upper gastrointestinal endoscopy. One meta-analysis study showed that the use of pharyngeal anesthesia together with intravenous or intramuscular sedation facilitates endoscopic examination or improves patient tolerance. Topical anesthesia is known to be associated with some serious side effects, including aspiration, bronchial asthma relapse, anaphylactoid reaction, and methemoglobinemia. Although these things are rare, they still need to be waried.

Sedation and Analgesia

Selection of sedation agents is highly dependent on the operator and based on maximizing patient comfort while minimizing risk. The choice of sedation generally consists of administering benzodiazepines alone or in combination with opiates to give a synergistic effect. The most commonly used benzodiazepines are midazolam and diazepam. The efficacy of both is comparable, but endoscopic prefer midazolam because of its faster action time, shorter duration of action, and high amnestic effects. Opioids, such as pethydine and fentanyl, have analgesia and sedation effects. Fentanyl has a faster action and clearance time and a lower incidence of nausea. Compared with traditional sedation (benzodiazepines), sedation using propofol provides similar side effects, better post-procedure patient satisfaction, decreases sedation time, and speeds recovery. In terms of side effects, propofol can cause hypoventilation, hypotension, and bradycardia are relatively common, but severe side effects are very rare. The need for sedation in endoscopic procedures (Table 3).

The Authority of Propofol Administration is in the Hand of Anesthesiologist

Administration of sedation for low-risk patients may be performed by non-anesthesiologists who have been certified specialized in the administration of propofol for gastrointestinal endoscopy.[2,3,5,12]

Table 3. The need of sedation in endoscopic procedures*

Procedure	Without sedation	Minimal sedation	Moderate sedation	Deep sedation
Esofagogastroduodenoscopy	v	v	v	v
Colonoscopy	v	v	v	v
Savary bougie/pneumatic baloon	-	v	v	v
Upper gastrointestinal polypectomy and lower gastrointestinal tract	-	v	v	v
Upper and lower gastrointestinal tract bleeding	v	v	v	v
Diagnostic or theurapetic ERCP (sphincterotomy, stone extraction, stent CBD)		v	v	v
PEG (SCBS)/gastrostomy	-	v	v	v
Foreign body extraction in upper or lower gastrointestinal tract	v	v	v	v
Ligation or STE esophageal varices (VE)	v	v	-	v
STE gastric varises	v	v	-	v
Enteroscopy: *single balloon* or *double balloon*	-	v	v	v
Diagnostic or theurapetic EUS	v	v	v	v

The Authority of Deep Sedation and General Anesthesia Administration is in the Hand of Anesthesiologist

Sedation Administration Procedure Including Analgesic for Endoscopy

Administration of sedation in endoscopic procedures is as needed, depending on the judgment of the endoscopic practitioner and upon the patient's request. In the implementation, some of the following points need to be considered:

Implementation

Personnel

There is one endoscopic nurse who monitors the patient continuously.

Patient preparation and monitoring

Intravenous access is needed for sedation and using venous catheters. It is recommended to provide oxygen supplementation due to frequent oxygen desaturation in patients breathing with room oxygen alone. Patient monitored using pulse oximetry and, if available, automatic noninvasive blood pressure measurements are done (at baseline and every 3-5 min intervals). Patients with a history of heart or lung disease should have a continuous electrocardiography.[5,8] Patients with dehydration, obesity, and old age need special attention before the administration of sedation drugs.

Level of sedation

Simple endoscopic procedures may be performed with mild to moderate sedation. More complicated (EUS and ERCP) or longer procedures need to be considered the use of deep sedation or anesthesia.[3,5,8,9] If endoscopist requires deep sedation, it should be considered consultation to a trained anesthesiologist/ non-anestesiologist. If endoscopist requires general anesthesia, it should be consulted to an anesthesiologist.

