

## PRACTICE

## THERAPEUTICS

# Procedural sedation and analgesia for adults in the emergency department

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This is one of a series of occasional articles on therapeutics for common or serious conditions, covering new drugs and old drugs with important new indications or concerns. The series advisers are Robin Ferner, honorary professor of clinical pharmacology, University of Birmingham and Birmingham City Hospital, and Albert Ferro, professor of cardiovascular clinical pharmacology, King's College London. To suggest a topic, please email us at [practice@bmj.com](mailto:practice@bmj.com).

A 59 year old woman presents to the emergency department with an isolated anterior dislocation of her left shoulder after a fall. Other than controlled asthma, she is healthy. Her last meal was four hours before the injury. After adequate analgesia using intravenous fentanyl, and despite an initial attempt to reduce her dislocation using relaxation techniques, it becomes evident that she needs sedation to complete the procedure successfully.

## What drugs are used for procedural sedation and analgesia?

Patients in the emergency department often need to undergo painful, distressing, or unpleasant diagnostic and therapeutic procedures as part of their care. The use of various analgesic, sedative, and anaesthetic agents has been outlined in several well referenced guidelines.<sup>1-4</sup> The American Society of Anesthesiologists (ASA) describes four levels of non-dissociative sedation—from minimal sedation to general anaesthesia—in addition to dissociative sedation (box).<sup>2</sup> In practice, prolonged deep sedation or general anaesthesia is rarely used in the emergency department in the absence of a clinician with appropriate training in anaesthesia.

Several classes and combinations of drugs are commonly used for the procedural sedation of adults in the emergency department.<sup>4 5</sup> Although combinations of benzodiazepines and opioids have been used for procedural sedation, utilising the availability of their reversal agents (flumazenil and naloxone), evidence for the use of other sedatives is emerging and is

supported by guidelines based on prospective randomised trials and observational studies.<sup>4 5</sup>

## Classes of drugs commonly used for sedation in the emergency department

Opioids: shorter acting, intravenously administered synthetic opioids such as fentanyl, alfentanil, or remifentanyl are most often chosen as primary analgesics in procedural sedation. Pupillary constriction is a common sign of clinical effect. Their most notable side effect is central depression of respiration. Opioids have no amnestic properties and produce varying levels of somnolence or sedation depending on individual patient factors, such as age and comorbidities.<sup>6</sup>

Benzodiazepines: those such as midazolam result in anxiolysis, sedation, amnesia, anticonvulsant activity, and, to a lesser degree, muscle relaxation.<sup>6</sup> This class of drug has no analgesic properties. As a single agent, benzodiazepines are most useful for procedures requiring minimal sedation.<sup>4</sup>

Barbiturates: in the past, methohexital was the barbiturate most commonly used in procedural sedation. These drugs were popular for use in adult procedural sedation but are no longer recommended as primary agents, owing to their narrow therapeutic window and relatively high side effect profile when compared to newer agents.<sup>7</sup> They will therefore not be discussed further in this paper.

Nitrous oxide: a tasteless, odourless, ultra short acting volatile agent with analgesic, anxiolytic, and sedative properties. It is non-invasive (not administered intravenously) and has relatively few contraindications. It has near immediate onset but also exhibits acute tolerance.<sup>8</sup>

Propofol: a dose dependent sedative and intravenous general anaesthetic agent used for uncomfortable or distressing procedures. Propofol has no analgesic properties so should not

### Levels of sedation as described by the American Society of Anesthesiologists<sup>2</sup>

#### Non-dissociative sedation

- Minimal sedation and analgesia: essentially mild anxiolysis or pain control. Patients respond normally to verbal commands. Example of appropriate use: changing burns dressings
- Moderate sedation and analgesia (formerly known as "conscious sedation"): patients are sleepy but also aroused by voice or light touch. Although their airway and respiration are self maintained, these may be suppressed with deeper levels of sedation (which is a continuum). Example of appropriate use: direct current cardioversion
- Deep sedation and analgesia: patients require painful stimuli to evoke a purposeful response. Airway or ventilator support (or both) may be needed. Example of appropriate use: major joint reduction (dislocated hip prosthesis)
- General anaesthesia: patient has no purposeful response to even repeated painful stimuli. Airway and ventilator support is usually required. Cardiovascular function may also be impaired. Example of appropriate use: not appropriate for general use in the emergency department except during emergency intubation

