Adverse events related to procedural sedation for gastrointestinal endoscopy in adults

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INTRODUCTION

Research and development in the field of gastrointestinal (GI) endoscopy has greatly expanded the diagnostic and therapeutic capabilities of these procedures. Adequate patient tolerance is essential for successful completion of a safe examination and compliance with subsequent follow-up. As a result, endoscopists have developed skills in administering procedural sedation to facilitate procedures and enhance patient comfort. However, some patients may attain a level of sedation that is deeper than intended and/or experience adverse events related to sedation such as hypoxemia.

This topic review will focus on adverse events related to procedural sedation administered by endoscopists.

The endoscopist's approach to mild to moderate sedation for GI endoscopy in adults is discussed in more detail separately. (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists".)

Anesthetic management for GI endoscopy delivered by anesthesia clinicians, including the use of propofol, deep sedation, and general anesthesia, is discussed separately. (See "Anesthesia for gastrointestinal endoscopy in adults".)

Monitored anesthesia care (MAC) for adults including MAC-related complications is discussed separately. (See "Monitored anesthesia care in adults".)

GENERAL PRINCIPLES

Preparing for emergencies — Serious adverse events associated with procedural sedation administered by the GI endoscopist are uncommon; however, endoscopists and nursing staff are required to have the skills and equipment necessary to recognize and manage complications related to procedural sedation [1,2]. Emergency support strategies endorsed by professional societies include [3] (see "Basic airway management in adults"):

- Emergency airway equipment for establishing a patent airway.
- Suctioning oral secretions, bag-mask ventilation, and providing supplemental oxygen.
- Pharmacologic antagonists for benzodiazepines and opioids (table 1). (See 'Pharmacologic antagonists' below.)
- Specific skills of the procedural team including the ability to manage the patient's airway, establish intravenous access, and provide advanced life support. (See "Advanced cardiac life support (ACLS) in adults".)

Patient selection — The goals for pre-sedation evaluation are to identify patients with underlying conditions that may increase risk and to create a plan for procedural sedation that minimizes risk, while managing coexisting medical conditions. Patients who are at risk for adverse events related to intravenous sedation (eg patients at risk for difficult airway) are referred to an anesthesia clinician to provide procedural sedation and airway management. Pre-sedation evaluation and anesthesia consultation are discussed separately. (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Presedation evaluation'.)

CARDIORESPIRATORY EVENTS

Incidence and risk factors — The estimated incidence of adverse cardiorespiratory events related to endoscopic procedures ranges from 0.27 to 0.9 percent in different series depending on the patient population, specific procedure, and sedation type (endoscopist-administered or anesthesia-directed) [2,4-6]. Sedative medications depress the respiratory drive, and adverse cardiorespiratory events include hypoxemia, hypotension, cardiac arrhythmia, and

cardiorespiratory arrest. For example, in a database study including over 300,000 endoscopic procedures performed with intravenous moderate sedation, the rate of adverse cardiorespiratory events was 0.9 percent, and risk factors included age >60 years, American Society of Anesthesiologists (ASA) class ≥III, and inpatient status [5].

Patient and procedure-related factors that have been associated with increased risk for adverse events with intravenous sedation are discussed in more detail separately. (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Presedation evaluation'.)

The incidence of adverse events for specific procedures is discussed separately:

- Upper endoscopy (See "Overview of upper gastrointestinal endoscopy (esophagogastroduodenoscopy)", section on 'Complications'.)
- Colonoscopy (See "Overview of colonoscopy in adults", section on 'Adverse events'.)
- Endoscopic retrograde cholangiopancreatography (ERCP) (See "Overview of endoscopic retrograde cholangiopancreatography (ERCP) in adults", section on 'Complications'.)

Hypoxemia

Causes — Insufficient oxygenation is termed hypoxemia, and this typically results from hypoventilation and/or airway obstruction (eg, obstructive sleep apnea) in patients given intravenous sedation. In addition to their sedative effects, opioids and benzodiazepines inhibit the central responsiveness to carbon dioxide, leading to decreased respiratory drive. (See "Measures of oxygenation and mechanisms of hypoxemia" and "Clinical presentation and diagnosis of obstructive sleep apnea in adults".)

