OVERSEDATION

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INTRODUCTION

Sedation for interventional pain procedures generally ranges from minimal sedation with oral anxiolytics to moderate (conscious) sedation using intravenous (IV) benzodiazepines with or without added opioids [1,2]. Because of the risks of oversedation and potential increase for neurologic injury during certain interventional procedures, deep sedation and general anesthesia should be utilized only for more painful and invasive procedures [2,3]. Both the American Society of Anesthesiologists (ASA) and the International Pain and Spine Intervention Society (IPSIS) indicate that sedation is typically not needed for most interventional pain procedures [1,2,4]. IPSIS considers the use of moderate/conscious sedation appropriate for those with significant anxiety, a history of prior vasovagal reaction, or for procedures "that are prolonged and/or painful" [1,2].

Nevertheless, despite medical society guidance against routine sedation, IV conscious sedation is commonly employed by interventional pain physicians in the United States [5,6]. An extensive survey of centers randomly selected from the American Pain Society revealed that roughly 50% of physicians used IV sedation for epidural steroid injections, and 90% used sedation for disc access and spinal cord stimulation trials [5]. Another survey found that 82% of physicians administered a sedative agent during interventional spine procedures, with 36% using propofol [6].

Oversedation occurs when the level of sedation is deeper than intended for the procedure. Patient factors (*e.g.*, previous exposures to alcohol or sedatives, weight, nutritional status) may render a patient at increased risk for oversedation and result in the patient becoming unexpectedly non-responsive or unconscious during conscious sedation. Likewise, dosing errors such as excessive opioid (e.g., fentanyl) or benzodiazepine (*e.g.*, midazolam) medications or sedative hypnotic agents (e.g., propofol) may result in overly deep levels of sedation. IPSIS advises that these deep levels of sedation are almost never necessary for interventional pain procedures, should be used only in exceptional circumstances, and should be performed under the supervision of trained anesthesiology personnel who independently monitor the patient and are not involved in performing the interventional procedure.

Sedatives (See Table 1)
The most common IV sedatives include midazolam (benzodiazepine), fentanyl (opioid), and propofol (sedative hypnotic). The choice of agent(s) depends on the regulatory requirements, the physician's goals, and the patient's needs and comorbidities. If the goal is anxiolysis, midazolam is the proper choice. If the goal is analgesia, fentanyl is often chosen. The combination of midazolam and fentanyl has synergistic effects; lower doses of each

can be used to provide both anxiolysis and analgesia. However, if these agents are administered together in excessive doses, oversedation with hypoventilation and apnea may ensue. Specific regulatory requirements may preclude sedative hypnotic (propofol) use, but if chosen, subanesthetic intermittent, small-bolus dosing is generally used, administered by a separate anesthesia provider, and titrated to effect with careful timing. Regardless of the selected sedative, all repeat dosing should be titrated to achieve the desired effect, and the patient should remain conversant throughout the procedure.

Reversal Agents (See Table 1)
Before administering a reversal agent in an overly sedated patient, the patient should be stimulated first to awaken and reestablish appropriate dialogue. The choice and dosing of reversal agent(s) depend on the sedative agent(s) administered and the patient's condition. If a combination of midazolam and fentanyl is utilized and the patient is apneic and unresponsive, the full naloxone dose of 0.4 mg (IVP or intranasal) is the correct reversal agent. Alternatively, if the patient is responsive but overly sedated, titrated flumazenil may be considered to reverse midazolam, or titrated naloxone to reverse fentanyl. The risks and side effects of each reversal agent should be considered before administration [7]. While reversing administered benzodiazepines with flumazenil in those with chronic benzodiazepine use incurs the risk of precipitating seizures, using naloxone to reverse the effects of administered opioids also carries risks, including the abrupt cessation of analgesia, tachycardia, hypertension, and pulmonary edema [7]. After successful reversal, continued monitoring is indicated in the recovery area because the sedative effects may persist beyond the reversal agent. There is no reversal agent for propofol. The effects of small doses of propofol are terminated by redistribution, with total clearance occurring via rapid extrahepatic metabolism [7].