#### Dissociative sedation

Dissociative sedation is described as a trance-like cataleptic state characterised by profound analgesia and amnesia, with retention of protective airway reflexes, spontaneous respirations, and cardiopulmonary stability. Example of appropriate use: fracture reduction (distal radius fractures in young adults)

be used as a single agent in moderately painful procedures. In subhypnotic doses, propofol has antiemetic and antipruritic properties.<sup>6,9</sup>

Phencyclidines (ketamine): ketamine is closest to a true "complete" anaesthetic agent in that it produces anxiolysis, amnesia, immobilisation, and profound analgesia.<sup>7</sup> It is suitable for brief, painful procedures requiring sedation.

Etomidate: a fast acting anaesthetic agent with no analgesic properties.<sup>6</sup>

## How well do sedative agents work?

There is no standardised definition for successful procedural sedation in the emergency department, other than successful completion of the procedure itself. Success rates therefore do not depend entirely on sedation, but can be affected by technical aspects of the procedure. The American College of Emergency Physicians states that the literature supporting the safety and efficacy of procedural sedation and analgesia in the emergency department is robust.<sup>5</sup> Studies reporting the success rate for completion of orthopaedic procedures in the emergency department vary. A retrospective chart review of 165 patients found that success rates varied from 64% (95% confidence interval 55% to 73%) with midazolam to 96% (77% to 100%) with propofol.<sup>10</sup> In a prospective cohort of 98 adult patients presenting with a dislocated hip prosthesis, a success rate of 96% (90% to 0.99%) was achieved using intravenous morphine and propofol.<sup>11</sup>

A prospective randomised comparison of 214 emergency department patients found that, as well as being equally safe, procedural success rates were similar for etomidate (89%; 81% to 93%) and propofol (97%, 92% to 99%).<sup>12</sup> A prospective cohort of 92 adult patients undergoing procedural sedation had a success rate of 99% (94% to 100%) with intravenous ketamine,<sup>13</sup> and a large randomised control trial of 284 emergency department patients described efficacious sedation rates of 91% (85% to 95%) with ketofol (1:1 mixture of ketamine and propofol) and 89% (83% to 93%) with propofol.<sup>14</sup> A systematic review using pooled data on 228 patients found no significant difference in the effectiveness of midazolam and propofol (effect difference 2.9%, -6.5% to 15.2%).<sup>15</sup>

## How safe are they?

Potential adverse effects for all sedative agents include loss of airway reflexes and tone, respiratory depression and apnoea, cardiovascular instability, nausea and vomiting, hallucinations, and emergence phenomena. There is a paucity of routinely

collected national safety and efficacy data for procedural sedation in the emergency department.

A systematic review that compared propofol and midazolam in 3300 patients reported no deaths and one serious adverse event where propofol was used (profound desaturation requiring intubation).<sup>15</sup>

A large registry series of 979 adult patients from a Canadian adult tertiary care centre found that adverse effects during procedural sedation and analgesia in the emergency department were rare (incidence ~1.4%) and were of doubtful clinical significance when managed appropriately.<sup>16</sup> The table<sup>||</sup> outlines possible adverse effects in more detail.

In a prospective observational study of 108 patients, propofol induced procedural sedation was reported to have the lowest rate of respiratory depression when compared with methohexital, a fentanyl-midazolam combination, and etomidate.<sup>20</sup>

A prospective cohort study of 92 adult patients found that ketamine was safe for adult procedural sedation in the emergency department; no serious adverse effects were associated with its use, although 13% of patients experienced agitation during recovery.<sup>13</sup>

## How are the drugs administered and what are the precautions?

### General principles

Although distinctions are made between deep sedation and general anaesthesia, sedation is a continuum where deep sedation may easily lapse into general anaesthesia. Several guidelines based on systematic review of the literature recommend that deep and dissociative sedation are managed with a similar level of governance to that for general anaesthesia.<sup>2-4, 21</sup>

International consensus guidelines recommend that minimal sedation—for example, with 50% nitrous oxide-oxygen blends—can be administered by a single physician or nurse practitioner with current life support certification anywhere within the emergency department.<sup>4</sup>

