New drugs and formulations can help achieve good postoperative pain relief

Postoperative pain management can be difficult to achieve, and inadequate knowledge about pain management can increase patient distress leading to a delayed recovery and postoperative complications. This article describes the assessment tools and early recognition signs of pain and aims to provide readers with a deeper insight into effective pain management options that can be used to ensure early postoperative pain control

What is pain?

Pain is an unpleasant sensory and emotional experience associated with acute or potential tissue damage. Such 'nociceptive' pain arises through stimulation of specific pain receptors (nociceptors). By contrast, neuropathic pain arises from a site of sensory nerve damage and is experienced because the damaged nerve becomes hyperexcitable and continues to activate the pain system after the damage has been repaired. Neuropathic pain can be spontaneous or evoked. Central pain refers to pain that arises from inside the brain and can be the most difficult to treat. An exceedingly rare form of this type of pain is psychological pain, which can be the hardest to treat.

Roadblocks to relief

Pain perception is affected by many factors, which vary from person to person. Some of these include age, gender, previous experience to pain, culture and a person's specific coping skills to pain.[1] This, and the fact that there is no relation between tissue damage and physical pain make it impossible to judge the amount of pain an individual is likely to suffer postoperatively. Therefore, because each person's experience of pain is different, it is best to manage it on an individual basis according to each patient's perception of their pain.[2]

There are significant barriers to managing postoperative pain, which can be thought of as 'roadblocks to pain relief'. Despite an acute pain relief protocol in many health care centres, postoperative pain management is unsatisfactory especially after intermediate and major surgical procedures on an extremity or on the spine.[3] These barriers can be divided into three categories:

- The health care system: Includes high cost of drugs, lack of reimbursement, lack of availability and accessibility to patient and restrictive regulation of controlled drugs.[4]
- Health care professionals: Fear of administration of opioids because of side-effects and addiction risks, lack of appropriate training in scoring and assessing pain.
- Related to patient: Concerns about drug addiction, fear of disturbing the nursing staff — thinking that they might be too busy or have more seriously ill patients to look after,[5] poor drug compliance and possible side-effects.[6]

Assessment tools

Assessment of postoperative pain should include the following domains broadly:

1. Pain attributes

These may include:

Pain intensity. Availability of a 'pain score' provides an important index for monitoring improvement in pain management. In this process, the patient ranks their intensity of pain (current, worst, average) using the 0 to 10 numeric rating scale (NRS) in which 0 stands for no pain and 10 the worst pain (Figure 1). It is one accepted method of evaluating pain and it may be used verbally or visually. Comparison of verbal numeric rating scale (VNRS) with visual analogue scale (VAS) for the management of acute pain showed that VNRS performs as well as the VAS in assessing changes in pain.[7]

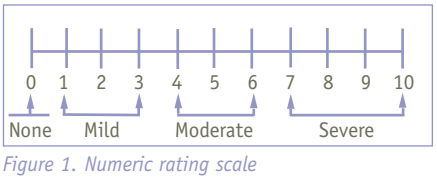


Figure 1. Numeric rating scale

For patients who have problems in communicating verbally (such as those with strokes and coma), it is important to use behavioural observations (such as moaning, wincing) and physiological indices (such as increase in heart rate, respiratory rate) when making pain assessments.

Pain location. This system is based on asking patients to indicate on their bodies where they feel the pain, and it can help assess the distribution of pain. A coding system based on a grid of regions has been established.[8] This system may be useful in detecting changes in multiple areas over time.

Onset and duration of pain. Should be reported by the patient or by someone aware of the patient's condition.

Pain description. The short form McGill pain questionnaire (SF-MPQ)[9] is helpful, because this gives patients a list of endorsed pain descriptors. It focuses on 15 representative descriptors, 1–11 representing sensory dimensions of pain and 12–15 the affective dimensions.

Factors exacerbating pain. Patients should be

asked questions like: 'what makes your pain feel better?' and 'what makes your pain worse?'. This will help to find out which factors affect their pain. Check lists of various factors are available to assist patients.

2. Behavioural manifestations

Observation of patients' behaviour is useful to help assess the severity of pain. The frequency of these behaviours should also be recorded if possible. General areas of observation include:

Posture. Includes frequent movement, limping, and movement in a guarded fashion.
Facial expression. Includes crying.
Avoidance of movement. Includes distress and suffering.