Table 1. Common Sedative and Reversal Agents (Titrated to Effect) [adapted from (7)]

Sedatives/Dosing	Reversal Agents	Initial Dose	Repeat Dose
Midazolam 0.5-1 mg IVP (benzodiazepine)	Flumazenil	0.2 mg IVP over 15 seconds	0.2 mg IVP 1-minute intervals, not to exceed 5 mg
Fentanyl 0.025-0.1 mg IVP (opioid)*	Naloxone	0.4 mg IVP 0.4 mg intranasal	0.04-0.08 mg IVP 2-minute intervals, usually not necessary to exceed 2 mg [8]
Propofol 10-20 mg IVP (sedative hypnotic)	N/A	10-20 mg IVP	10-20 mg IVP, intermittent dose

**Using a lower initial dose of fentanyl is advised in the elderly and others potentially more susceptible to opioid effects.*

TYPICAL PRESENTATION

Case: Woman with neck pain

An 80-year-old woman was referred to the interventional pain clinic by her neurosurgeon for a cervical interlaminar epidural steroid injection to be performed using sedation. She provided a history of extreme needle phobia and an episode of "passing out" after receiving a steroid shot many years ago. Despite rarely providing sedation, the physician agreed to provide conscious sedation. IV access was achieved using a 22G Jelco catheter with extension tubing that flushed well with normal saline. Monitoring included nasal cannula end-tidal carbon dioxide (ETCO2), intermittent non-invasive blood pressure, electrocardiogram (EKG), and pulse oximetry. Nasal cannula oxygen was flowing at 2 L/min. Over the next fifteen minutes, the following occurred:

- The patient received midazolam 2 mg and fentanyl 50 mcg intravenous push (IVP). The patient appeared comfortable.
- Over the next several minutes, the monitoring nurse noted that the patient's ETCO2 had risen from 40 to 60 mmHg. The capnogram then showed a flat line. Assuming a monitor malfunction, the nurse adjusted the ETCO2 cartridge without effect.
- The pulse oximetry reading decreased from 95% to 85%, and then the display revealed no waveform. The nurse checked the pulse oximetry finger probe, assuming it had detached from the index finger of the tucked right arm. The continuous EKG rhythm displayed a reduction in the initial heart rate from 100 to 40 beats per minute (bpm). The non-invasive blood pressure monitor displayed an initial reading of 90/60; however, no subsequent readings were displayed after several cycles of cuff inflation and deflation.
- The nurse then called the patient's name, shook her arm, and alerted the entire staff that the patient was unresponsive and did not appear to be breathing.

OVERSEDATION PROTOCOL (OPIOID/BENZODIAZEPINE COMBINATION)*

1. If oversedation results in apnea, immediately stop the procedure and call for help. In the office setting, call EMS (911 or local equivalent) and explain the nature of the emergency.
2. If prone, roll the patient to the supine position to initiate Basic Life Support (BLS) and Advanced Cardiac Life Support (ACLS) [9].
3. Immediately begin bag-mask ventilation with high-flow oxygen until spontaneous ventilation resumes. Continue monitoring.
4. Administer naloxone 0.4 mg IVP if the patient is unresponsive, apneic, and an opioid has been administered. If the patient is oversedated but responsive, consider using titrated doses of flumazenil for benzodiazepine overdose or naloxone for opioid overdose. Oversedation resulting from a combination of benzodiazepine and opioids should preferably be treated with titrated naloxone because of the risk of flumazenil-induced seizures in those receiving chronic benzodiazepines.
5. If a previously placed IV catheter infiltrates or becomes dislodged, choose intramuscular/intranasal naloxone 0.4 mg as an alternative. After administering the alternative route of naloxone, placing another IV catheter is advised for additional IV dosing, if required.
6. Because the duration of the sedative agent may exceed that of the reversal agent, the patient should be monitored in the recovery area for a sufficient time (e.g., 45-60 minutes) to ensure that the patient does not become re-sedated.

7. Follow-up: Notify the patient's emergency contact or family.
8. Consider debriefing the team and reviewing procedures to prevent future occurrences.