However, oxygen desaturation is a late indicator of hypoventilation or airway obstruction, and use of capnography facilitates earlier detection of these problems. This is discussed separately. (See "Carbon dioxide monitoring (capnography)".)

Hypoxemia has been commonly reported with endoscopic procedures, while it is often transient and responds to supplemental oxygen [7-11]. For example, in a study including 101 patients undergoing endoscopy without routine use of supplemental oxygen, transient hypoxemia (ie, oxygen saturation <90 percent) was observed in 25 patients (25 percent), while sustained hypoxemia (>60 seconds) requiring supplemental oxygen occurred in 30 patients (30 percent) [9].

Risk factors for hypoxemia include baseline oxygen saturation <95 percent, urgent procedure, advanced or therapeutic procedure with longer duration (eg, endoscopic retrograde cholangiopancreatography), history of comorbid illness, and possibly obstructive sleep apnea [1,12-15].

Prevention — Supplemental low-flow oxygen (eg 3 liters/minute) is routinely provided and continuous pulse oximetry monitoring is routinely performed during endoscopic procedures, and this is discussed separately. (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Sedation management'.)

Management

General measures — For patients who develop hypoxemia despite supplemental oxygen, initial management includes maneuvers to open the patient's airway (eg, head-tilt chin-lift (picture 1)), increasing the oxygen flow rate via nasal cannula (up to 10 L/minute), and/or providing supplemental oxygen via face mask, and aspirating air through the endoscope to reduce abdominal distension. For most patients, hypoxemia resolves with initial measures. Basic airway management in adults is discussed separately. (See "Basic airway management in adults".)

For patients who do not respond (ie oxygen saturation ≤90 percent) despite initial measures, subsequent measures include use of an air-mask-bag unit (AMBU) and/or reversal agent(s), and for patients having an upper endoscopy, removal of the endoscope. (See 'Pharmacologic antagonists' below.)

Airway management is discussed in more detail separately. (See "Anesthesia for gastrointestinal endoscopy in adults", section on 'Airway management'.)

Pharmacologic antagonists — Pharmacologic antagonists (ie reversal agents) to treat oversedation are rarely necessary but should be available for patients with hypoxemia from respiratory depression who do not respond to supplemental oxygen and basic airway management (see 'General measures' above and "Basic airway management in adults"):

- Naloxone – For patients who develop respiratory depression after being given an opioid agent and a benzodiazepine, naloxone is typically given for initial pharmacologic therapy. Naloxone is an opioid antagonist that is used to reverse respiratory depression and sedation caused by opioids (eg, fentanyl), and thus, ventilation is improved. Additional supportive measures such as fluid resuscitation and vasopressor agents may be required to manage hypotension resulting from opioid overdose. (See "Acute opioid intoxication in adults", section on 'Basic measures and antidotal therapy'.)

Dosing and administration for naloxone can be found in the table (table 1). In most patients, titration of the naloxone dose will safely reverse opioid effects while preserving some analgesia. However, sudden reversal of analgesic effects may cause pain and sympathetic surge resulting in hypertension and tachycardia. Older adults and those with cardiovascular disease may be particularly susceptible to adverse effects related to naloxone. The use of naloxone is discussed in more detail separately. (See "Respiratory problems in the post-anesthesia care unit (PACU)", section on 'Opioids and anesthetic agents' and "Acute opioid intoxication in adults", section on 'Management'.)

- Flumazenil – Oversedation caused by benzodiazepines is uncommon because the most commonly used agent, midazolam, has a short duration of action. Flumazenil, a benzodiazepine antagonist, is rarely necessary but may be given to patients who developed respiratory depression after receiving an opioid and a benzodiazepine and were given naloxone, but did not respond.

  Dosing and administration of flumazenil are listed in the table (table 1).

  Flumazenil should be used cautiously in patients who chronically use benzodiazepines, because it may result in agitation or increased risk of seizures. Benzodiazepine withdrawal and use of flumazenil are discussed in more detail separately. (See "Benzodiazepine poisoning and withdrawal".)

Patients who required reversal agent(s) are monitored for a minimum of 90 minutes after the procedure because they are at risk for recurrence of oversedation. The half-life of reversal agents is shorter than the medications that resulted in oversedation. Postprocedure care and other criteria for discharge following an endoscopic procedure are discussed separately. (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Postprocedure care'.)