3. Past and current pain treatments

Patients should be asked about any pharmacological or non-pharmacological strategies used for pain relief in the past.

4. Patients' expectations of pain

The 0–10 NRS scoring system can be used as a rough estimate of patients' satisfaction with their current pain management, where 0 is 'completely unsatisfied' and 10 'completely satisfied'.

Pharmacological management of pain

There are different pain management modalities used to treat postoperative pain.

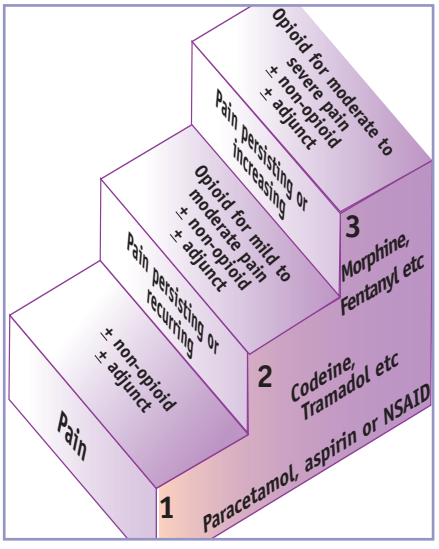


Figure 2. World Health Organization (WHO) analgesic ladder[10]

The World Health Organisation (WHO) analgesic ladder[10] was introduced for pain control in cancer patients (Figure 2). However, it is also used in the management of acute pain because it uses a local strategy for acute pain management.

The first rung of the ladder is to start with peripherally-acting drugs like paracetamol and non-steroidal anti-inflammatory drugs. If pain is not relieved, addition of a weak opioid, such as codeine, together with appropriate agent(s) to control pain while minimising side-effects are recommended. If pain still persists, the final rung of the ladder suggests adding a stronger opioid, such as morphine so that the centrally and peripherally acting drugs are given together.

The world Federation of Societies of Anaesthesiologists recommends (Figure 3) treating acute pain with stronger analgesics and local anaesthetic blocks. Then, as the pain diminishes, with peripherally acting drugs.

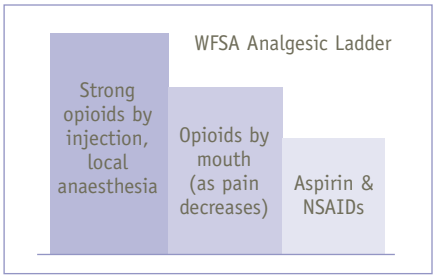


Figure 3. World Federation of Societies of Anaesthesiologists (WFSA) analgesic ladder

Non-opioid analgesics

Non opioid analgesics are the main analgesic treatment for mild-to-moderate postoperative pain. Common drugs include non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol and cyclooxygenase-2 (COX-2) inhibitors.

NSAIDS. A heterogeneous group, which act by inhibiting both forms of COX to reduce the production of prostaglandins and thereby reduce the inflammatory response. Some of the common NSAIDs and their number needed to treat (NNT) include: Diclofenac 50mg (2.3), Ibuprofen 400mg (2.4), Naproxen 550mg (3.0) and Ketorolac 60mg (1.8).[11] The NNT is the number of patients who need to receive the active drug for one patient to achieve at least 50% relief of pain compared with placebo over a 4–6 hour treatment. NSAIDs are rarely effective as a sole agent in control of acute postoperative pain.[12] When used together with opioids, they work synergistically and have a significant opioid sparing effect.[13] In patients undergoing cardiothoracic surgery aged less than 70 years, the adjunctive use of NSAIDS with narcotic analgesia reduces both the VAS 24-hour pain score and the narcotic needs.[14]

The choice of NSAIDs should be based upon availability, duration of action and cost. If pain is expected to persist for a longer period of time it is better to choose an agent with a longer half-life. Use should be carefully monitored because of side effects. Prolongation of bleeding time should be considered in postoperative patients. Inhibition of prostaglandins in the gastric mucosa makes it more prone to bleeding and ulceration.[15] Care should be exercised when using these in patients with asthma. A clinically unimportant transient reduction in renal function was noted in a meta-analysis to show the effects of NSAIDs on postoperative renal function.[16] However, NICE advise that NSAIDs should not be withheld from patients with normal preoperative renal function because of concerns about postoperative renal impairment.[15] Routes of administration include topical (not normally used in postoperative management), oral, rectal, intramuscular and parenteral.