** A specific protocol for propofol oversedation is not presented here because it relies exclusively on ventilation and cardiopulmonary support. Propofol's effects generally dissipate in a few minutes with careful small-bolus dosing due to its rapid redistribution and metabolism.*

RISK MITIGATION/PREVENTION

Informed consent

The physician should obtain informed consent for sedation, reinforcing with the patient that IV sedation is elective and not a necessary component of the procedure. When providing education regarding conscious sedation, the physician should ensure that the patient has reasonable expectations, including the following:

- The purpose of moderate sedation is to provide anxiolysis and/or pain relief.
- The patient should not expect to be deeply sedated or rendered unconscious; rather, they should expect to remain conscious, conversant, and able to respond appropriately to verbal stimuli.
- Patients should be informed that they may experience some minor pain during the procedure. Sedation combined with local anesthesia should make even fairly complex interventional procedures tolerable.
- The physician should obtain IV sedation consent, which covers the risks and potential complications of oversedation.

Overdose prevention

- All IV medications should be titrated carefully to effect, with special caution given to the elderly patient (delayed circulation times and increased sedative effects) and those who have consumed opioid or benzodiazepine medications pre-procedurally.
- Administering the lowest necessary dose of a sedative agent to achieve anxiolysis and analgesia prevents oversedation. Additional sedation can be administered, but the administered medication cannot be withdrawn.
- Regardless of agent choice (benzodiazepine, opioid, or sedative hypnotic), the sedated patient must remain conversant throughout the procedure. However, if the patient becomes unresponsive, the procedure should be paused or a reversal agent administered to allow the return of consciousness. Respiratory arrest (apnea with hypoxemia) demands termination of the procedure and manual ventilation with 100% oxygen until spontaneous ventilation resumes.
- IV sedation may be safely administered in various clinical settings, provided the facility is appropriately equipped for intraprocedural patient monitoring.
- The staff and interventional physician should be trained in the administration of conscious sedation and its recovery, the appropriate use of reversal agents, and the management of oversedation, hypoventilation, and respiratory arrest.

