

Sedation for cases without local anaesthetic

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Introduction

This overview will focus on sedation for painful diagnostic and therapeutic procedures, where the use of local analgesia is not feasible.

The first public demonstration of ether anaesthesia took place in 1846 in the Massachusetts General Hospital. It is unlikely that the anaesthetist, William Morton, could have foreseen that, one day, it would be possible to control the level of anaesthesia to meet specific requirements. This is possible through the development of rapid- and short-acting drugs, regulated by computer-driven infusions that visualise the relationship between drug and effect. The grey area between wakefulness and general anaesthesia is known as sedation (Figure 1).

It is in this area that local analgesia plays a pivotal role. When pain is controlled by topical, local, or regional analgesia, sedation serves the main purpose of helping the patient to cope with fear, anxiety, claustrophobia, distress, and physical discomfort. Under these circumstances, minimal or moderate sedation levels¹ are adequate to ensure patient comfort (Figure 2).

However, for many painful procedures, the use of local analgesia is not feasible (Table I). Since most sedatives have little, or no, analgesic effects, sedation in itself is not enough to block the intense pain of painful procedures. Therefore, the use of systemic analgesics is mandatory to supplement the sedation, and attenuate the painful stimuli.

Table I: Painful procedures, where the use of local analgesia may not be feasible

Painful injections of local analgesia, e.g. dentistry, plexus blocks
Injection of large areas with local analgesia, e.g. tumescent technique
Interventional radiology
Gastrointestinal tract “-oscopies”, endoscopic retrograde cholangiopancreatography
Bronchoscopies
Dermatology: Photodynamic therapy, laser, cauterisation
Transcutaneous neurosurgical procedures: Rhizotomies, nerve root blocks
Bone marrow aspiration