Paracetamol. This has analgesic and antipyretic but little anti-inflammatory properties. Its postulated mechanism of action is to inhibit the COX-3 enzyme in the central nervous system, while sparing the peripheral prostaglandin production. It has fewer side-effects than NSAIDs and is better absorbed orally. Evidence suggests that it is a weaker analgesic than NSAIDs with a NTT of 3.8 (paracetamol 1000mg). However, it has beneficial effects when used in combination with NSAIDs.[17] The use of paracetamol as a single pre-emptive dose in abdominal surgery with peri-operative epidural analgesia does not reduce the analgesic consumption and pain intensity post

operatively.[18] Routes of administration include oral, rectal and parenteral. The regular administration of the parenteral form (proparacetamol) was shown to reduce the opioid requirement in postoperative orthopaedic patients by 46 per cent.[19]

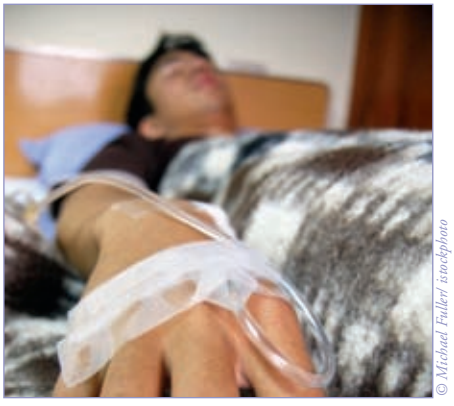
Cyclooxygenase 2 inhibitors. These agents act on COX-2, which is induced in response to surgical trauma and spare the COX-1 (constitutive form). This has beneficial effects on the gastric mucosa and renal tubular function due to the production of normal physiological prostaglandin. Some common COX-2 inhibitors and their NNT include: Rofecoxib 50mg (2.3) and Valdecoxib 20mg (1.6). They have no inhibitory action on platelets and therefore reduce postoperative blood loss, and they cause a lower incidence of gastrointestinal (GI) ulcerations at lower doses.[20] Therefore, they have a number of advantages over NSAIDs postoperatively but require caution with regard to renal side-effects.[21] There are significantly greater numbers of thrombotic cardiovascular events, which offset the increased number of serious GI adverse effects observed with NSAIDs.[22] This is most noted with Rofecoxib, which has a 3.9-fold increase in the incidence of serious thromboembolic adverse events compared with placebo after 18 months of use.[23] COX-2 inhibitors (especially Rofecoxib) used by elderly patients with hypertension may be associated with significant oedema and increased blood pressure.[24]

Opioid analgesics

Opioids can be taken by oral, sublingual, transmucosal, transdermal, rectal, inhaled, intravenous and intramuscular routes. They activate the G-protein coupled mu, delta and kappa receptors located at supra-spinal and spinal levels and in peripheral tissue. Mild to superficial pain can be relieved by weak opioids such as codeine and dextropropoxyphene whereas severe pain arising from deep or visceral structures requires the use of stronger opioids like morphine, pethidine and buprenorphine. Often they can be used in combination with peripherally acting drugs — such as paracetamol — in minor surgical procedures. Morphine is the most commonly used opioid for postoperative pain. Desirable effects are sedation and anxiolysis whereas the unfavourable effects include respiratory depression, bradycardia, hypotension and specific vagal effects. Gastrointestinal effects include reduced peristalsis and therefore constipation. Opioids are inactivated in the liver with metabolites excreted in bile and urine. Care must be taken in patients with renal impairment to avoid the accumulation of morphine-6-glucuronide. Patients tolerate morphine quite well and its benefits outweigh the side-effects making it so useful in postoperative analgesia.[25] Although the risk of addiction with morphine use remains a fear among patients, numerous studies have indicated that this risk is minimal.[5]

Patient-controlled analgesia

Different patients vary in their opoid requirements, which brought the concept of patient-controlled analgesia (PCA). It allows the patient to self-administer small



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doses of opioids, preferably morphine, at frequent intervals. It allows for variations in opioid requirements with patient tolerance, changes in intensity of pain and variability in pharmacokinetics. It is essential for the patient to understand how it works to avoid its misuse and overdosage.