Guidelines recommend that for deeper levels of sedation (moderate and dissociative), using intravenous agents, a physician should be present to administer the sedative, in addition to the practitioner carrying out the procedure.<sup>4</sup> A history and physical examination should be performed before the procedure.<sup>3,4</sup> Assessment of ASA (physical status classification) grade is recommended, although a retrospective registry analysis showed no correlation between ASA grade and complications in 303 adult patients undergoing deep sedation for hip reduction.<sup>22</sup> Particular attention to airway assessment is

recommended. However, a meta-analysis of the components of the “LEMON” airway assessment tool showed poor to moderate discriminative power for identifying difficult laryngoscopy but higher discriminative power when used in combination.<sup>23</sup>

For moderate sedation, resuscitation room facilities are recommended, with continuous cardiac and oxygen saturation monitoring, non-invasive blood pressure monitoring, and consideration of capnography. During deep sedation, capnography is recommended, and competent personnel should be present to provide “cardiopulmonary rescue” in terms of advanced airway management and advanced life support.<sup>3 4</sup>

A well designed randomised controlled trial showed that capnography may provide early warning of ventilatory changes that could result in hypoxia during sedation of patients receiving supplemental oxygen.<sup>24</sup> This has not been confirmed in patients breathing room air.<sup>25</sup> Ongoing assessment of the level of consciousness using the Glasgow coma scale or sedation scale is recommended; use of the motor component only of the scale is safe and effective in sedated patients.<sup>3 4</sup>

Consensus guidelines also recommend the checking of equipment, careful management of drugs, optimal patient positioning, pre-procedural fasting for deeper sedation other than in emergency situations, careful documentation, post-sedation advice, and audit of standards.<sup>4</sup> There are no published checklists that refer directly to sedation, but checklists are now widely used in operating theatres and before pre-hospital emergency anaesthesia, and these have been shown, in uncontrolled trials, to improve patient safety.<sup>26</sup>

## Specific advice

Patients in pain should be provided with analgesia before proceeding to sedation.<sup>4</sup> The intravenous route is generally the most predictable and reliable method of administration for most of these agents. Local factors, including availability, familiarity, and clinical experience will affect drug choice, as will safety, effectiveness, and cost factors. The table summarises advice on selection, administration, and cautions.

## How cost effective is procedural sedation and analgesia?

There may be cost savings associated with providing sedation in the emergency department for procedures that can be performed safely in either the emergency department or the operating theatre, as well as with certain drug choices. A matched cohort economic evaluation comparing children who were sedated in the emergency department with those who were admitted to theatre in 2010 estimated that each sedation in the emergency department saved £614 (€746; \$1033) (95% confidence interval £441 to £787).<sup>27</sup>

A cost effectiveness analysis showed that choosing a sedation strategy with propofol over midazolam resulted in average savings of \$17.33 (\$10.44 to \$24.13) per sedation performed.<sup>28</sup>

## Case resolution

Because the patient has already received intravenous fentanyl, various options are available to sedate her for shoulder relocation. Nitrous oxide may provide enough sedative effect. Propofol could also be used because the procedure is short. Had she not just received intravenous fentanyl, administration of a sub-dissociative dose of ketamine analgesia with propofol sedation would be an ideal combination.

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**Tips for patients**

Different drugs are available to help avoid awareness of painful procedures in the emergency department. These are usually injected into a vein, but occasionally they may be inhaled as a gas or swallowed as a pill

Painkillers or analgesic agents such as fentanyl or morphine reduce pain without causing unconsciousness

Sedative agents such as propofol, midazolam, or etomidate make you sleepy and unaware of the procedure. You may not remember events for a few minutes after receiving these drugs. Ketamine is another drug that "dissociates" you from feeling discomfort. You will be able to respond after receiving this drug but will not feel the pain of the procedure

Although these drugs may rarely cause side effects such as nausea, vomiting, altered perception of reality, or hallucinations on waking, and occasionally may affect your breathing, these effects are minimised by careful monitoring and early treatment should they occur

Your sedation in the emergency department will be performed in a fully monitored setting by staff dedicated to the sedation as well as to the procedure

## Table

Table 1 | Drugs used for procedural sedation and analgesia in adults in the emergency department