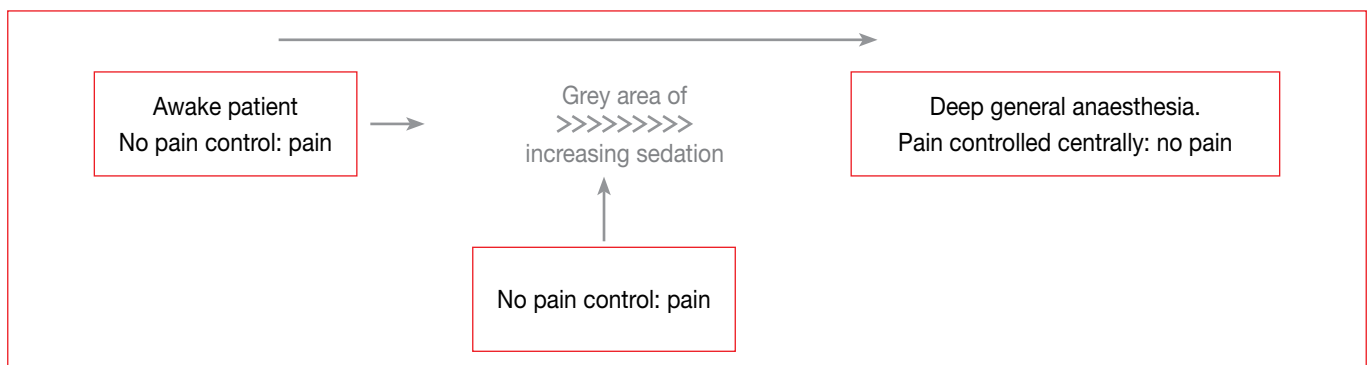


Figure 1: The relationship between pain perception, and sedation and anaesthesia

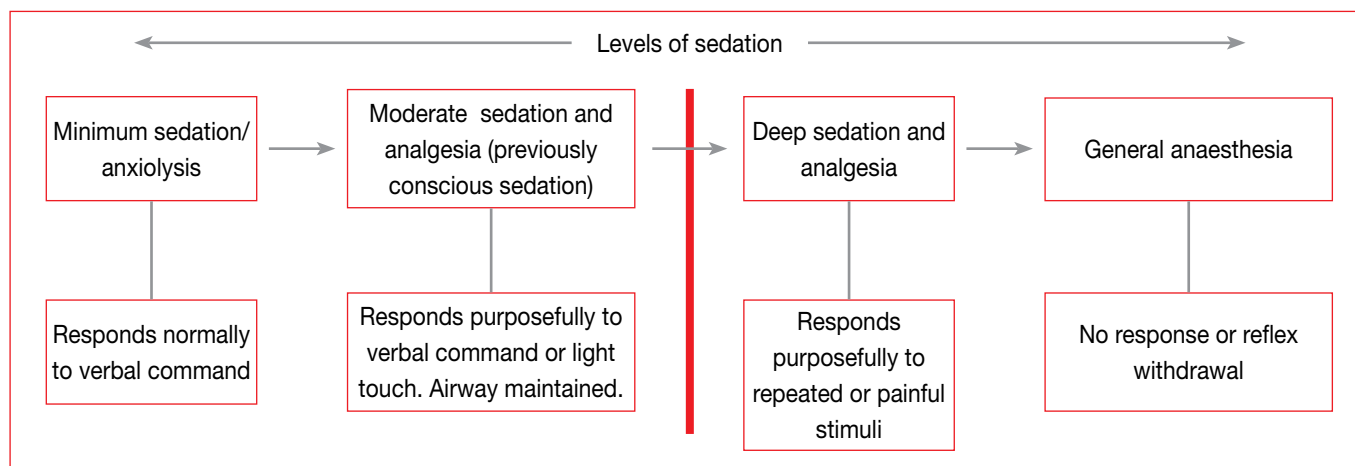


Figure 2: The levels of sedation

From: American Society of Anesthesiologists' task force on sedation and analgesia by non-anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology*. 2002;96:1004-1017.

Analgesia, like sedation, is a continuum between the perceived absence of pain and maximum pain.²

When a noxious stimulus is applied to a conscious patient who did not receive any pain control, the patient is certain to experience pain (Figure 1). If this patient is sedated, the patient will still experience some pain, depending on the extent of the painful stimulus, and on the patient's personal pain threshold. With increasing sedation, conscious pain perception is abolished, and the patient eventually falls unconscious, and under general anaesthesia. At this point, the interaction between analgesia and anaesthesia becomes inseparable,² and there will be no pain perception, even though the patient did not receive any pain control. The threshold at which sedation turns into general anaesthesia is unknown, and is dependent on factors like the intensity of the painful stimulus, and the patient's pain threshold. Most sedation scales use response to verbal command and reaction to pain as an indication of the level of sedation.³⁻⁵ It is generally accepted that a patient who is not responding to verbal command or light touch, is deeply sedated, and a patient who does not show a purposeful response to a painful stimulus, is under general anaesthesia.¹

The problem of predicting pain

When addressing the acute and intense nature of painful stimuli, the following is important:

- The perception of pain is subjective, and has a strong emotional component.⁶
- Pain perception varies between cultural and ethnic groups,⁷ as well as between males and females.^{8,9} Therefore, it is not possible to predict accurately how an individual will react to a specific painful procedure, and how much analgesia is needed.
- When analgesia is offered, it is impossible to predict whether the level of analgesia is sufficient for the next

painful surgical stimulus.

- Even though pain can be quantified, to some extent, by using a visual analogue scale, it cannot easily be measured scientifically.
- It is possible during sedation to monitor the patient's perception of pain, by keeping the patient responsive using moderate, rather than deep, sedation.
- During a non-painful procedure, the emphasis is on sedation. During a painful procedure, the emphasis is on systemic pain control, augmented by sedation, to help the patient tolerate the pain.

The problem of planning the sedation

When planning the sedation, the following needs to be taken into account:

The nature of the procedure: how much pain?

Even though pain cannot be measured, through experience, practitioners know how much pain a certain procedure will cause, and how patients will react to this pain, in general. Therefore, practitioners have a general idea of how much analgesic will be required. For example, will intravenous paracetamol suffice, or should intravenous opiates be added?

