Procedural sedation in the emergency centre

M Stander, L A Wallis, on behalf of the Emergency Medicine Society of South Africa (EMSSA)

Background. The performance of safe and effective procedural sedation in the emergency centre has become a core competency in emergency medicine internationally. However, in South Africa clear guidelines are lacking and this guideline attempts to set out the standard for the routine safe use of procedural sedation by clinical staff in emergency centres.

Method. The Emergency Medicine Society of South Africa (EMSSA) appointed a task group to analyse the international literature and guidelines, and a draft document was produced which was revised by consensus input from an expert panel.

Introduction

A proportion of patients presenting to emergency centres need to undergo procedures that can be unpleasant and painful. The provision of safe and effective analgesia and procedural sedation is a critical aspect of the provision of care in an emergency centre. Given the nature of an emergency centre, which is often overwhelming and noisy and appears chaotic to patients, the entire clinical experience for the patient and ultimately outcome can be improved if appropriate and effective procedural sedation is provided. The Emergency Medicine Society of South Africa (EMSSA) recognised the lack of uniformity on this topic and set up an expert panel responsible for the drafting of this practice guideline.

This document is intended as a guide for emergency medicine specialists and all medical practitioners involved in the provision of emergency procedural sedation in emergency centres in South Africa.

Procedural sedation definition

Procedural sedation refers to a technique of administering sedatives or dissociative agents, with or without analgesics, to induce a state that allows patients to tolerate unpleasant procedures while maintaining cardiorespiratory function and retaining the ability to respond purposefully to verbal commands and/or tactile stimulation. This technique is appropriate for both adult and paediatric patients.

3. Levels of sedation

3.1 Minimal sedation (anxiolysis) is a drug-induced state during which patients respond normally to verbal commands. Cognitive function and co-ordination may be impaired, but ventilatory and cardiovascular systems are unaffected.

3.2 Moderate sedation (previously referred to as conscious sedation) is a drug-induced depression of consciousness during which patients respond purposefully to verbal or light tactile stimulation. The techniques and drugs (in the doses used) are not likely to produce loss of protective airway reflexes.

3.3 Deep sedation is a drug-induced depression of consciousness during which patients cannot be aroused easily but respond purposefully after repeated or painful stimulation. These patients may require assistance in maintaining a patent airway and may need ventilatory support.

3.4 General anaesthesia refers to a state of drug-induced loss of consciousness during which patients are not rousable and may have impaired cardiorespiratory function requiring varying degrees of support.

3.5 Dissociative sedation is a trance-like cataleptic state characterised by profound analgesia and amnesia with retention of protective airway reflexes, spontaneous respiration and cardiopulmonary stability. Ketamine is the only approved dissociative agent.

Progression from one stage to the next is a continuum, and it is often difficult to predict how a patient will respond to a specific sedative agent. It is essential that practitioners possess the skills necessary to rescue a patient from one level deeper than the desired level of sedation.

Recommendations in this guideline are not intended to represent the only diagnostic and management options that emergency practitioners can apply. The individual physician’s judgement is of utmost importance. However, procedural sedation is the recognised and validated standard of practice for painful and intimidating procedures.

4. Scope of practice guideline

This practice guideline:
- applies to the administration of dissociative agents, sedative agents or sedative and analgesic agents together
- does NOT apply to:
  - administration of agents to facilitate airway management or tracheal intubation
  - patients who have already undergone tracheal intubation and ventilation
- refers to the use of moderate sedation and analgesia, and deep sedation and analgesia, in order to facilitate diagnostic or therapeutic procedures
- refers to the use of sedative, analgesic and dissociative agents in the emergency centre
- refers to adult and paediatric patients.
5. Objectives of procedural sedation
The objectives are:
- to provide adequate analgesia, anxiolysis, sedation and amnesia during the performance of painful diagnostic or therapeutic procedures
- to minimise variations in patients’ cardiovascular and respiratory physiological parameters
- to maintain the patient’s protective airway reflexes.

6. Contraindications to procedural sedation
6.1 Contraindications
Contraindications include:
- lack of appropriate monitoring equipment, or inability to monitor patient during procedure
- lack of personnel experienced in airway management or interpretation of monitoring equipment
- lack of resuscitation and airway management equipment
- children under the age of 2 years should not receive procedural sedation unless under the care of an emergency medicine physician experienced in paediatric emergency medicine
- allergy or sensitivity to the prescribed medication (refer to the listed contraindications to specific medications as described in the latest edition of the South African Medicines Formulary (SAMF)).

