Techniques of opioid administration

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Abstract

Opioids continue to be the main pharmacological treatment for severe acute pain. Traditional methods of opioid administration (oral, intramuscular, subcutaneous) are more effective in managing pain if the treatment regimens are individualized and dosages are titrated to effect (pain relief). Oxycodone, an opioid agonist similar in potency to morphine, has proved useful as an oral step-down analgesic in the treatment of acute postoperative pain for a number of surgical procedures (orthopaedic, abdominal, gynaecological). It is also a valuable alternative opioid to morphine intravenous patient-controlled analgesia (IV PCA) in those patients who experience severe unpleasant side effects, such as nausea and hallucinations. Other PCA modalities available for opioid administration in the treatment of acute pain include epidural and transmucosal (intranasal, sublingual, buccal). Transdermal delivery of highly lipid-soluble opioids is available for the treatment of severe pain in chronic and palliative care. This passive drug delivery system is not suitable for the routine management of severe acute pain because rapid and reliable changes to the delivery rate are not possible. However, advances in transdermal delivery system technology have led to the development of a non-invasive PCA system for the management of acute postoperative pain, which utilizes the process of iontophoresis. This has the potential to be a valuable modality in the future management of acute postoperative pain.

Keywords Acute pain; analgesia; patient-controlled analgesia; postoperative pain; transdermal

Learning objectives

After reading this article, you should be able to:

- discuss the principle of opioid titration to effect
- explain the significance of lipid solubility in relation to analgesic efficacy and adverse effects
- identify the difference between transdermal and iontophoretic drug delivery.

Opioids continue to be the main pharmacological treatment for severe acute pain. The management of acute pain has improved with the introduction of advanced techniques for the administration of opioids (e.g. patient-controlled and epidural analgesia) and the more recent innovative non-invasive modalities. However, the traditional methods of administration still remain in common use.

Conventional routes of administration

The key to making the traditional methods of opioid administration more effective is to individualize treatment regimens for patients by titrating the drug dose and frequency to suit the patient. The principle is to titrate the dose against effect (pain relief) and minimize adverse effects. If the drug has been delivered and absorbed and the patient still complains of pain then it is safe to administer another smaller dose (5 minutes after an intravenous injection, 60 minutes after an intramuscular or subcutaneous injection and 90 minutes after oral morphine). If this second dose is ineffective, repeat the process or change the route of administration to achieve faster pain control.

Oral opioids

Oral opioids are required in larger doses compared with the parenteral route to take into account the effect of first-pass metabolism in the liver. An equianalgesic dose of the parenteral opioid is required in the oral formulation (Table 1). Immediate-release oral

Equianalgesic doses and half-lives of common opioids

Opioid	i.m./i.v. (mg)	Oral (mg)	Half-life (hours)
Morphine	10	30	2–3
Pethidine	100	400	3–4
Oxycodone	14	20–30	2–3
Codeine	130	200	2–4
Fentanyl	0.15–0.20	–	3–5
Alfentanil	0.75–1.50	–	1–2
Sufentanil	0.02	–	2–3
Remifentanil	0.05–0.1	–	1–2
Diamorphine	5	60	0.5[a]
Methadone	10	10–15	15–40
Hydromorphone	1.5	7.5	3–4
Tramadol[b]	100	100	5–7
Buprenorphine	0.40	0.80[c]	3–5
Pentazocine	60	150	3–5
Nalbuphine	10–20	–	2–4
Butorphanol	2.0	–	2–3

- Published reports vary in the suggested doses considered to be equianalgesic with morphine; therefore, titration to clinical response in each patient is necessary.
- Suggested doses are the results of single-dose studies only, therefore, use of data to calculate total daily dose requirements may not be appropriate.
- There may be incomplete cross-tolerance between drugs. In patients who have been receiving one opioid for a prolonged period, it is usually necessary to use a dose lower than the expected equianalgesic dose when changing to another opioid and titrating to effect.

Source: Macintyre PE, Ready LB. Acute pain management: a practical guide, 2nd edn. London: WB Saunders, 2001.

[a] Rapidly hydrolysed to morphine.
[b] Only part (about one-third) of its analgesic effect results from action on μ-opioid receptors.
[c] Sulingual. IM, intramuscularly; IV, intravenously.

Table 1

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opioids (e.g. morphine (Oramorph, Sevredol), oxycodone, hydromorphone) are preferred for the management of acute pain, because, in most cases, analgesia is obtained in 45–60 minutes. Fixed-interval dosing (e.g. 4-hourly) is preferable to a 'when required' regimen to ensure adequate relief of moderate-to-severe pain. In addition, medication for breakthrough pain should be prescribed within a dose range based on the previous 24 hours' requirements.

Oxycodone as step-down analgesia: oral oxycodone has been used for, and proved to be effective in, the treatment of acute postoperative pain for many surgical procedures – abdominal, pelvic, breast, gynaecological, orthopaedic – on both an inpatient and a day-surgery basis.