Expected duration

An estimate of the expected duration is important, because patients may be able to tolerate intense pain for short periods of time, for example, the cauterisation or laser of one small lesion. If the intense pain is repeated over a longer time, or increases over time, the patient may not be able to tolerate the procedure.

Age of patient: the elderly and children

It is undecided as to whether the elderly tolerate pain better than younger patients. However, it is known that elderly

patients are more sensitive to analgesics and sedatives,¹⁰ and that drug doses must be reduced and titrated to effect. On the other hand, children may perceive pain, even in the absence of a painful stimulus. This is often seen in the dentist's chair, where even after administration of local analgesia, children can interpret pressure as pain.

Patients' emotional state

Patients' emotional state may influence their perception of, and reaction to, painful stimuli, and needs to be taken into account.¹¹

The problem of safe systemic analgesia

When using intravenous analgesics, the principles of safe sedation practice, as set out in the South African Society of Anaesthesiologists (SASA) Sedation Guidelines 2010¹² should be kept in mind:

- Administer the minimal dose necessary to make the patient feel comfortable and safe
- Titrate the drug to the patient's needs
- Be knowledgeable about the time of onset of the drug's action.

It is prudent to scrutinise the drugs being used, in order to ensure a safe sedation (Table II). Sedation often involves the combination of more than one type of drug. Since these drugs act synergistically, it is mandatory to reduce doses accordingly, and titrate to effect.

Table II: Checkbox to determine choice of analgesic

Is the practitioner knowledgeable about the use of the drug?
What is the purpose of choosing the drug: Analgesia, sedation, synergism?
Does the drug suit the nature of the procedure, regarding pain intensity and duration of procedure?
What is the time-to-onset and time-to-peak effect: Sufficient time for the drug to reach the peak effect?
Is the drug duration of action in keeping with procedure duration?
Are there any possible delayed adverse events?
Is the drug safe in terms of hemodynamic stability, respiratory control, and allergic potential?

Step 1: Consider oral analgesics before the procedure

The use of preoperative analgesics has two benefits:

- During longer procedures, it will provide some additive analgesia during the procedure.
- More importantly, the preoperative analgesics will

provide analgesia postoperatively, when the short-acting systemic analgesics used during the procedure have been stopped, and the effects have worn out.

Step 2: Start the sedation with a small dose of sedative, e.g. 0.5-1 mg intravenous midazolam

This serves two purposes:

- Testing the waters: the patient's reaction to the small dose gives the practitioner some idea of how sensitive the patient is to sedatives. If this small dose causes instant drowsiness, the sedationist will realise that the patient will probably only need a little sedation to achieve the desired effect. If, on the other hand, there is little, or no, visual effect, supplemental doses of midazolam can be given as bolus intravenous injections to render the patient calm and relaxed. These should be titrated in small incremental doses against effect.
- Amnesia is ensured early in the sedation process. This is beneficial where the nature of the procedure intrudes on a patient's personal privacy. If the patient experiences and remembers the procedure as pleasant, the patient may be more willing to return for repeat procedures. This is especially important in procedures that have to be repeated at regular intervals, such as colonoscopies for cancer screening. However, relying on amnesia as a means of pain control should be discouraged. Even though the amnesia gained is beneficial in certain circumstances, the main goal should be to take care of the patient's pain in itself.

Note: Midazolam has no analgesic effect. Use of midazolam should result in a conscious, compliant patient.

In combination with other depressant drugs, especially opiates, with which it acts synergistically, midazolam may result in loss of upper airway muscle tone, with airway obstruction and respiratory depression.

Step 3: Addition of systemic analgesics, in addition to sedation maintenance

Sedation is usually maintained with an intravenous infusion of a hypnotic, like propofol, or etomidate.

Systemic analgesia is added either:

- As small bolus doses from a separate syringe
- Mixed in the same syringe as the sedation maintenance, or
- As a separate infusion, in addition to the sedation maintenance.

Note: Even though some studies suggest that propofol may have analgesic properties,¹³ these are not potent enough to manage the intense pain of many painful procedures. Appropriate analgesic agents should be added for optimal effect.