Minimal effective analgesic concentration (MEAC) is defined as the minimum plasma concentration of the drug at which effective pain relief occurs when a drug is given by constant infusion. Its variation among different patients accounts for the vast difference in analgesic requirements. This is illustrated by the large variation in drug demand seen with patient controlled analgesia systems. This varies between 13 and 44mg/hour for pethidine, 30 and 100mcg/hour for fentanyl and 0.3 to 9 mg/hour for morphine in different patients.[26]

Prescription of anti-emetics, oxygen and opioid antagonists should go hand-in-hand with PCA. Routes of administration include intravenous, intramuscular, subcutaneous and epidural. The ideal dose of morphine for PCA is 1mg but variations exist among patients depending upon their analgesic requirements. Overdosage is prevented by ensuring a lock-out period (period during which no analgesic is delivered) of 5 to 10 minutes. Patients who receive epidural fentanyl-bupivacaine PCA have better pain relief than morphine PCA epidurally or intravenously.[27] It has been shown that pain relief by PCA is better and more acceptable by patients. However, a minority of patient's particularly older people find it difficult to use.[28,29] Intrathecal morphine plus PCA reduces morphine consumption and improves the analgesic effect over PCA alone postoperatively.[30] Other studies of morphine PCAs and combinations with ketamine showed that there was a significantly lower consumption of morphine, but no patient benefit.[31,32]

Epidural analgesia

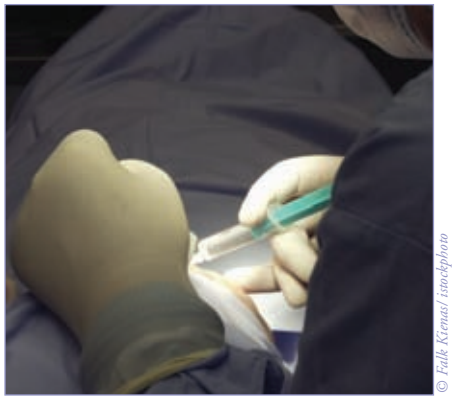
Epidural analgesia is especially used in lower abdomen, pelvic and lower limb surgery. It is produced by the administration of an opioid, local anaesthetic agent or combinations of the two into the epidural space outside the dural sac using an indwelling catheter. Opioids used on their own include morphine and pethidine, while combination analgesics include fentanyl or diamorphine with bupivacaine. The epidural use of local anaesthesia and opioids together resulted in a synergistic effect, which was superior to use of either alone, when pain was assessed during patient movement. This allows for improved activity and earlier patient mobilisation.[33] Side-effects include nausea, vomiting, urinary retention and pruritis. Infection is mainly via the epidural catheter track and reduction of colonization at the catheter tip can be achieved by maintaining

sterile skin around the catheter insertion site.[34] A meta-analysis of epidural versus parenteral opioid analgesia (in colorectal surgery) showed that although it improved analgesia and reduced postoperative ileus there was no reduction in hospital stay.[35,36]

Overdosage may result in respiratory depression and requires a high level of vigilance. During transition from epidural to oral analgesia, the timing of oral analgesia administration is crucial to effective pain management. Oral analgesia should be administered either before or at the same time as the removal of the epidural catheter.[37]

Local anaesthetic infiltration

This is a simple way of achieving effective pain relief around a wound site. Wound infiltration with local anaesthetic agents after surgical excision of breast lumps has proven to be effective in clinical settings.[38] This may provide several hours of analgesia but might only delay the need for continuous analgesia. This may in turn be circumvented by continuous catheter techniques for regional analgesia such as femoral nerve, brachial plexus and inter-pleural analgesia.[39] The use of pre-emptive



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local analgesia has shown some benefit in reducing postoperative pain.[40] Bupivacaine is the most commonly used local anaesthetic because diluted solutions produce very limited motor block. Even topical local anaesthetics in the form of EMLA (Eutectic mixture of lidocaine and prilocaine) can reduce postoperative pain after haemorrhoidectomy.[41]