There is no reversal agent for oversedation due to propofol, and oversedated patients are managed with supportive measures (eg, airway management) until the drug wears off. Use of propofol for GI endoscopy is discussed separately. (See "Anesthesia for gastrointestinal endoscopy in adults", section on 'Propofol'.)

Cardiac arrhythmias — Cardiac arrhythmias are not uncommon in patients who have continuous electrocardiographic monitoring during endoscopic procedures; however, most arrhythmias are not associated with hemodynamic instability [16,17]. For example, during elective procedures, sinus tachycardia may be associated with patient anxiety or discomfort while sinus bradycardia may be induced by vagal stimulation or related to use of beta blockers.

Management of cardiac arrhythmias associated with hemodynamic instability is discussed separately. (See "Sinus tachycardia: Evaluation and management" and "Sinus bradycardia".)

Hypotension — Intravenous procedural sedation may be complicated by hypotension (systolic blood pressure <90 mmHg) that is related to reduced cardiac output or peripheral resistance [18,19]. Hypotension during procedural sedation may be due to a vasovagal episode or related to sedatives that have mild vasodilatory effects and can depress sympathetic outflow to the cardiovascular system [17]. If hypovolemia is suspected, volume supplementation with intravenous crystalloid solution (eg, normal saline solution) can be beneficial, and this is discussed separately. (See "Cardiovascular problems in the post-anesthesia care unit (PACU)", section on 'Hypotension'.)

The risk of hypotension may be higher in patients on antihypertensive medications or those with preprocedure volume depletion (eg, recent bowel preparation). (See "Bowel preparation before colonoscopy in adults".)

Hypotension related to the use of propofol is discussed separately. (See "Anesthesia for gastrointestinal endoscopy in adults".)

OTHER ADVERSE EVENTS

Other adverse events related to intravenous sedation include:

- Pulmonary aspiration – Aspiration of gastric contents into the lungs that results in pneumonia is an uncommon complication of upper endoscopy, and the preprocedure assessment includes identifying risk factors for aspiration (eg, history of gastroparesis, acute upper GI bleeding) [2]. Conditions that increase aspiration risk and management of such patients are discussed separately. (See "Anesthesia for gastrointestinal endoscopy in adults", section on 'Airway management' and "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Presedation evaluation'.)

- Injection site pain – Propofol, which is typically used for anesthesia-directed procedural sedation, can cause pain at the injection site, and this is addressed separately. (See "Monitored anesthesia care in adults", section on 'Propofol'.)

EVENTS RELATED TO PHARYNGEAL ANESTHESIA

Topical (pharyngeal) anesthesia is not routinely used prior to endoscopy; however, it may be useful for some patients (eg, those having upper endoscopy with minimal or no intravenous sedation). (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Topical anesthesia'.)

Aspiration — The risk of aspiration of gastric contents may be increased when topical (pharyngeal) anesthesia is used in combination with intravenous sedation for upper endoscopy. Topical pharyngeal anesthesia results in transient inhibition of the airway reflexes (eg, cough, gag). (See "Aspiration pneumonia in adults", section on 'Predisposing conditions' and 'Other adverse events' above.)

Methemoglobinemia — Topical anesthetics, especially benzocaine spray, are a common cause of methemoglobinemia, which may be suspected in patients with cyanosis (eg, pale or blue-colored skin and lips) in the presence of a normal arterial oxygen pressure (PaO_2). The appearance of blood in patients with methemoglobinemia has been described as dark red, chocolate, or brownish to blue in color, while pulse oximetry is inaccurate in monitoring oxygen saturation in the presence of methemoglobinemia. The diagnosis and management of methemoglobinemia is discussed separately. (See "Methemoglobinemia".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Endoscopy preparation, sedation, and special considerations".)

SUMMARY AND RECOMMENDATIONS

- **General principles –** For patients undergoing gastrointestinal (GI) endoscopy, adequate tolerance is essential for successful completion of a safe examination. However, some patients may attain a level of sedation that is deeper than intended and/or experience adverse events related to sedation such as hypoxemia or hypotension. (See 'Introduction' above.)