Table III: Comparison of the opioids in use

	Alfentanil	Fentanyl	Sufentanil	Remifentanil
Potency	++	+++	++++	+++++
Bolus dose	1 µg/kg	0.25 µg/kg	0.02 µg/kg	Only with infusion pump
Time to peak effect	1.5 minutes	2-3 minutes	5-6 minutes	1-2 minutes
Duration of action (dose-dependent)	< 5 minutes	30 minutes	30 minutes	2-3 minutes
Comments	Useful for short painful procedures. Duration of action increases with prolonged infusion.	Duration too long for use as infusion.	Duration of action increases with prolonged infusion.	High potential for bradycardia, muscle rigidity. Not recommended for use outside operating room, unless highly trained and experienced.

The problem of safe and potent systemic analgesics

In 2012, the following systemic analgesics are available for use during painful procedures:

- Opioids
- Tramadol
- Ketamine
- Dexmedetomidine
- Paracetamol
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Ketofol.

The opioids

The good

Opiates are potent analgesics, and their use is invaluable during painful procedures. Morphine and pethidine are among these, and in the past, have been used extensively during sedation. Due to these two drugs' long time-to-peak effect, long duration of action, and active metabolites, with possible delayed adverse events, their use in sedation outside the operating room is no longer justified. They have, to a large extent, been replaced by synthetic opioids (the fentanyl-group) with predictable onset, time-to-peak effect and duration of effect.

The bad

Opioids are capable of inducing variable degrees of respiratory depression, especially when used in combination with other respiratory depressant drugs, for example, midazolam and propofol. They may also cause cardiac depression with bradycardia. Practitioners administering these drugs intravenously must be trained and competent in airway management, and in the practice of rescue and resuscitation.¹² When used in combination with other sedatives, the opioids should be reduced, or titrated. Given rapidly, they can induce chest wall rigidity. One way of circumventing some of these side-effects, is to give the opioids by infusion, rather than boluses. They are

known to induce nausea and vomiting. Sedation guidelines recommend the use of a capnogram, and availability of the opioid-specific antagonist, naloxone, when opioids are used to augment sedation. Naloxone reverses both the respiratory and analgesic effects of the opioids. Therefore, it should be reserved for severe respiratory depression, or respiratory arrest. Reversal of analgesia may cause a profound sympathetic response. The post-procedural period is especially important, because of the lack of stimulation that may cause the patient to drift into deeper levels of sedation, with possible delayed respiratory depression.

Table III shows the main differences of the opioids in use.

Tramadol

An atypical opioid, tramadol not only displays μ -receptor agonist activity, but also inhibits reuptake of noradrenalin and serotonin.

The good

Tramadol is less likely to cause respiratory depression than the opioids in the fentanyl group.

The bad

Tramadol is not as potent and rapid-acting as the opioids in the fentanyl group. It should not be used in combination with other serotonergic drugs, since such combinations may precipitate the serotonin syndrome.

Dose: 1 mg/kg over 5 minutes.

Ketamine

Ketamine has stood the test of time, and is well-known for its analgesic properties, even in small, non-anaesthetic doses.

The good

Ketamine induces a state of cortical dissociation with profound analgesia, sedation and amnesia. Unlike the opioids, it has a wide therapeutic range, with relative

preservation of airway reflexes and tone. Spontaneous breathing is maintained. Since it is the drug least likely to cause fatal cardiorespiratory depression, it is probably the safest drug to use in terms of unintentional loss of consciousness.

The bad

The use of ketamine is sometimes associated with non-purposeful movements. Its sympathomimetic effects may result in tachycardia and hypertension. This may have detrimental effects in patients with chronic hypertension or ischaemic heart disease. However, these effects are rarely seen with the doses recommended for sedation.

Ketamine causes an increase in secretions in the mouth and airways, which may mandate the use of antisialogues.

With the low doses used in sedation, an antisialogogue in adult patients is seldom indicated.

Its recovery is associated with emergence delirium, especially in adults. The concomitant use of benzodiazepines can reduce the incidence, but will also deepen the sedation and prolong recovery. Ketamine, at small sedative doses (0.1-0.3 mg/kg), should be free from such effects.