Special attention

The administration of sedation and analgesia should consider the various organ disorders which have occurred in patients, among others: liver function disorders, kidney function, lung function, heart function and geriatric patients.[3,5]

Antidotum and cardiopulmonary resuscitation equipment

Antidotum (naloxone and flumazenil) and cardiopulmonary resuscitation equipment should be available in the action room of endoscopy procedure.[5]

Recovery period

Observations performed by endoscopic nurses include assessment of consciousness, hemodynamics, and respiration. Transfer/discharge of patient can be done after fulfilling Aldrete criterion. Outpatients are not allowed to bring their own vehicle/drive up to 24 hours after the procedure.

Observation of Endoscopy Procedure

Observation includes all patient managements, namely: (1) Vital signs assessed by regular intervals (oxygen saturation, heart rate and blood pressure); (2) Complications due to sedation and treatment; (3) Check list criteria for discharge.[5]

Pharmacological Characteristics of Sedation and Analgesic Drugs for Endoscopy

Currently the drugs still used in gastrointestinal endoscopic measures are diazepam, midazolam, propofol, fentanyl and pethidine. The characteristics of these drugs among others:

Diazepam

Pharmacokinetics

Dose of sedation is 0.04-0.2 mg/kg body weight. Distribution: easily soluble in the lipid and penetration into the blood brain barrier occurs quickly. Biotransformation: converted in the liver into water-soluble end product. Excretion: especially through urine. The enterohepatic circulation causes secondary peak levels in plasma 6-12 hours after administration.[14,15]

Table 4. Anesthesia recovery period from Aldrete[13]

The value of 2 clinical feature		1	0
Consciousness	Conscious, good orientation	Can be awakened	Can not be awakened
Color	Pink, O2 required for O2 saturation> 92%	Pale/ blackish need O2 for O2 saturation > 90%	Cyanosis, with O2 saturation < 90%
Activity	Four extremities can be moved	Two extremities can be moved	The extremity does not move
Respiration	Can breath and cough	Shallow breath, shortness of breath	Apneu or obstruction
Cardiovascular	Blood pressure changed < 20%	Blood pressure changed 20-30%	Blood pressure changed 50%

Effects on organ systems

Cardiovascular: minimal suppressive effect although at induction dose. Arterial blood pressure, cardiac output, and peripheral vascular resistance usually slightly decrease, while heart rate increases. Respiration: decreases the ventilatory response to CO_2. Central nervous system (SSP): lowers oxygen consumption in the brain, blood flow to the brain, and intracranial pressure.[14,15]

Midazolam

Pharmacokinetics

Absorbtion: usually given intravenously with sedation dose of 0.01-0.1 mg/kg body weight. Injection of midazolam causes minimal venous irritation, sometimes can cause thrombophlebitis. Distribution: soluble in water at low pH, but imidazole ring causes increased solubility in lipids. The maximum effect is achieved after about 2 minutes and gives 30 minutes of sedation. Elderly patients tend to be more sensitive and recover longer. Biotransformation: Midazolam is converted in the liver into water-soluble end product. Its half-life is about 2 hours with a clearance of 6-11 mL/min per kg. Excretion: especially excreted in urine. Kidney failure can prolong the period of sedation.[14,15]

Effects on organ systems

Cardiovascular: lowers blood pressure and peripheral vascular resistance as well as changes in heart rate variability. The effect in decreasing blood pressure is greater than diazepam. Respiration: lowers the ventilation response to CO_2. CNS: lowers oxygen consumption in the brain, blood flow to the brain, and intracranial pressure. Cause antegrad amnesia. Has a mild muscle relaxant effect. It has no direct analgesic effect.[14,15]

Propofol

Pharmacokinetics

Absorbsi: can only be given intravenously for induction of anesthesia and moderate to deep sedation. Propofol administration causes pain during injection, which can be reduced by administering lidocaine and choosing a large antecubital vein. The dose is reduced for the elderly and the concurrent use of other sedatives. Generally, the onset of action is 30-60 seconds sedation, with action duration of 4-8 minutes. Distribusi: highly soluble in lipid, so that it has short onset of action. The recovery time of a single bolus is also very fast due to very short half-life distribution (2-8 minutes). Biotransformasi: clearance of propofol takes place in the liver as well as extrahepatic, thus speeding up the recovery period after IV administration. The conjugate is an inactive metabolite. Pharmacokinetics of propofol appears to be not affected by moderate cirrhosis. Ekskresi: propofol metabolites are excreted in the urine, but chronic kidney disease does not affect the clearance of propofol itself.[14,15]