6. Relative contraindications
Relative contraindications include:
- facial, dental or airway abnormalities that would preclude tracheal intubation
- patients at high risk of vomiting and aspiration
- haemodynamically or neurologically unstable patients.

7. Patient evaluation
Obtain a history and perform a physical examination to identify medical illnesses, medications, allergies and anatomical features that may affect procedural sedation and airway management. The time and nature of last oral intake must be documented.

7.1 Medical history and examination
The medical history and formal physical examination to be performed before administering sedation are to include the following:
- health and risk assessment history, including allergies, current medications, current health problems, previous hospitalisations, previous sedation and anaesthetic history
- vital signs and weight
- mental health status
- assessment of airway opening and patency
- the airway should also be assessed for potential difficulties to bag-mask ventilation as well as difficult laryngoscopy
- respiratory status
- cardiovascular status
- nil per os (NPO) status
- developmental status (in paediatric cases).

7.2 Consent
As part of the consent process, staff members must clearly explain the proposed treatment or procedure. The explanation should include the following:
- potential benefits and drawbacks
- any possible adverse affects of treatment
- any significant/reasonable alternatives
- the likelihood of success.

7.3 High-risk patients
Patients at high risk for complications due to procedural sedation include individuals with:
- upper airway obstruction (stridor when awake)
- sleep apnoea or significant snoring
- mandibular hypoplasia, craniofacial abnormalities or history of difficult airway during anaesthesia or sedation
- active vomiting, delayed gastric emptying
- significant gastro-oesophageal reflux, particularly with history of aspiration
- pre-existing significant neurological dysfunction or depressed level of consciousness
- hypovolaemia, cardiac disease or other potential for alteration in perfusion
- pneumonia, reactive airway disease or other disorder of gas exchange or pulmonary mechanics
- history of sedation failure
- multiple trauma
- head trauma
- patients who have ingested a central nervous system depressant such as alcohol.

7.4 High-risk techniques
Sedation techniques with higher risk for complications include:
- deep sedation, regardless of intended depth or drugs administered
- non-elective sedation
- combination drug therapy, particularly opioids and hypnotics
- medications administered in large doses instead of titrated to effect
- use of opioids for sedation instead of analgesia.

8. Pre-procedure preparation and equipment
The procedure should be performed in a clinical environment where monitoring can be done and where access to resuscitative drugs and equipment is immediately available. The relevant reversal agents must also be available.

8.1 Equipment
The following equipment should be present:
- oxygen and delivery devices (nasal cannula and face mask)
- suction and suction catheters
- resuscitation trolley and defibrillator and intubation equipment
- vital signs monitor (including blood pressure, cardiac monitor and saturation)
- positive-pressure breathing device
- oral airways of appropriate size
- advanced cardiac life support medications.

Intravenous (IV) access must be established and maintained, except when using an intramuscular technique for the administration of ketamine in children.
9. Fasting before procedural sedation
There is no evidence to show that patients need to be fasted, and recent food intake is not a contraindication. The risks and benefits of performing procedural sedation on each individual patient need to be considered carefully in choosing the timing and target level of sedation.

10. Staff4,9,10
Sedation and performance of a procedure require at least two appropriately qualified staff (a doctor and a nurse or two doctors); one to perform the procedure, and one to be solely responsible for the administration of medication, monitoring and documentation.

Observation and monitoring should be done from the start of sedation until discharge criteria have been met.

The staff responsible for administering the IV analgesia and sedation should be trained in the recognition of complications associated with IV sedation. Personnel providing procedural sedation and analgesia must have an understanding of the drugs administered, ability to monitor the patient’s response to the medications given, and the skills necessary to intervene in managing all potential complications.

11. Monitoring and documentation6,7
Assessment of the patient should be done at baseline and every 5 minutes once the first analgesia/sedation dose has been administered.

The following should be documented:
- vital signs (blood pressure, heart rate, respiratory rate)
- electrocardiograph rhythm
- oxygen saturation
- airway patency
- use (or not) of supplemental oxygen
- level of consciousness
- pain
- medications given, including route, dose and person administering.