Class	Drug	Dosage and administration*	Advantages	Cautions†
Opioids	Fentanyl	0.5-1 µg/kg IV over 2 min until appropriate analgesia reached	Short acting analgesic; reversal agent (naloxone) available	May cause apnoea, respiratory depression, bradycardia, dysphoria, muscle rigidity, nausea, and vomiting; hypotension is described but is uncommon when used as a single agent; use lower aliquots and/or longer dosing intervals for older people or those with renal or hepatic dysfunction <sup>9</sup>
	Morphine	50-100 µg/kg IV then 0.8-1 mg/h IV as needed	Reversal agent (naloxone) available; prolonged analgesic properties (longer duration of action) than fentanyl, alfentanil, sufentanil, and remifentanil	Uncommon first line agent for procedural analgesia; slow onset and peak effect time and less reliable than fentanyl, alfentanil, sufentanil, and remifentanil
	Remifentanil	0.025-0.1 µg/kg/min IV	Ultra-short acting; no solid organ involved in metabolic clearance	Difficult to use without an infusion pump
Benzodiazepines	Midazolam	Small IV doses of 0.02-0.03 mg/kg until clinical effect ("sleepy," ptosis, dizziness, slurred speech) achieved; repeat dosing of 0.5-1 mg for 3-5 min, with total dose <5 mg	Familiar emergency drug; minimal effect on respiration; reversal agent (flumazenil) available	No analgesic effect; may cause hypotension, particularly when given rapidly or combined with opioids (may need to decrease midazolam dose); paradoxical excitation can occur (uncommon)
Volatile agents	Nitrous oxide	50% nitrous oxide-50% oxygen mixture delivered by physician or patient holding mask over mouth and nose	Rapid onset and recovery; cardiovascular and respiratory stability; few contraindications	Acute tolerance may develop; specialised equipment needed; for prolonged use, requires a well ventilated space, possibly with scavenging system of waste gases
	Propofol	Intermittent bolus of 10-30 µg/kg IV over 1-5 min or continuous infusion of 100 µg/kg/min for 3-5 min then reduce to ~50 µg/kg/min titrated to effect	Rapid onset; short acting; anticonvulsant properties	May cause rapidly deepening sedation, airway obstruction, apnoea, hypotension secondary to myocardial depression; consider reducing the dosage (by 50%, or more) in elderly patients or those with reduced physiological reserve
Phencyclidines	Ketamine	0.2-0.5 mg/kg IV over 2-3 min; 2-4 mg/kg intramuscularly	Rapid onset; short acting; potent analgesic even at low doses; cardiovascular stability; bronchodilator; synergy with propofol; few contraindications	Avoid in patients with a history of psychosis because it may (re-)activate psychiatric disease; may cause nausea and vomiting; emergence reactions‡ common, but midazolam 0.03 mg/kg IV may attenuate or eliminate these reactions, <sup>9 13</sup> and quiet spaces for recovery may also help <sup>17</sup> ; consider adding an anti-sialagogue, such as glycopyrrolate
Etomidate	Etomidate	0.1-0.15 mg/kg, slow (30-60 s) IV injection; may re-administer every 3-5 min	Rapid onset; short acting; cardiovascular stability in non-hypovolaemic patients; respiratory depression rare <sup>6 9</sup>	May cause myoclonus, pain on injection, nausea, vomiting, lower seizure threshold (caution when using in patients with seizure disorders/epilepsy—may induce seizures), <sup>6</sup> and adrenal suppression (importance unclear in trauma <sup>7 9</sup> ); recommended IV dose lasts 5-15 min

\*Dosing regimens and protocols should be verified for each individual institution before starting any procedural sedation technique. The doses given are suggestions only and doses and injection intervals may need to be adjusted on the basis of individual clinical presentation and comorbidities. IV=intravenous.

†Combinations of sedatives and analgesic drugs: synergistic combinations of these agents can augment their depressive effects on respiration and slow the patient's return to consciousness compared with the use of each drug alone.<sup>4</sup> Dosages should therefore be appropriately reduced when multiple agents are used. Certain combinations have better safety profiles. For instance, before propofol induced deep sedation, low dose ketamine (at sub-dissociative levels) seems to be a safer analgesic than fentanyl; a small prospective trial for this indication showed that ketamine was associated with fewer significant intra-sedative adverse events (47% (95% CI 31% to 64%) v 84% (67% to 93%)).<sup>18</sup>

‡Emergence reactions are undesirable psychological reactions that can occur during recovery from sedative regimens when ketamine is a key component. They can vary in severity and composition but commonly involve vivid dreaming, a sensation of floating or leaving one's body, and misinterpretations of true sensory stimuli (illusions). These are often associated with excitement, confusion, euphoria, and fear.<sup>19</sup>