    - **Preparing for emergencies –** Serious adverse events associated with procedural sedation administered by the GI endoscopist are uncommon; however, endoscopists and nursing staff are required to have the skills and equipment necessary to recognize and manage complications related to procedural sedation. Emergency support

strategies include (see 'Preparing for emergencies' above and "Anesthesia for gastrointestinal endoscopy in adults"):

- Emergency airway equipment for establishing a patent airway.
- Suctioning oral secretions, bag-mask ventilation, and providing supplemental oxygen.
- Pharmacologic antagonists for benzodiazepines and opioids.
- Specific skills of the procedural team include managing the patient's airway, establishing intravenous access, and providing advanced life support.

- **Pre-sedation evaluation –** The goals for pre-sedation evaluation are to identify patients with underlying conditions that may increase risk and to create a plan for procedural sedation that minimizes risk, while managing coexisting medical conditions. Pre-sedation evaluation and anesthesia consultation are discussed separately. (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Presedation evaluation'.)

- **Sedation management –** Supplemental low-flow oxygen is routinely provided and continuous pulse oximetry monitoring is performed during endoscopic procedures, and this is discussed separately. (See "Gastrointestinal endoscopy in adults: Procedural sedation administered by endoscopists", section on 'Sedation management'.)

- **Adverse events –** For patients given intravenous procedural sedation, hypoxemia (insufficient oxygenation) typically results from hypoventilation and/or airway obstruction. In addition to their sedative effects, opioids and benzodiazepines inhibit the central responsiveness to carbon dioxide, leading to decreased respiratory drive. (See 'Hypoxemia' above.)

  For patients who develop hypoxemia despite supplemental oxygen, initial management includes maneuvers to open the patient's airway (eg, head-tilt chin-lift (picture 1)), increasing the oxygen flow rate via nasal cannula (up to 10 L/minute) and/or providing supplemental oxygen via face mask, and aspirating air through the endoscope to decrease abdominal distension.

  Topical (pharyngeal) anesthesia is not routinely used prior to upper endoscopy; however, it may be useful for some patients (eg, those having upper endoscopy with minimal or no intravenous sedation). Adverse events associated with pharyngeal anesthesia include

aspiration of gastric contents and methemoglobinemia. (See 'Events related to pharyngeal anesthesia' above.)

The incidence of adverse events for specific endoscopic procedures is discussed separately:

- Upper endoscopy (See "Overview of upper gastrointestinal endoscopy (esophagogastroduodenoscopy)", section on 'Complications'.)
- Colonoscopy (See "Overview of colonoscopy in adults", section on 'Adverse events'.)
- Endoscopic retrograde cholangiopancreatography (ERCP) (See "Overview of endoscopic retrograde cholangiopancreatography (ERCP) in adults", section on 'Complications'.)

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Topic 2599 Version 19.0

GRAPHICS

Reversal agents for opioids, benzodiazepines, and anticholinergic agents

Drug class	Reversal agent	Dose of reversal agent (IV)	Time between repeat doses	Maximum cumulative initial dose	Additional dosing if necessary
Opioids	Naloxone	40 mcg	2 to 5 minutes	10 mcg/kg	Infusion at 1 to 10 mcg/kg per hour, with careful titration of the infusion rate according to patient response.
Benzodiazepine	Flumazenil	0.2 mg	1 minute	1 mg	After a 20 minute interval, if sedation is evident, additional 0.2 mg doses may be administered to a maximum of 1 mg. After another 20 minute interval, this dosing may be repeated. No more than 3 mg should be administered in a single hour.
Anticholinergic agent	Physostigmine	0.5 to 1 mg (slow IV push)	5 to 10 minutes	2 mg	

IV: intravenous.

Data from:

1. *Nicodemus HF, Rose JB. Delayed emergence in pediatric patients. In: Complications in Anesthesia, 1st ed, Atlee JL (Ed), Saunders, Philadelphia 1999.*
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Graphic 106215 Version 3.0

Head-tilt/chin-lift maneuver

To relieve upper airway obstruction, the clinician uses two hands to extend the patient's neck. While one hand applies downward pressure to the patient's forehead, the tips of the index and middle fingers of the second hand lift the mandible at the chin, which lifts the tongue from the posterior pharynx. The head-tilt/chin-lift maneuver may be used in any patient in whom cervical spine injury is **NOT** a concern.

Graphic 70710 Version 7.0

Contributor Disclosures

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