Capnometry can be considered to provide additional information regarding the early identification of hypoventilation, but is not an essential requirement of procedural sedation.2,3,11

Documentation should include the date and time of start of sedation, start of procedure and time of conclusion of post-procedure care. Adverse events that should be recorded include apnoea or airway obstruction requiring intervention, vomiting, aspiration, and over-sedation, inadequate sedation, sedation failure or need for reversal agents.

12. Drugs administered4,8,11,12
Ketamine, midazolam, fentanyl, propofol and etomidate can all safely be administered for procedural sedation and analgesia in the emergency centre. Morphine can safely be used as an analgesic adjunct (refer to Appendix 2 for drugs and dosages).

Medication doses must be calculated, drawn up and labelled before commencement of the procedure. Appropriate antagonists must be available and only used if absolutely necessary. Antagonists should not be given directly after the procedure in order to ‘reverse’ the patient’s sedation and analgesia.

Drugs should be given slowly and in small incremental doses. Analgesic agents should generally be administered before sedative agents, as over-sedation may result if analgesic medications are given after sedation.

The therapeutic affect should be assessed before the next incremental dose is determined and the patient should be observed for the following:
- decrease in oxygen saturation
- ability to maintain patent airway
- appropriate response to physical stimulation and/or verbal command
- significant changes in vital signs.

Adjust doses according to patient’s age, level of debilitation, drug combinations, tolerance, pulmonary reserve, previous narcotic use and length of procedure.

13. Post-procedure care and discharge criteria1,8
The patient should not be left alone at any stage. A trained staff member should remain with the patient until discharge.

13.1 Post-procedure assessments
Post-procedure assessments should be documented:
- every 15 minutes for 1 hour
- then every 30 minutes for 1 hour
- then hourly or until discharge criteria have been met.
- If the patient receives a reversal agent, they should be observed after the procedure for a minimum of 1.5 additional hours.

13.2 Discharge criteria
The following criteria need to be fulfilled before the patient can be discharged:
- Vital signs, level of consciousness, cardiovascular and respiratory status have returned to pre-sedation levels.
- A responsible, designated adult is able to accompany patient and transport is available.
- The patient/caregiver has received appropriate verbal and written discharge instructions.
- Discharge forms are completed and discharge medication has been dispensed.
- Pain is adequately controlled.
- Nausea/vomiting is controlled.
- Oxygen saturation is at pre-intervention status.
- No signs or symptoms that may jeopardise the safety of recovery (bleeding, swelling, extreme pain, dizziness, etc.).
- Follow-up for extended care has been provided.
- For children: age-appropriate responses are present.

All patients MAY NOT DRIVE home and should not drive for up to 24 hours following discharge. The same precaution would apply to patients who operate heavy machinery.

Patients with special handicaps, including the blind with or without a guide dog, the deaf and mute, and patients with mental illness and/or mental handicap, may need extra precautions on discharge at the discretion of the attending doctor.

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The authors declare that there are no conflicts of interest.

References


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**Appendix 1. American Society of Anesthesiology patient classification status**

| ASA I | Normal healthy patient |
| ASA II | Patient with mild systemic disease; no functional limitation, e.g. smoker with well-controlled hypertension |
| ASA III | Patient with severe systemic disease; definite functional impairment, e.g. diabetes and angina with relatively stable disease, but requiring therapy |
| ASA IV | Patient with severe systemic disease that is a constant threat to life, e.g. patient has dyspnoea on mild exertion and chest pain |
| ASA V | Unstable moribund patient who is not expected to survive 24 hours with or without the operation |
| ASA VI | Brain-dead patient whose organs are removed for donation to another |
| E | Emergency operation of any type – added to any of the 6 above categories (e.g. ASA II E) |

