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. The fentanyl HCl iontophoretic transdermal system (fentanyl ITS) 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

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.

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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 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 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

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	15	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
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

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

- 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.[3]

Table 1

required' regimen to ensure adequate relief of moderate-to-severe pain. In addition, medication for breakthrough pain should be prescribed with a dose range based on the efficacy of previous doses (Table 2).

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 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 4–6-hour 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 hours as needed for pain relief, although 4-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 two to determine the 12-hourly doses, rounding down to the closest tablet strength.[2]

The release of oxycodone from the oxycontin tablet is biphasic – there is a rapid initial absorption phase within 37 minutes followed by a slow absorption phase over 6.2 hours. Peak pain relief for oxycontin tablets occurs at approximately 1 hour and last for 12 hours, with peak plasma concentrations at 2–3 hours after administration.[1,2]

Example of oral opioid administration

A 58-year-old patient, with postoperative knee arthroplasty, switching from patient-controlled analgesia (PCA) morphine to oral morphine. Patient's PCA opioid use in last 24 hours was 50 mg (50 mg intravenously = 150 mg orally)

Patient's likely 24-hour oral opioid requirement based on prior opioid intake:
Oramorph/Sevredol, 20 mg, 4 hourly (6 × 20 mg = 120 mg), plus
Oramorph/Sevredol, 10–20 mg, 1–2 hourly as needed.
If oxycodone or hydromorphone were to be used, the oral dosing regimen would have to account for the increased potency of these drugs in comparison with morphine

Table 2

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 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. Absorption of opioids is variable from the injection site; the first dose may result in a blood concentration that provides little, if any, pain relief. For a parenteral (or an enteral) opioid to be effective it must reach a certain therapeutic blood level, and this level may vary 4-fold amongst patients.[3] Age-related changes in pharmacokinetics and pharmacodynamics influence the dose of opioid required for analgesia (Table 3). Consequently, the most reliable indicator of opioid dose is the patient's age.[3]

The dose interval has to be set so that the opioid dose has had its maximum effect before another dose is administered. A reasonable dose interval, to allow safety and flexibility, would be 1–2 hours. The use of algorithms and guidelines for intramuscular administration has become increasingly popular in the management of acute pain (Figure 1).

Subcutaneous injection via an indwelling cannula in the subcutaneous tissue of the upper outer aspect of the arm or thigh is a useful alternative route of administration. Morphine is most commonly used because pethidine is too irritating and painful when administered by this route as a single injection. The rate of absorption of morphine after subcutaneous injection is similar to that of an intramuscular injection; therefore the guidelines for titration are the same (Figure 1).

Advanced methods of administration

Intravenous bolus is a superlative means of establishing rapid analgesia. It may be used for patients who are hypotensive or hypovolaemic, when absorption of the drug after intramuscular or subcutaneous administration is less predictable; to achieve initial pain relief (e.g. after surgery or trauma); and, to deal with episodes of inadequate analgesia or incident pain. The technique is often limited to specialized areas where nursing staff are trained in the use of an algorithm for the administration of intravenous opioids (Figure 2). There is less variability in blood levels if smaller doses are administered more often, making it easier to titrate the drug to suit each patient. The maximum effect of intravenous fentanyl may be seen within 5 minutes, whilst intravenous morphine may take up to 15 minutes. The time to peak effect must be considered when dosing intervals are prescribed.