Oxycodone differs from oral morphine in that it has a higher bioavailability (up to 87%) and a slightly longer half-life. An approximate conversion ratio of 1:1 is recommended between parenteral morphine and parenteral oxycodone. When transferring patients from parenteral to oral oxycodone, the dose should be based on a 1:2 ratio (i.e. 1 mg intravenous oxycodone:2 mg oral oxycodone). This same conversion ratio also applies when switching from parenteral morphine to oral oxycodone[1] (i.e. 1 mg intravenous morphine:2 mg oral oxycodone). These ratios are only a guide. Inter-patient variability requires that each patient is carefully titrated to an appropriate dose.

Dosage regimens: oxycodone's slightly longer half-life than morphine permits a 4- to 6-hourly dosing of the immediate-release oral formulation (Oxynorm) to maintain analgesia. Pain relief occurs as early as 15 minutes and peaks at approximately 1 hour.[1,2] The usual adult dose is 10–30 mg every 4 hour as needed for pain relief, although four times a day dosing regimens have also proved to be effective.

The use of controlled-release oxycodone (Oxycontin) is indicated for the treatment of moderate-to-severe pain when continuous analgesia is required for prolonged periods. Calculate the equivalent total daily dose of oral oxycodone and divide by 2 to determine the 12 hourly doses, rounding down to the closest tablet strength.[2]

A new oral preparation (Targinact™) combines this opioid agonist with an antagonist. As both oxycodone and naloxone enter the gut, naloxone has a much higher affinity for, and preferentially binds to, the opioid receptors counteracting opioid-induced constipation by blocking the binding of oxycodone. At least 97% of the naloxone is eliminated in the healthy liver, preventing it from significantly affecting analgesic efficacy; oxycodone passes through the liver into the central nervous system (CNS) where it exerts its analgesic effect.[3]

The maximum daily dose of Targinact is limited to 40 mg/20 mg (a dose ratio of 2:1 oxycodone hydrochloride to naloxone hydrochloride) corresponding to twice daily administration of Targinact 20 mg/10 mg prolonged-release tablets.[3]

Rectal opioid

Rectal opioid suppositories may be useful in patients unable to take oral medication and in whom other methods are unsuitable. Drugs absorbed from the lower half of the rectum bypass the portal vein and first-pass metabolism in the liver. Drug absorption varies with the site of placement in the rectum (the upper part of the rectum enters the portal system), the contents of the rectum and its blood supply. Suppository formulations containing morphine, oxycodone or hydromorphone are available.

Intramuscular injections

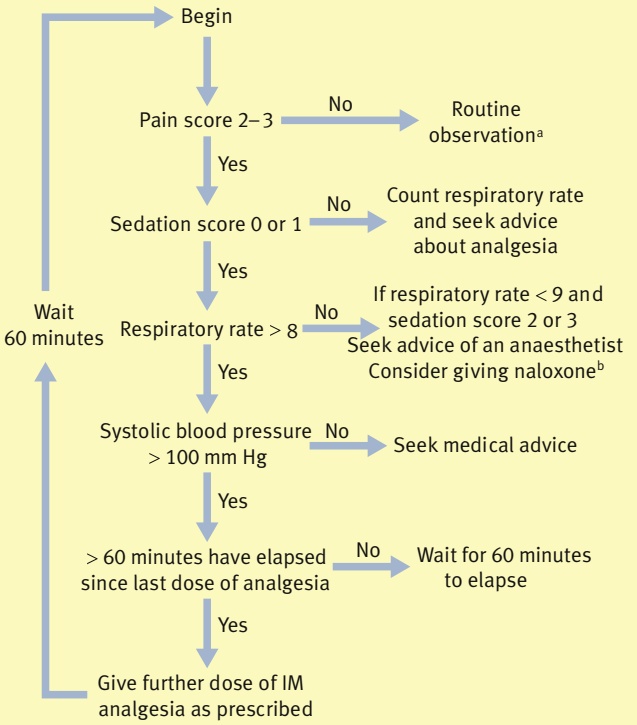
Intramuscular injections of opioids are useful in acute pain management if there is a lack of personnel trained to administer intravenous injections or if continued venous access is difficult. Traditionally, intramuscular opioids are prescribed 4-hourly as needed, but this fixed-interval dosing does not take into account the 2–4 hour half-life of typical opioids (Table 1). An intramuscular opioid injection takes 30–60 minutes to be effective. For a parenteral (or an enteral) opioid to be effective it must reach a certain therapeutic blood level, and this level may vary fourfold amongst patients. The most reliable indicator of opioid dose is the patient's age.[4] The use of algorithms and guidelines for intramuscular administration has become increasingly popular in the management of acute pain (Figure 1).

Protocol for hourly intramuscular injection of opioid analgesia in postoperative adult patients

Morphine hourly IM dose	
Weight	**Dose**
40–65 kg	7.5 mg
66–100 kg	10 mg

Pethidine hourly IM dose	
Weight	**Dose**
40–65 kg	50 mg
66–100 kg	75 mg

If weight is < 40 kg or > 100 kg seek advice of anaesthetist or APS



IM, intramuscular
[a] If the pain score is 1 and 4–6 hours have elapsed since the last intramuscular opioid injection, consider oral analgesia
[b] Respiratory depression: prepare and administer naloxone as per prescription until respiratory rate > 12 and sedation score < 2
See Figure 2 for pain and sedation scores
Source: Pain Management Service, Swansea NHS Trust

Figure 1