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**Appendix 2. Medications and dosages**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosing (&gt;46 kg)*</th>
<th>Paediatric dosing (≤46 kg)*</th>
<th>Precautions/contraindications/side-effects</th>
<th>Special considerations &amp; reversal agent</th>
<th>Preanaesthetic Category</th>
<th>Contraindications with alcohol</th>
<th>Duration</th>
<th>Metabolised/Liver Excercised/Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etomidate</td>
<td>Initial dose: 0.1 - 0.3 mg/kg</td>
<td>Under 10 years: No dose established</td>
<td>Commonly causes myoclonus, pain upon injection, no clinical significance</td>
<td>No reversal agent</td>
<td>Prophylaxis Category C</td>
<td>None</td>
<td>3 - 5 min</td>
<td>Excreted: Liver Excercised: Kidney</td>
</tr>
</tbody>
</table>

* Dosages for children <10 years not established.
### Appendix 2. Medications and dosages (continued)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosing (&gt;45 kg)*</th>
<th>Paediatric dosing</th>
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<th>Special considerations &amp; reversal agent</th>
<th>Precautions/contraindications/side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fentanyl</strong> (Sublimaze) Analgesic Sedative effects</td>
<td><strong>Initial dose:</strong> 1 - 2 µg/kg slow IV push (over 1 - 2 min); may repeat dose after 30 min <strong>Usual maximum:</strong> 100 µg within 30 min <strong>IV dose rate:</strong></td>
<td><strong>Initial dose:</strong> 1 µg/kg</td>
<td><strong>Onset:</strong> 1 - 2 min <strong>Peak:</strong> 3 - 5 min <strong>Duration:</strong> 30 - 60 min <strong>Metabolised:</strong> Liver <strong>Excreted:</strong> Kidney</td>
<td>Reduce dose by 1/4 to 1/3 when used with other CNS-depressing drugs or in the elderly or debilitated Muscle rigidity from high doses may prevent adequate chest wall expansion and respiration. This is reversed with neuromuscular blockers or naloxone, but patient must be artificially ventilated</td>
<td><strong>Precautions:</strong> Elderly/debilitated Bradyarrhythmias Head injury Respiratory disease <strong>Contraindications:</strong> Hypersensitivity <strong>Side-effects:</strong> CNS/respiratory depression Hypotension Muscle rigidity Bradycardia Nausea and vomiting Pruritus Seizures</td>
</tr>
<tr>
<td><strong>Flumazenil</strong> (Anexate) Reversal of benzodiazepines</td>
<td>Reversal of benzodiazepine-induced sedation <strong>Onset:</strong> 1 - 2 min <strong>Peak effect:</strong> 6 - 10 min In high-risk patients it may be necessary to increase interval between doses to over 1 minute</td>
<td><strong>Initial dose:</strong> 0.2 mg IV over 15 s Wait 45 s, additional 0.2 mg doses at 1-min intervals until maximum of 4 additional doses have been given Maximum cumulative dose is 1.0 mg Repeat above in 20 min if needed No more than 3 mg in 1 h</td>
<td>No manufacturer-published data</td>
<td>Can precipitate seizures in those with seizures controlled by benzodiazepines, with tricyclic depression overdose, and at high risk for seizures</td>
<td><strong>Precautions:</strong> Re-sedation: monitor for re-sedation, respiratory depression for up to 120 min. Re-sedation least likely in low-dose sedation (e.g. &lt;10 mg midazolam) <strong>Contraindications:</strong> Hypersensitivity Tricyclic antidepressant overdose Benzodiazepine dependency <strong>Side-effects:</strong> Visual disturbances Diaphoresis Seizures Arrhythmias</td>
</tr>
</tbody>
</table>
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<tbody>
<tr>
<td><strong>Ketamine</strong></td>
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<tr>
<td>Analgesic</td>
<td>Initial dose: 1 - 2 mg/kg IV</td>
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<td>Atropine should NOT be given routinely as it has been shown to be associated with a higher incidence of respiratory complications Barbituates and ketamine should not be injected using the same syringe</td>
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<tr>
<td>Dissociative agent</td>
<td>IV dose rate: Give slowly over 1 min</td>
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<td></td>
<td>IV: 0.5 - 1 (2) mg/kg, max. dose 100 mg</td>
<td></td>
<td>Onset: 30 s - 1 min IV, 3 - 5 (4) min IM</td>
<td></td>
<td>Contraindications: History of cardiovascular disease or hypertension</td>
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<td></td>
<td>IM: 4 mg/kg (range 3 - 5 mg/kg), max. dose 50 mg/kg (IM preferred route)</td>
<td></td>
<td>Duration: 5 - 15 min IV, 12 - 25 min IM</td>
