Clinical update: postoperative analgesia

Pain is a complex sensation, the sensory appreciation of afferent nociception that elicits an affective and autonomic component. Acute postoperative pain differs from chronic or cancer pain because it is more transitory, and any affective component relates to anxiety about the outcome of the surgical condition and perhaps concern for suboptimum analgesia. By contrast, chronic pain is persistent, often with fluctuating intensity, and the affective component contains a greater depressive element. Unfortunately, poorly controlled and persistent pain occurs after surgery and can be severe, which might increase the risk of a chronic pain state.[1] For patients awaiting surgery, the possibility of severe acute postoperative pain is a major concern.[2] Moreover, uncontrolled postoperative pain can lead to delayed recovery from surgery, pulmonary dysfunction and hypoxia, and restriction of mobility with subsequent increased risk of thromboembolism.[1,3]

Surveys in the UK,[3,4] the USA,[5] and elsewhere[1] have identified an unacceptable prevalence of poor pain control after surgery. Simple standardised analgesic regimens can lead to better pain control and reduced postoperative complications.[5] The introduction of acute pain services in hospitals has promoted improvements in postoperative pain management.[1,6,7]

Patients recovering from surgery and trauma should have frequent measurement of their pain intensity to optimise treatment[1,8,9] (pain is considered the fifth vital sign),[9] typically by visual analogue scale (VAS) or verbal rating scores.[1,8] The VAS can be used to guide choice and dose of analgesics, and to document successful therapy. Furthermore, increased pain or analgesic requirements might signify a postoperative complication such as concealed haemorrhage, infection, or bowel leak, and surgical review may be warranted. Patients administered repeat doses of opioids should also have their sedation level monitored and scored as a useful early warning of opioid overdose.[1] In these situations, alternative opioid-sparing techniques should be used (see below).

Patients undergoing minor surgery can be adequately managed with oral analgesics, such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), tramadol, and/or oxycodone. Those undergoing more extensive surgery usually require parenteral opioids or local analgesic techniques (regional block), sometimes in combination. The requirement for parenteral opioids can be minimised by co-administration of one or more adjunctive analgesics and/or regional block, with the intention of minimising opioid-related side-effects such as sedation, respiratory depression, nausea, and vomiting. However, with the possible exception of NSAIDs, there is little evidence to support the belief that opioid-sparing regimens reduce opioid-related side-effects.[10] A consensus statement outlined guidelines for the management of postoperative nausea and vomiting.[11]

Postoperative analgesia has often relied on parenteral opioids, but an oral regimen can be effective for nearly all minor, intermediate, and some more extensive (major), surgical procedures. The key issue is whether the patient can swallow or not. Suggested analgesic regimens are outlined in the panel. A more comprehensive presentation of alternative regimens and a critical appraisal of the literature can be found elsewhere.[1,9,12]

Paracetamol has analgesic and antipyretic, but not anti-inflammatory, activity. It is believed to be a centrally-acting cyclo-oxygenase (COX) inhibitor with weak peripheral effects.[2] Because this drug does not cause gastric irritation and is relatively non-toxic in therapeutic doses, it should be considered as a basic building block of most postoperative analgesic regimens. However, 5 g may be enough to cause centrilobular hepatic necrosis in an adult, and so care should be taken when paracetamol is administered in regular repeat doses for more than a few days. An intravenous formulation is available, which facilitates its administration in patients under anaesthesia (before the end of surgery, aiming to reduce opioid-induced sedation and respiratory depression in the recovery room) or who cannot swallow. The recommended dose of paracetamol is 15 mg/kg, with a maximum daily dose of 60 mg/kg. This dose, however, has a 24-h morphine-sparing effect of less than 10 mg and there is no evidence that this significantly reduces opioid side-effects.[10,13]

NSAIDs and COX-2 inhibitors are useful analgesic adjuncts that can improve pain relief while reducing opioid requirements postoperatively.[1,12,14] Unfortunately, NSAIDs have undesirable effects that include platelet

inhibition (and bleeding), renal impairment, and peptic ulceration, which are particularly worrisome in the postoperative period. In general, the risk and severity of NSAID-associated side-effects are increased in the elderly population.[1] Selective COX-2 inhibitors have been introduced into perioperative clinical practice; they have similar analgesic efficacy to that of NSAIDs but a lower bleeding risk, and are presumed to have less gastrointestinal toxicity. Unfortunately, an increased incidence of thrombotic complications might preclude their use in many patients.[15] Interestingly, when given long term, NSAIDs such as diclofenac and ibuprofen seem to have similar rates of thrombotic complications to those of some COX-2 inhibitors, indicating they have predominantly COX-2 activity.[16] Thus naproxen may be a preferable NSAID for postoperative analgesia in such at-risk patients.