Peripheral nerve blocks

These can be used alone or in combination with other analgesic agents to provide effective pain relief. In one study a combination of a continuous lumbar plexus block with PCA was superior to PCA alone by reducing the opioid requirements, side-effects and enhancing patient satisfaction.[42] The use of such a modality at home in children seemed feasible in those children with a suitable family environment, and shortened the hospital stay.[43] Preoperative popliteal nerve blocks were also shown to avoid patient discomfort, augment general anaesthesia, provide good postoperative pain control, and have a high patient satisfaction with no significant complications.[44] Ilio-inguinal nerve blocks are often performed after inguinal hernia repair and provide efficient pain relief. However, a recent study showed that neurological complications can occur, which resulted in the study being aborted.[45]

Non-pharmacological measures

Certain non-pharmacological measures can prove to be useful in managing postoperative pain. These include cognitive-behavioural therapies, heat or cold applications, massage, exercise and transcutaneous electrical nerve stimulation (TENS).

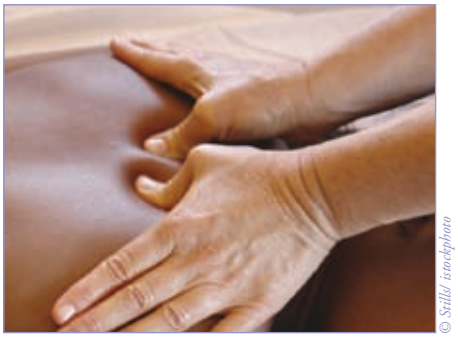
Cognitive-behavioural therapies can be used to provide patient comfort. Good explanation of the surgical procedure before hand, with the aim of relieving patient anxiety can play an important role. The results of one study showed that patients exposed to music intra-operatively or post-operatively reported significantly lower pain intensity at one to two hours post operatively, and required less morphine.[46] Use of lavender aromatherapy can reduce the demand for postoperative opioids in the immediate postoperative period.[47]

Cold applications decrease pain by reducing muscle spasm and inflammation in the acute setting. Cryotherapy has been clinically applied to relieve pain, in which a cryosurgical probe was used to block peripheral nerve function and achieve analgesia.[48] Heat applications are then used to facilitate perfusion and help clear accumulated fluids.

> The WHO pharmacological ladder should form the basis of managing pain in all clinical settings, augmented by institution of non-pharmacological measures.

Massage, exercise and immobilisation are also used to reduce pain. In one randomised controlled trial (RCT) massage therapy was shown to be an effective and safe adjuvant therapy for the relief of acute postoperative pain in patients undergoing major operations.[49]

Although exercise is not a normal way of reducing postoperative pain there is one report noting that it could be used for anterior cruciate ligament surgery. Lower body positive pressure exercise was effective at reducing ground reaction forces, while safely facilitating gait postoperatively, thereby reducing pain significantly and improving mobility.[50]



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TENS is the use of small electrical pulses to the body via electrodes placed on the skin to reduce pain. It accomplishes this in two ways. The first way is by using TENS at a high frequency (90–120Hz), which triggers the blockage of pain nerve pathways to the brain. The second way is by using low frequencies (2–5Hz) where there is stimulation of the body to produce endogenous endorphins, which block pain signals. One study showed that the use of TENS in lower abdominal surgery reduced opioid intake and mixing high and low frequencies had a slightly greater opioid-sparing effect than using either in isolation.[51]

This, however, is not true for all post operative pain. Another study concluded that there was no use for TENS in the postoperative management of pain after knee arthroplasty because there was no significant reduction in the requirement for PCA with or without TENS.[52]

Conclusions

Effective postoperative analgesia is of utmost importance to reduce patient distress and suffering. This also promotes early recovery and reduces postoperative complications. The WHO pharmacological ladder should form the basis of managing pain in all clinical settings, augmented by institution of non-pharmacological measures. It is important for medical staff to communicate early with the patient, and to recognise early signs of pain and treat it in the beginning with the appropriate analgesic agent suitable for the patient. To improve the standard of care and reduce postoperative patient suffering, postoperative pain management should be taken seriously and given the importance it deserves.

Declaration of competing interests

The authors declare that they have no competing interests.

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