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<td>Active pulmonary infection or disease</td>
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<td></td>
<td>Oral: 4 - 5 mg/kg</td>
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<td>Full recovery: 30 - 120 min</td>
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<td>Age 3 mo. or less</td>
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<td></td>
<td>Different formulations available: 10 mg/ml, 50 ng/ml, 100 mg/ml</td>
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<td>Initial IV dose: Over 60 s (rapid administration may cause respiratory depression)</td>
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<td>Head injury not a contraindication</td>
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<td></td>
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<td></td>
<td>Metabolism: Liver</td>
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<td>Glaucoma or acute globe injury not a contraindication</td>
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<td></td>
<td>Excretion: Kidney</td>
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<td>Psychosis</td>
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<td>Conditions with intracranial hypertension</td>
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<td></td>
<td>Seizure or CNS disorders</td>
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<td></td>
<td>History of airway instability, tracheal surgery or stenosis</td>
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<td>Side-effects: Nystagmus, resp. depression, hypersalivation, laryngospasm, non-purposeful movements, emesis, ↑ HR, BP, ICP</td>
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<td></td>
<td>‘Emergence reaction’ – unpleasant</td>
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<td></td>
<td>Dreams/hallucinations (most common in females age &gt;10)</td>
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<tr>
<td><strong>Midazolam</strong></td>
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<td></td>
<td>Contraindications: Elderly/debilitated</td>
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<tr>
<td>(Dormicum)</td>
<td>Initial dose: 0.02 - 0.1 mg/kg IV initially</td>
<td></td>
<td>Onset: 1½ - 5 min</td>
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<tr>
<td>Anxiolytic</td>
<td>If further sedation is required, may repeat with 25% of initial dose after 3 - 5 min</td>
<td></td>
<td>Peak: 10 - 15 min</td>
<td></td>
<td>Hypersensitivity</td>
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<tr>
<td>Amnesic</td>
<td>Not to exceed 2.5 mg/dose (1.5 mg for elderly persons) and 5 mg cumulative dose (3.5 mg for elderly persons)</td>
<td></td>
<td>Duration: 60 - 90 min</td>
<td></td>
<td>Acute narrow-angle glaucoma</td>
</tr>
<tr>
<td>Skeletal muscle relaxant</td>
<td>Usual maximum: Average adult &lt;60 years – 5 mg within 30 min</td>
<td></td>
<td>Metabolised: Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticonvulsant</td>
<td>Elderly adult &gt;60 years – 3.5 mg within 30 min</td>
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<td>Excreted: Kidney</td>
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<td></td>
<td>IV dose rate: 1 mg over 1 min. Wait 2 min after each increment to fully evaluate effects. Maintain level with 25% of initial IV dose</td>
<td></td>
<td>Recovery is dose dependent, usually 1 - 2 h</td>
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<tr>
<td></td>
<td>Intravenous: 0.05 - 0.1 mg/kg IV 3 min before procedure; not to exceed a total cumulative dose of 0.4 mg/kg or 6 mg</td>
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<td>Reduction by 1/3 to ½ when used with other CNS-depressing drugs or in the elderly or debilitated</td>
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<tr>
<td></td>
<td>Oral: 0.5 - 0.75 mg/kg</td>
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<td>Manufacturer recommends not more than 1.5 mg over at least 2 minutes in patients with decreased pulmonary reserves</td>
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<td></td>
<td></td>
<td>Reversal agent: Fumazenil (Anexate)</td>
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</tbody>
</table>
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<th>Paediatric dosing</th>
<th>Onset</th>
<th>Special considerations &amp; reversal agent</th>
<th>Precautions/contraindications/side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphine</strong></td>
<td>Initial dose: 0.05 - 0.1 mg/kg slowly</td>