Dose: 0.1-1 mg/kg

Dexmedetomidine

Dexmedetomidine is a highly selective alpha-2 receptor agonist.

The good

It has sedative, analgesic, and anxiolytic effects, with little, or no, respiratory depression. In combination with simple analgesics, it is particularly useful as an oral agent for painful procedures. The resultant sedation is markedly different from that caused by propofol and the benzodiazepines.¹⁴ It mimics natural sleep, resulting in a patient who is responsive when roused. It potentiates opioid-induced analgesia.¹⁴ Administration is by continuous intravenous infusion.

The bad

Dexmedetomidine has limited analgesic properties, and co-administration of an opioid for painful procedures is indicated. There are no amnesic properties. Possible side-effects include profound bradycardia, sinus arrest, and hypotension, especially in patients with heart block, or a high resting vagal tone. The time-to-peak effect and long half-life are drawbacks in procedural sedation.

Dose: 0.5 µg/kg over 10 minutes, then 0.2-1 µg/kg titrated to effect.

Paracetamol

The use of intravenous paracetamol is well established for the relief of mild-to-moderate postoperative pain.

The good

Intravenous paracetamol has a fast onset of action, with pain relief that occurs within 5-10 minutes.¹⁵ Its analgesic effect is comparable to morphine 10 mg intramuscular and ketorolac 30 mg intravenously.^{16,17} It does not cause respiratory compromise, and is hemodynamically friendly. The long duration of action, 4-6 hours, is of benefit in post-procedural pain management.

The bad

The peak analgesic effect, after intravenous administration of paracetamol, occurs after one hour. It is not potent enough to be used as single agent during painful procedures.

Dose: 1 g over 15 minutes.

The NSAIDs

The good

One of the advantages of the NSAIDs in the perioperative period is the variety of available routes of administration. It is possible to administer NSAIDs topically, orally, sublingually, intravenously, intramuscularly, and rectally. They improve the quality of analgesia produced in combination with the opioids, and have a useful opioid-sparing effect.

The bad

The NSAIDs alone will not produce sufficient analgesia during painful procedures. They are also associated with a significant number of adverse effects. It is important to remember that gastrointestinal adverse events can occur, irrespective of the route of NSAID administration.

Ketofol

Ketofol is a combination of propofol and ketamine in one syringe, in a concentration of 5 mg/ml each. A bolus of 3 ml over 1-2 minutes provides analgesia and sedation for 10-15 minutes.

Other methods used to relieve pain

Tender, loving care

Information on what is to be expected, reassurance, and a pleasant, relaxed ambience, considerably help patients to tolerate painful procedures.

Hyoscine (Buscopan®)

Anticholinergic drugs that inhibit gut motility may be helpful in procedures like endoscopies, but can cause tachycardia and hypotension. The half-life of hyoscine is short, about 10 minutes, so incremental doses may be needed.

The problem of inadequate pain relief

With patient variability in pain perception, it could be possible that systemic pain relief does not abolish a patient's pain, and that deep sedation is needed to keep the patient comfortable.

Under these circumstances, it should be realised that:

- Deeper levels of sedation are associated with more adverse events^{1,18}
- Shorter-acting drugs should be used to prevent delayed recovery
- Longer recovery times should be expected
- Patients under deep sedation should receive the same standard of care as patients under general anaesthesia
- Sedation practitioners must be able to manage, rescue, and recover, a patient, who enters a deeper level of sedation than intended^{1,12}

Failed sedation can be defined as “the failure to achieve a desired level of sedation, such that the procedure has to be abandoned, or the need arises to convert to general anaesthesia”.¹² Failed sedation may be attributed to patient factors, drug factors, or procedure-related or operator factors. A previous episode of failed sedation may necessitate the provision of general anaesthesia for future procedures.¹²

Conclusion

When the use of local analgesia is not possible during painful procedures, systemic analgesics need to alleviate the painful stimuli. Sedatives should not be used to compensate for inadequate analgesia. When combining benzodiazepines or other sedatives with opioids, the effects of both drug groups are potentiated, and the risk of adverse events and progression to deeper levels of sedation increases.

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