Tramadol, like NSAIDs, provides effective analgesia in patients undergoing minor or intermediate surgery.[17] Its antinociceptive activity is mainly due to inhibition of reuptake of norepinephrine and serotonin in the central nervous system. The commonest side-effects include nausea, vomiting, and delirium. Tramadol is contraindicated in advanced renal failure, epilepsy, carcinoid syndrome and phaeochromocytoma, and in patients receiving monoamine oxidase inhibitors; caution should be exercised in those receiving tricyclic or selective serotonin-reuptake inhibitors. Intravenous tramadol 1–2 mg/kg should be administered slowly over 30 min, or before the patient emerges from anaesthesia, to reduce the incidence of nausea and vomiting.[1]

Opioids are effective postoperative analgesics and are the main drugs for moderate to severe pain. Opioids can be given orally (the low bioavailability of morphine requires that the oral dose must be more than that used parenterally), intravenously, subcutaneously, transdermally, intra-articularly, or transmucosally. Also, an anaesthetist can administer opioids into the spinal or epidural space. Opioid dose should be individually titrated because of considerable interpatient variation in requirements, and in adults age is a better determinant of dose than weight—patients older than 60 years need a 20% reduction in dose per decade. Intravenous patient-controlled analgesia, in which the patient has control over the timing of each dose, is now a standard method of providing postoperative analgesia. This technique enhances analgesia compared with intermittent opioid administration. Unlike the above

***Panel:* Suggested steps to improve postoperative analgesia[1]**

1 Measure pain in all patients after surgery, with visual analogue scale (VAS) or verbal rating scale, aiming to maintain score of ≤3 (out of 10) on movement.

2 Determine whether patient is no longer nil by mouth and can swallow tablets. Oral analgesic regimens, including oral opioids, should be used in preference to parenteral therapies.

3 For minor or intermediate surgery, use strict (not when needed) paracetamol+NSAID (or COX-2 inhibitor); use oral oxycodone or tramadol for breakthrough pain. Continue for 24–72 h (according to extent of surgery) and then use paracetamol or NSAID as needed.
- Paracetamol 1–1·5 g (intravenous, oral, or rectal) four times a day. Maximum dose 5 g a day, restrict therapy to <5 days.
- Naproxen 250 mg orally three times a day, diclofenac 50 mg orally or rectally twice a day. Reduce dose and restrict therapy to <5 days if dehydration, renal impairment, or patient is elderly.
- Tramadol 100–150 mg orally four times a day. Reduce dose if renal failure or patient is elderly.
- Oxycodone 5–10 mg orally every 4 h as needed.

4 For major surgery, use paracetamol±NSAID (or COX-2 inhibitor)±tramadol+morphine via patient-controlled pump; if anaesthetist has done local anaesthetic block, there will be reduced morphine requirements. Initial start with oral opioid regimen may be suitable in selected patients. Patient should be referred to acute pain service (if available).
- Anaesthetist should administer appropriate amount of morphine intraoperatively; titrate additional doses, each 1–2 mg, in recovery room to control pain before transfer to surgical ward.
- Settings for patient-controlled anaesthesia: morphine 2 mg (1 mg if age >60 years) bolus, 5–8 min lockout period; no background infusion.
- If patient-controlled anaesthesia is unavailable: morphine 0·10 mg/kg intramuscularly or subcutaneously every 2 h as needed.
- If pain intensity is unexpectedly high, notify surgical team to review patient.
- Continue multimodal regimen until 24–72 h after surgery (according to extent of surgery), then convert to oral analgesic regimen (as for minor/intermediate surgery).

Adult doses given; adjust for weight and age in children. NSAID=non-steroidal anti-inflammatory drug, COX-2=cyclo-oxygenase 2. Special populations: chronic pain patients and those on chronic opioid or opioid antagonist therapy (eg, oxycodone, morphine, methadone, naltrexone, and transdermal buprenorphine and fentanyl) require particularly individualised attention that includes preoperative planning of appropriate analgesic regimen and close supervision from acute pain service (or equivalent).

less potent drugs, opioids influence the emotional aspects of pain such as anxiety and fear, as well as altering the actual pain threshold, rendering pain more tolerable. Opioids act on specific opioid receptors in the brain and spinal cord, and can be categorised according to endorphin receptor affinity and activity: pure agonists (morphine, oxycodone, codeine), partial agonists, partial antagonists, and pure antagonists (eg, naloxone). Some (eg, morphine) are more active at the supraspinal μ receptor, while others are more active at spinal δ and κ receptors. Pethidine is not recommended for postoperative analgesia because repeat doses may lead to accumulation of its metabolite, norpethidine, which can lead to confusion and seizures.[1]

The most important opioid side-effects are ventilatory depression (which may be severe and produce hypoxia), sedation, nausea and vomiting, and inhibition of gastrointestinal motility. Vigilance and monitoring are necessary to avoid excessive sedation and severe respiratory depression, and oxygen therapy should be routinely administered in the early postoperative period.

Acute postoperative pain is best treated by a multimodal approach, with drug combinations to enhance analgesia and reduce potential side-effects.[1] Paracetamol is a mainstay of most regimens, to which NSAIDs (or COX-2 inhibitors) and tramadol can be added, with opioids completing this combination.[1,12,14,17] Other adjuvant analgesic agents, such as ketamine or clonidine, may be used in those who are on maximum multimodal therapy but have inadequate pain relief, but these therapies are best managed by specialist anaesthetists or pain-medicine practitioners. The use of local anaesthetic techniques, ranging from simple subcutaneous wound infiltration by the surgeon to complex peripheral and central (spinal and epidural) blocks by the anaesthetist, can improve postoperative pain relief markedly. Regional block techniques reduce the need for systemic opioid therapy and may be associated with a reduction in opioid-related side-effects.[1,2,3] Many studies have identified possible beneficial effects with regional block, in particular improved analgesia,[1,18,19] but whether this improves outcome after surgery is unclear.[12,18]

Improved pain relief after surgery can be assisted by the routine measurement of pain intensity, and routine use of simple multimodal analgesic regimens. These simple efforts, applied widely, can dramatically improve surgical patients' postoperative pain experience.[3]

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