Effects on organ systems

Cardiovascular: lowers arterial blood pressure due to decreased systemic vascular resistance (inhibition of sympathetic vasoconstrictor activity), cardiac contractility, and preload. Factors which exacerbate hypotension, among others: large doses, rapid injections, and old. Propofol significantly disrupts normal baroreflex response to hypotension, particularly in normocarbia or hypocarbia conditions. Patients with impaired ventricular function may experience significant decrease in cardiac output due to decreased ventricular filling pressure and contractility. Respirasi: at induction doses, causes severe respiratory depression to apnea. In the conscious patient, infusion of propofol (subanesthetic dose) inhibits breathing impulse from hypoxic states and depress normal responses to hypercarbia. Propofol can cause release of histamines, but the wheezing incidence in asthma and nonasmic patients is quite rare and therefore not contraindicated. SSP: lowers blood flow to the brain and intracranial pressure. Antiemetic effect appears when the concentration in the blood reaches 200 ng/mL so it is recommended for outpatients.[14,15]

Propofol Medium Chain Triglycerides/Long Chain Triglycerides (MCT/LCT) (Propofol Lipuro®)

Propofol MCT/LCT has some advantages compared to propofol LCT (propofol original) which usually being used, among others: (1) Pain is proportional to the original propofol that has been added lidocaine, but has an equivalent effect[16,17,18]; (2) Pharmacokinetic profile of MCT / LCT is better than LCT, namely: rapid clearance, reduced immunological disorders, reduced lung gas exchange disturbances and haemodynamic effects.[16,19,20,21]

Pethidine

Pharmacokinetics

Absorption: absorption occurs rapidly with peak plasma levels reached in about 20-60 minutes.

Distribution: Pethidin has a strong bond with proteins, while the bonds with fat are of low affinity. Biotransformation: undergoes biotransformation in the liver with a half-life of about 3 hours. In patients with cirrhosis of the liver, bioavailability increases by 80% and its half-life is elongated. Excretion: the final product is eliminated by the kidneys, a small portion undergoes biliary excretion.

Effects on organ systems

Cardiovascular: Pethidin increases heart rate and decreases cardiac contractility. In some individuals, it triggers the release of histamine which causes a great decrease in systemic vascular resistance and arterial blood pressure. Respiration: causes respiratory depression and in susceptible people, can cause histamine-related bronchospasm. CNS: sometimes causes CNS excitation characterized by tremors, muscle twitches, and seizures. Gastrointestinal: Opioids generally slows gastric emptying by decreasing peristalsis. There may be biliary colic due to opioid-induced contractions in the Oddi sphincter.[14,15]

Fentanyl

Pharmacokinetics

Single dose of fentanyl has duration of 30 minutes. Distribution: distribution in the body takes place quickly, which is 5-20 minutes. High solubility in fat causes rapid onset of action and short duration of action. Biotransformation: converted into an inactive end product. Excretion: excreted in the urine and partially excreted with bile. Enterohepatic recirculation may occur up to 4 hours after the last IV dose.

Effects on organ systems

Cardiovascular: Administration in high doses causes vagus-mediated bradycardia. Not suppresses contractility of heart muscle. However, blood pressure may drop because of bradycardia, venodilation, and decreased sympathetic reflex. Respiration: suppress respiration rate. Increases resting PaCO2 and dulls the response to CO2 challenge, causes CO2 response curve decreases to the right. Decreases the bronchoconstrictive response to airway stimulation, such as intubation. **CNS**: reduces oxygen consumption in the brain, cerebral blood flow, and intracranial pressure, but the effect is milder than benzodiazepine. Stimulation of medulla CTZ causes a high incidence of nausea and vomiting. Gastrointestinal: slows gastric emptying by lowering peristalsis. Biliary colic may be occurred due to contractions of Oddi sphincter.[14,15]

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