<td>0.05 - 0.1 mg/kg slowly</td>
<td><strong>Onset:</strong> 1 min</td>
<td>Reduce dose by 1/3 to ⅛ when given with other CNS-depressing drugs or in the elderly or debilitated</td>
<td><strong>Precautions:</strong> Elderly/debilitated, Respiratory conditions, Seizure disorders, Head injury <strong>Contraindications:</strong> Hypersensitivity <strong>Side-effects:</strong> CNS/respiratory depression, Hypotension, Nausea/vomiting, Dizziness</td>
</tr>
<tr>
<td>Analgesic Sedative effects</td>
<td><strong>Bolus dosages:</strong> 2.5 mg elderly/debilitated, 5 - 10 mg healthy adult</td>
<td><strong>Peak:</strong> 15 min</td>
<td><strong>Duration:</strong> 2 - 4 h</td>
<td><strong>Metabolised:</strong> Liver</td>
<td><strong>Excreted:</strong> Kidney</td>
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<tr>
<td></td>
<td><strong>Usual maximum:</strong> 10 mg within 30 min</td>
<td><strong>Reversal agent:</strong> Naloxone (Narcan)</td>
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<tr>
<td></td>
<td><strong>IV dose rate:</strong> Administer slowly: Wait 5 min to evaluate effects</td>
<td>0.01 mg/kg every 2 - 3 min. May repeat as needed</td>
<td>If does not produce desired outcome, a subsequent dose of 0.1 mg/kg may be administered</td>
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<tr>
<td></td>
<td><strong>Onset:</strong> 1 - 2 min</td>
<td><strong>Duration:</strong> 5 - 10 min</td>
<td></td>
<td>Monitor for re-sedation</td>
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<td></td>
<td></td>
<td><strong>Precautions:</strong> Avoid bolus dosing and use smaller infusion doses in elderly/debilitated patients</td>
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<td></td>
<td></td>
<td>May cause hypotension in 3 - 10% of adult patients and 17% of paediatric patients</td>
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<td></td>
<td><strong>Contraindications:</strong> Patients with soybean and egg hypersensitivity</td>
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<td></td>
<td>Caution in elderly and hypovolaemic patients (consider fluid bolus in hypovolaemic patients before injection of propofol)</td>
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<td></td>
<td><strong>Side-effects:</strong> Painful injection. This is improved by mixing the drug with a small amount (0.25 mg/kg) of intravenous lignoocaine</td>
<td></td>
</tr>
<tr>
<td><strong>Naloxone</strong></td>
<td>0.4 mg - 2 mg IV</td>
<td>0.01 mg/kg every 2 - 3 min. May repeat as needed</td>
<td><strong>Onset:</strong> 1 - 2 min</td>
<td>Can precipitate ventricular tachycardia and fibrillation in patients with cardiovascular disease or receiving potentially cardiotoxic drugs</td>
<td><strong>Precautions:</strong> Cardiovascular disease <strong>Contraindications:</strong> Hypersensitivity, Narcotic dependency <strong>Side-effects:</strong> Nausea/vomiting, Sweating, Tachycardia, hypertension, Pulmonary oedema</td>
</tr>
<tr>
<td>Reversal of narcotics</td>
<td>May repeat as needed in 2 - 3-min intervals prn</td>
<td><strong>Duration:</strong> 5 - 10 min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Propofol</strong></td>
<td><strong>Initial dose:</strong> 1 mg/kg bolus IV Manually ‘top up’ doses with boluses at half the initial dose</td>
<td><strong>Initial dose:</strong> 0.5 - 1 mg/kg over 20 - 30 s, or continuous infusion starting at 100 - 150 µg/kg/min Followed by maintenance infusion of 25 - 75 µg/kg/min (infusions should only be used by those experienced at using them)</td>
<td><strong>Onset:</strong> &lt;1 min</td>
<td>No reversal agent</td>
<td><strong>Precautions:</strong> Avoid bolus dosing and use smaller infusion doses in elderly/debilitated patients May cause hypotension in 3 - 10% of adult patients and 17% of paediatric patients <strong>Contraindications:</strong> Patients with soybean and egg hypersensitivity Caution in elderly and hypovolaemic patients (consider fluid bolus in hypovolaemic patients before injection of propofol) <strong>Side-effects:</strong> Painful injection. This is improved by mixing the drug with a small amount (0.25 mg/kg) of intravenous lignoocaine</td>
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<td>(Diprivan) Non-analgesic Sedative</td>
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*IV = intravenous; CNS = central nervous system; IM = intramuscular; HR = heart rate; BP = blood pressure; ICP = intracranial pressure; prn = as needed.

*Patients with higher tolerance may receive higher doses at the discretion of the physician.*