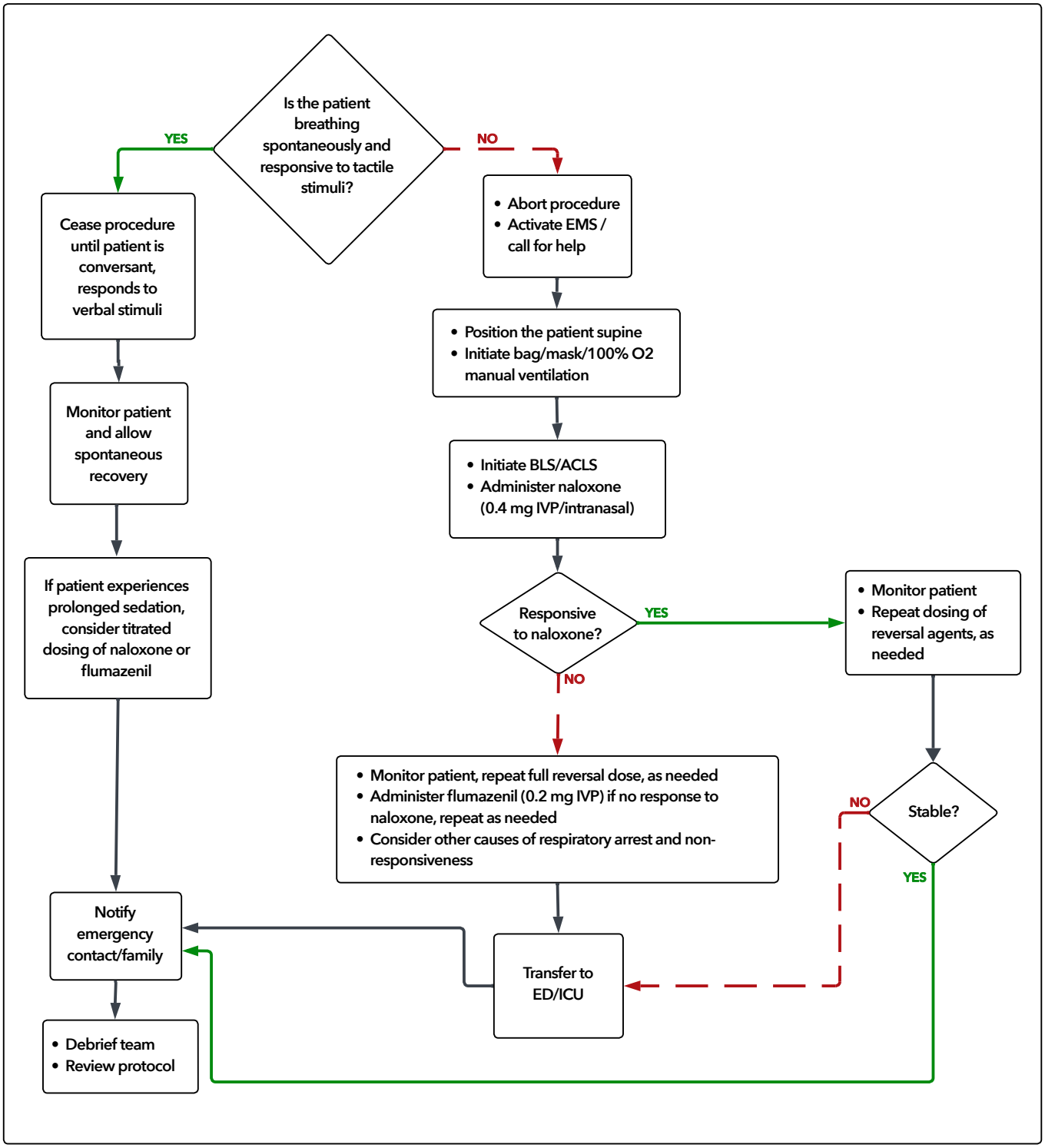
Advance Preparation

- Regardless of the service site, the facility should be appropriately equipped to manage emergencies (see ***Advance Preparation for Emergencies*** [10]).

KEY CONSIDERATIONS/TAKEAWAYS

- Despite medical society statements against the routine use of sedation, IV conscious sedation is commonly used in conjunction with interventional pain procedures. However, sedation is elective and not a necessary component of the procedure.
- Deep sedation and general anesthesia are not indicated for most interventional pain procedures and incur risks for certain procedures. If conscious sedation is utilized, appropriate monitoring, compliance with state medical board and institutional regulations, and formation of a high-performance procedure team led by the interventional physician are required.
- All sedative agents must be titrated to effect. The patient must remain conversant throughout the sedation process.
- If oversedation occurs and the patient becomes unresponsive to verbal stimuli, the procedure should be paused and/or a reversal agent administered to allow consciousness to return.
- In the case of overdose with apnea, the procedure should be aborted, and appropriate agent reversal and resuscitative efforts initiated.
- Overdose is an inherent risk of conscious sedation. Risk mitigation and prevention are essential elements of appropriate sedation.

SUSPECTED OPIOID / BENZODIAZEPINE OVERSEDATION



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DISCLAIMER

While these Emergency Protocols are intended to identify elements critical to the management of emergencies during interventional pain procedures, they are not intended to be inclusive of all proper emergency management protocols or exclusive of other methods of care reasonably utilized to obtain the same results. Nothing contained in these documents is intended to be used as a substitute for the care and knowledge of the individual clinician. They are guidelines based on evidence-informed expert consensus. IPSIS makes no representation and assumes no responsibility for the accuracy of the information contained or available through this website, and such information is subject to change without notice. Given the individual patient's clinical circumstances and preferences, the clinician's independent medical judgment should always determine patient care and treatment. Practitioners are advised to consider management options in the context of their training, background, and institutional capabilities when selecting recommended treatment options. IPSIS is not responsible, nor does it assume any legal liability or responsibility for the accuracy, completeness, clinical efficacy, or value of any such information or apparatus, product, or process described or referenced through this website or the information contained therein.